ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 1
January 1975
Pages 1–74

Mechanisms of Photochemical Air Pollution

By J. N. Pitts, Jr. and B. J. Finlayson[*]

Dedicated to Professors Philip A. Leighton and Francis E. Blacet

Selected aspects of the chemistry of photochemical air pollution is discussed and some important, unresolved problems dilineated. The reactive species considered include NO_2, O_3, $O(^3P)$, $O(^1D)$, $O_2(^1\Delta_g)$, OH and HO_2. Both the kinetics and mechanisms of the reactions constituting the major tropospheric sources and sinks of these species are treated where available. The application of this information in both computer and smog chamber simulations of photochemical smog is discussed.

1. Introduction

Photochemical air pollution was first overtly recognized in the Los Angeles Basin in the 1940's from the crop damage it caused[1]. This new type of smog was characterized by the formation of oxidants[2] in contrast to the well-known "London Smog" which contained primarily SO_2 and particulates[3]. *Haagen-Smit* and co-workers[4–7] demonstrated that a mixture of cracked gasoline or olefins and ozone acting on crops reproduced the smog damage, and showed that ozone was produced when a mixture of nitrogen dioxide and individual organics (olefins, alkanes, alcohols, carbonyl compounds, acids) or dilute auto exhaust was irradiated.

Since then these experiments have been reproduced under a variety of conditions. Figure 1 shows a typical time dependence[8–10] of the reactants and major products when a mixture of nitrogen oxides and propylene in the part-per-million (ppm) concentration range are irradiated in air with ultraviolet light ($\lambda \gtrsim 290$nm)[3, 11]. Initially, NO is rapidly converted to NO_2. Simultaneously, the olefin concentration decreases and acetaldehyde appears. When the NO concentration is sufficiently low, O_3 and peracetyl nitrate ($CH_3CO_3NO_2$) build up while the NO_2 and C_3H_6 concentrations fall.

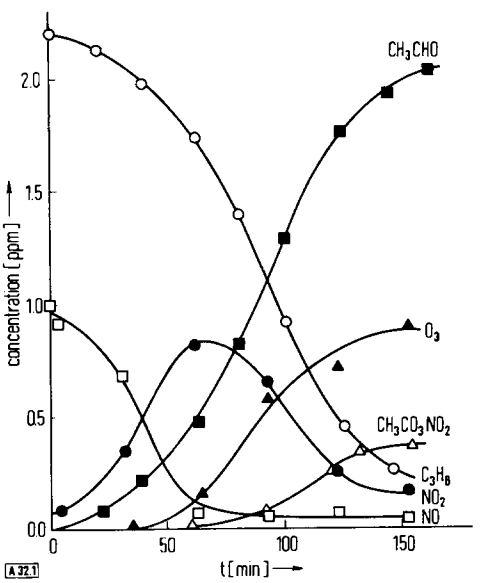


Fig. 1. Typical concentration-time profiles [8—10] for the reactants and major products in the photooxidation of propylene in the presence of NO and NO_2 (after [10]).

In this system NO_2 is the major light-absorbing species[3]. At wavelengths less than 430nm NO_2 dissociates forming NO and ground state oxygen atoms, $O(^3P)$, (see Section 2):

$$NO_2 \xrightarrow{\lambda < 430\,nm} NO + O(^3P) \quad (1)$$

In air this is rapidly followed by:

[*] Prof. Dr. N. Pitts, Jr. and Dr. B. J. Finlayson[**]
Department of Chemistry and
Statewide Air Pollution Research Center
University of California
Riverside, Calif. 92502 (USA)
[**] *Present address:*
Department of Chemistry,
California State University
Fullerton Calif. 92634 (USA)

$O + O_2 + M \rightarrow O_3 + M$ $\quad k_2^{[*]} = 2.1 \times 10^8$ (M = N_2) (2) [12, 13]

$O_3 + NO \rightarrow NO_2 + O_2$ $\quad k_3 = (1.1 \pm 0.2) \times 10^7$ (3) [14]

In the presence of propylene, we should include:

$O + C_3H_6 \rightarrow$ products (4)

$O_3 + C_3H_6 \rightarrow$ products (5)

The behavior shown in Figure 1 has challenged chemists to explain the following apparent anomalies. Starting with large quantities of NO and small amounts of NO_2, we see in the initial stages of the reaction an increase in NO_2, the species which we know is being lost photochemically by reaction (1). Secondly, the rate of olefin disappearance is much greater than that due solely to its reactions with O and O_3, as shown in Figure 2[10]. These anomalies imply that a chain reaction must be involved both in the NO—NO_2 conversion and in the olefin loss.

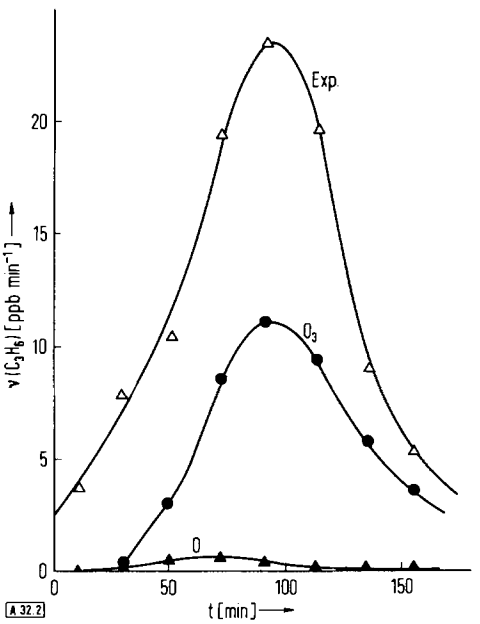


Fig. 2. Comparison of the experimentally determined rate v of propylene loss to that calculated from its reaction with O and O_3 [8—10] (after [10]).

The behavior described above is characteristic of photochemical smog formation involving any reactive hydrocarbon, singly or in complex mixtures such as auto exhaust. In 1961, *Leighton*[3] speculated that radicals such as R, RO_2, RO, OH, HO_2, and H might be involved. Further work since then has strengthened and clarified these ideas. One major contribution was the suggestion[15, 16] that CO, in conjunction with hydroxyl (OH) and hydroperoxyl radicals (HO_2) might participate in the NO to NO_2 conversion:

$OH + CO \rightarrow CO_2 + H$ (6) [17]

$k_6 = 9.8 \times 10^7$

$H + O_2 + M \rightarrow HO_2 + M$ (7) [18]

$k_7 = (2.13 \pm 0.4) \times 10^{10}$ (M = N_2)

$HO_2 + NO \rightarrow NO_2 + OH$ (8) [19]

$k_8 = (1.8 \pm$ factor of 3) $\times 10^8$

Thus, carbon monoxide, which was assumed to be unreactive in photochemical air pollution until the rate of reaction (6) was shown[20] to be fast, may now assume an important role under appropriate conditions. Some organics, such as formaldehyde, may act in a similar manner[21]:

$OH + HCHO \rightarrow H_2O + HCO$ (9) [22]

$k_9 = (8.4 \pm 2.1) \times 10^9$

$HCO + O_2 \rightarrow HO_2 + CO$ (10) [23]

$k_{10} = (3.4 \pm 0.7) \times 10^9$

$HO_2 + NO \rightarrow HO + NO_2$ (8)

Thus, any source of H, HO_2, or OH will contribute to the rapid oxidation of NO to NO_2 and, as we shall see, to the enhanced rate of olefin consumption.

Understanding the detailed course of the reactions involved in complex smog mixtures such as that in Figure 1 is the immediate goal of atmospheric chemists today. This necessitates an intimate knowledge of the kinetics and mechanisms (including intermediates *and* products) of all elementary reactions involved. Only then can we accurately and reliably predict the time dependence of the pollutant concentrations in such simulated smog experiments. Of course, even this mammoth task is only a step towards the ultimate aim—predicting the same time dependence in the real atmosphere where fresh pollutants are constantly being added, meteorology is changing, and some of *yesterday*'s "aged" smog is also present when the sun rises to initiate the reactions *today*. In order to meet even the initial goal, however, we lack kinetic and mechanistic information in many crucial areas, information which must be obtained by careful, quantitative research in a variety of systems ranging from the torr to part-per-billion (ppb) concentration ranges. This provides an unparalleled opportunity for chemists to apply their expertise to a societal problem facing all of us.

In this article, we briefly summarize current knowledge of selected areas of photochemical air pollution, and in doing so, delineate some of the present and future challenges to the chemist. This is not intended to be a comprehensive review but rather an examination of certain interesting aspects of smog chemistry which we hope will put the subject in perspective. We apologize in advance to the many scientists whose work is not included, or discussed in the detail it deserves, due to the limitations of space.

2. Photolysis of Nitrogen Dioxide (NO_2)

NO_2 is the major light-absorbing species in the solar actinic region ($\lambda > 290$ nm) and is an important (but not the sole) initiator of photochemical smog formation. It has been established[3] that the primary process on absorption of wavelengths less than ≈ 398 nm is dissociation, with a primary quantum yield of approximately unity:

$NO_2(X^2A_1) \xrightarrow{h\nu} NO(X^2\pi) + O(^3P)$ (1)

This is consistent with the NO_2 bond dissociation energy of 3.115 eV ($\lambda = 398$ nm)[24]. At wavelengths greater than 430 nm, there is no $O(^3P)$ production[3, 25–28]; only photophysical processes occur.

Bond rupture also occurs, however, at wavelengths between 398 and 430 nm[3, 25, 26, 29], as confirmed by a recent study[28].

[*] Rate constants throughout are given in l-mol-s units at 300 °K.

In this wavelength region the photon is not sufficiently energetic by itself to cause dissociation, and the excess energy must come from the rotational energy[26, 28, 35].

Recently, *Jones* and *Bayes*[28] measured relative quantum yields for NO formation at exciting wavelengths from 295 to 445 nm in 5 or 10 nm intervals using a photoionization mass spectrometer. This technique, which has proven to be powerful and will undoubtedly play a large role in kinetic and mechanistic studies in the future, uses photon absorption to ionize the species entering a quadrupole mass spectrometer. The advantages over ionization by conventional electron impact include (i) the possibility of selective ionization (through the choice of ionizing wavelength) of small quantities of species in the presence of large amounts of compounds which would otherwise interfere, (ii) minimization of fragmentation processes, hence greatly simplifying interpretation of the mass peaks, and (iii) partial confirmation of identification through the use of resonance lamps of varying photon energy[28, 30].

The quantum yields for NO[28] were put on an absolute basis using the results of previous work at 313 and 366 nm. Since reaction (1) is rapidly followed by

$$O + NO_2 \rightarrow NO + O_2 \qquad (11)$$

Φ_{NO} is anticipated to be 2.0 at $\lambda < 398$ nm in the absence of competing processes.

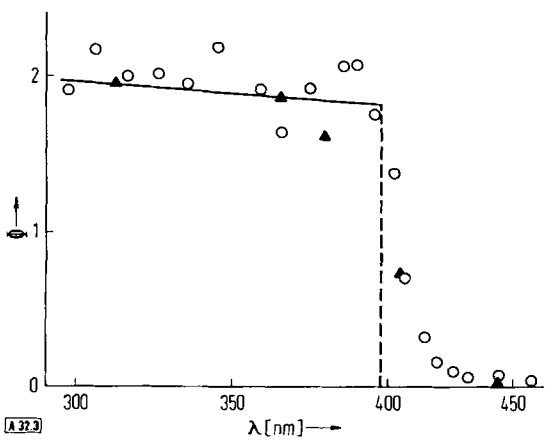


Fig. 3. Wavelength dependence of the quantum yield [28] for NO formation in the photolysis of NO_2; ○ from ref. [28]; ▲ from ref. [3, 26]. Dotted line gives the dissociation energy of NO_2 (3.115 eV) [24]. Solid line is the least squares fit to the data of ref. [28] (after [28]).

Figure 3 gives the results of this investigation[28] as well as those of earlier studies[3, 26]. It is seen that for $295 < \lambda < 398$ nm, Φ is close to 2 but decreases slightly with increasing wavelength. *Jones* and *Bayes*[28] suggested that the competing process which accounts for $\approx 3\%$ of the reaction at 313 nm and $\approx 8\%$ at 366 nm may be energy transfer to O_2. Thus these investigators[31, 32] observed the production of electronically excited $O_2(a^1\Delta_g)$ when mixtures of NO_2 and O_2 were irradiated in the region $330 < \lambda < 590$ nm. *Frankiewicz* and *Berry*[33, 34] also observed the production of small quantities of $O_2(b^1\Sigma_g^+)$ in the same system.

As mentioned above, the observed dissociation of NO_2 at $\lambda > 398$ nm can be qualitatively explained by the contribution of the rotational energy, in agreement with recent spectroscopic studies[35]; quantitatively, however, the calculated NO quantum yields are lower[28] than those determined experimentally. Further studies are necessary in order to resolve this discrepancy between theory and experiment.

3. The Role of Ozone in Photochemical Air Pollution

In air, the ground state oxygen atom, $O(^3P)$, produced in the photolysis of NO_2, is removed primarily by reaction (2) with O_2. At the present time, this is the only reaction known to produce O_3 although alternate reactions such as that of the Criegee diradical (see Section 3.2) with O_2 have been suggested[36].

$$R\dot{C}HOO\cdot + O_2 \rightarrow RCHO + O_3 \qquad (12)$$

3.1. Kinetics of the Ozone-Olefin Reaction

Table 1 gives typical room temperature rate constants for the reactions of O_3 with some species normally present in polluted urban atmospheres. Using these rates and typical ambient pollutant concentrations, one calculates that the only important loss processes of O_3 occur by reaction with olefins, NO, and to a lesser extent, NO_2. The rapid reaction (3) of O_3 with NO is the reason that O_3 does not begin to accumulate (Figure 1) until the NO concentration has decreased to a low value. This may also at least partially explain why oxidant levels in downtown Los Angeles have dropped as the NO emissions have risen; concurrently, ozone concentrations have increased in communities downwind due to the subsequent photolysis of the NO_2 formed by reaction (3)[41–43].

Table 1. Selected room temperature rate constants for some ozone reactions.

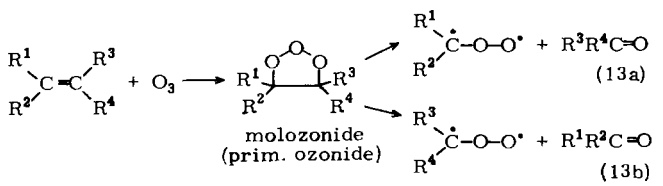
Compound	$k \times 10^{-3}$ [l mol^{-1} s^{-1}]	Ref.
Ethylene	0.93 ± 0.09	[37]
Propylene	7.5 ± 0.6	[37]
Isobutene	8.2	[38]
trans-2-Butene	165 ± 14	[37]
$(CH_3)_2C{=}CHCH_3$	296 ± 10	[38]
$(CH_3)_2C{=}C(CH_3)_2$	906 ± 48	[38]
Toluene	7.2×10^{-3}	[39]
$HC{\equiv}CH$	52×10^{-3}	[39]
CH_3CHO	20×10^{-3}	[39]
CH_4	$\leq 0.72 \times 10^{-3}$	[39]
CO	$\leq 0.6 \times 10^{-3}$	[39]
NO	$(1.1 \pm 0.2) \times 10^{4}$	[14]
NO_2	19 ± 3	[40, 14]

At low NO concentrations O_3 reacts primarily with olefins at rates of $\approx 10^3$—10^5 l mol^{-1} s^{-1}. While the rate constants of Table 1 are generally the most recently determined ones, there are significant disagreements in the literature values, particularly for olefins containing an internal double bond. It now appears that secondary attack of intermediates on the reactants makes the experimentally determined rate constant sensitive to the reaction conditions, particularly the O_2 concentration[38, 44]. Additionally, the rate of formation of the major carbonyl products may be nonlinear[45], at least under certain conditions, and hence those rate studies based solely on product formation may be in error. These factors have only recently come to light and indicate the need for

further kinetic studies over a wide variety of experimental conditions.

3.2. Mechanism of Gas Phase Ozone-Olefin Reactions

Until recently, the mechanism of the ozone-olefin reactions in the gas phase had generally been interpreted in terms of a modified liquid phase Criegee mechanism[46-48]. The initial electrophilic attack of ozone on the olefin is thought to produce a molozonide, or primary ozonide, which cleaves to the Criegee "zwitterion" (more likely a diradical in the gas phase) and a carbonyl compound [reactions (13a) and (13b)]:



(13a)

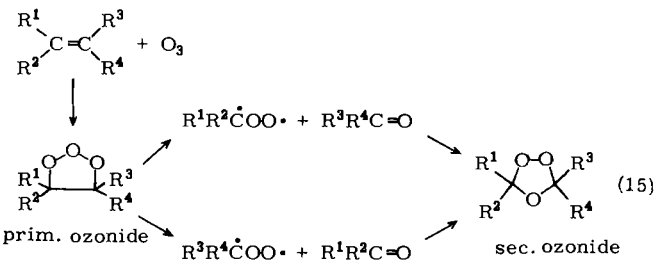
(13b)

According to *Scott*, *Hanst*, and co-workers[49,50], the diradical then decomposes, rearranges or reacts further. The extent of decomposition will be determined primarily by the size of the diradical since larger molecules will have a greater number of vibrational degrees of freedom over which to dissipate the excess energy without decomposing. For example, the Criegee diradical $CH_3\dot{C}HOO\cdot$ from the propylene reaction may decompose[49,50] as follows:

$$CH_3-\dot{C}H-O-O\cdot \xrightarrow{(a)} H_2O + CH_2=C=O$$
$$\xrightarrow{(b)} CH_3OH + CO \qquad (14)$$
$$\xrightarrow{(c)} CH_4 + CO_2$$

All of these products were observed in the propylene-ozone reaction[49,50].

On the other hand, secondary ozonide formation was observed by infrared spectroscopy[50] for the longer chain hydrocarbons (1-hexene, 2-pentene, and 3-heptene) where diradical decomposition is not expected to be extensive. Presumably this arises by recombination of the diradical and carbonyl fragments in a manner analogous to the liquid phase [reaction (15)].

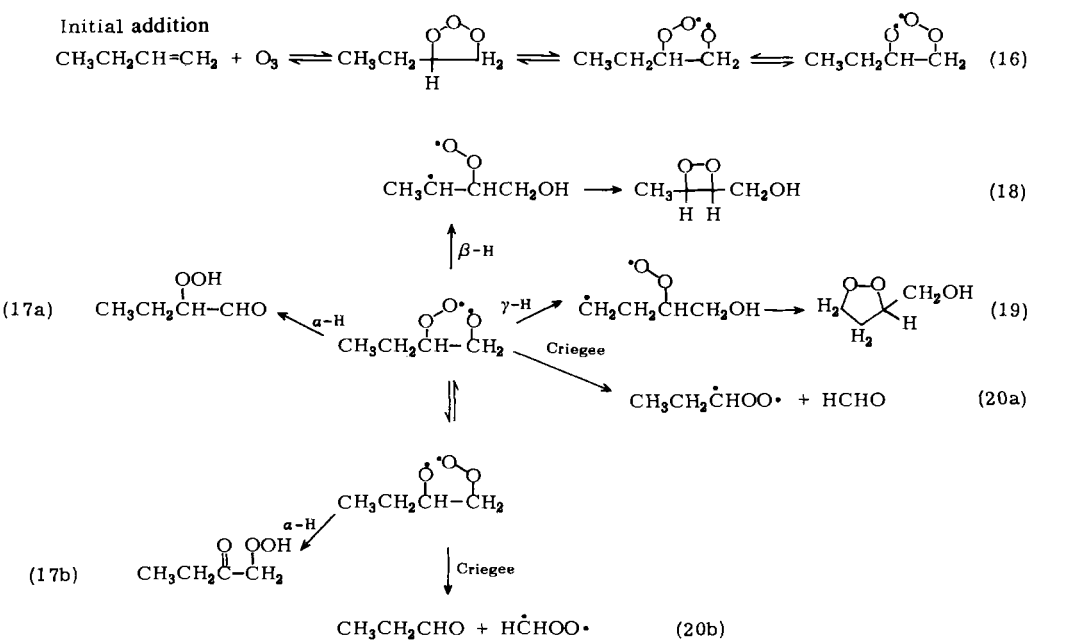


(15)

However, the formation of such ozonides has not been reported using alternate techniques such as GC. Such confirmatory studies are, in the authors' opinion, desirable.

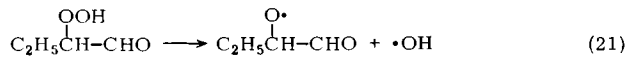
Subsequent studies using a variety of techniques over a wide range of experimental conditions have yielded results which are not easily explained by this mechanism, however. These include (i) the formation of a wide variety of "abnormal" ozonolysis products such as peroxides; aldehydes, and ketones one and two carbons shorter than the major carbonyl product; and carbonyl compounds having the same chain length as the reactant olefin[51-54], (ii) non-unit stoichiometry[38,52,55,56], (iii) the formation of radical intermediates at low pressures[58], including significant yields of H atoms[44,57,59], and (iv) the production of chemiluminescence[44,57,59-63].

In order to explain these observations, *O'Neal* and *Blumstein*[64] have proposed that, in addition to the Criegee path, α, β, and γ abstractions of the primary ozonide can occur. For example, for the 1-butene reaction with O_3, the following series of reactions are postulated; the relative importance of each of these paths under various experimental conditions can be calculated from the thermochemistry and unimolecular theory. The ΔH^0 values are −32.9 for reaction (16), −74.3 for (17a), −65 for (18), −80 for (19), and ≤4.4 kcal/mol for (20a).



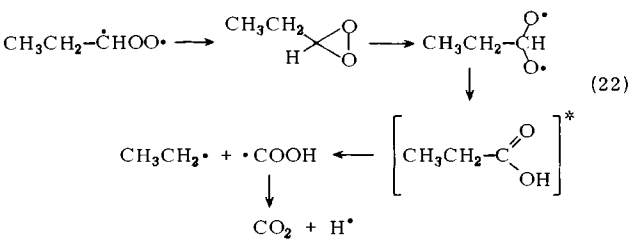
Chemiluminescence is then rationalized by the decomposition of the dioxetanes formed by β-hydrogen abstraction[44, 64, 65], leading to electronically excited species.

Reactions (16)—(20) are highly exothermic and hence will result in the formation of excited products. Decomposition of these energetic species will occur in competition with their collisional stabilization and hence be pressure dependent. For example, excited hydroperoxides formed by α-hydrogen abstraction, as in (17), are known[66] to cleave at the O—OH bond if sufficient energy is available [reaction (21)].



(21)

A novel feature of the *O'Neal-Blumstein* proposal is the postulated rearrangement of the Criegee diradical under certain conditions to the excited acid which may also decompose[64, 67] [reaction (22)].

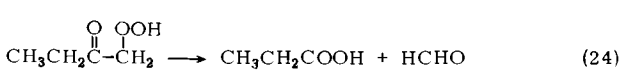


(22)

This may explain the production of H atoms[44, 57, 59] and also be consistent with the proposals of *Scott*, *Hanst*, and coworkers[49, 50] regarding the modes of decomposition of the diradical $CH_3\dot{C}HOO\cdot$ (see above). Acetic acid is known to decompose photochemically to CH_4 and CO_2[68] and thermally to $CH_2{=}C{=}O + H_2O$[69]. Ketene has been observed in significant yields from the reaction of *cis*-2-butene with ozone both at low[58, 70] and at high[70] total pressures, while CH_3COOH was not detected[58, 70].

At high pressures and for long chain diradicals the acid from the Criegee cleavage may be stabilized, in which case the final products are the same as those from the decomposition of the α-carbonyl hydroperoxide [reactions (23) and (24)].

(23)



(24)

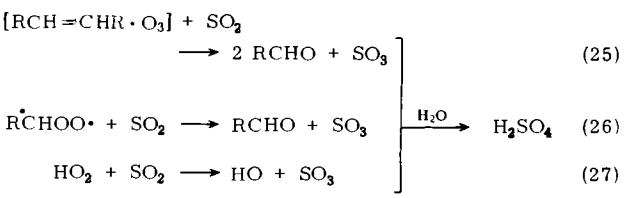
The only means of differentiating between these two paths is identification of the α-carbonyl hydroperoxide which is an intermediate in the α-hydrogen abstraction path but not in the Criegee path.

While this theory of ozone-olefin reactions is attractive, further experimental validation is needed before the theory, or selected aspects thereof, can be accepted. It is evident that much more work is needed on the intermediates (including radical species), stoichiometry, effects of oxygen, total pressure, and reactant concentrations using a variety of techniques in order to establish confidently the mechanisms and the bimolecular rate constants of these complex reactions.

Because of the uncertainties regarding the reaction mechanism, the precise role of ozone-olefin reactions in photochemical smog formation still remains obscure. One possibility is the production of H atoms followed by their reaction with O_2 to form HO_2[44]. Furthermore, if radicals such as HCO which are formed at 2 torr[58] are also produced at atmospheric pressure, they too may participate in the NO to NO_2 conversion by formation of HO_2, by reaction (10). Finally, it is interesting to speculate that the α-carbonyl hydroperoxide may be the phytotoxicant produced in ozone-olefin reactions[71, 72].

3.3. Effect of Sulfur Dioxide on Ozone-Olefin Reactions

When SO_2 is added to a mixture of ozone and olefin in the dark or to dilute auto exhaust which is subsequently irradiated, it is rapidly oxidized by some unidentified reaction intermediate or product to sulfuric acid aerosol[45, 73–75]. An ozone-olefin adduct[45], the Criegee diradical[45], and HO_2[44] have all been suggested as the oxidizing species [reactions (25)—(27)].



(25)

(26)

(27)

While further detailed studies are badly needed, this important finding may explain the high rates of oxidation of SO_2 in areas of photochemical smog[21] and would suggest that the use of high sulfur fuels in such areas be discouraged[43] because of the apparent toxicity of particulate sulfate[163] and its role in visibility reduction.

4. Reactions of $O(^3P)$ with Olefins and Arenes

At typical ambient pollutant levels $O(^3P)$ reacts to a small extent with hydrocarbons, in addition to its primary loss by reaction (2) with O_2.

4.1. Kinetics of Reactions of $O(^3P)$ with Olefins and Arenes

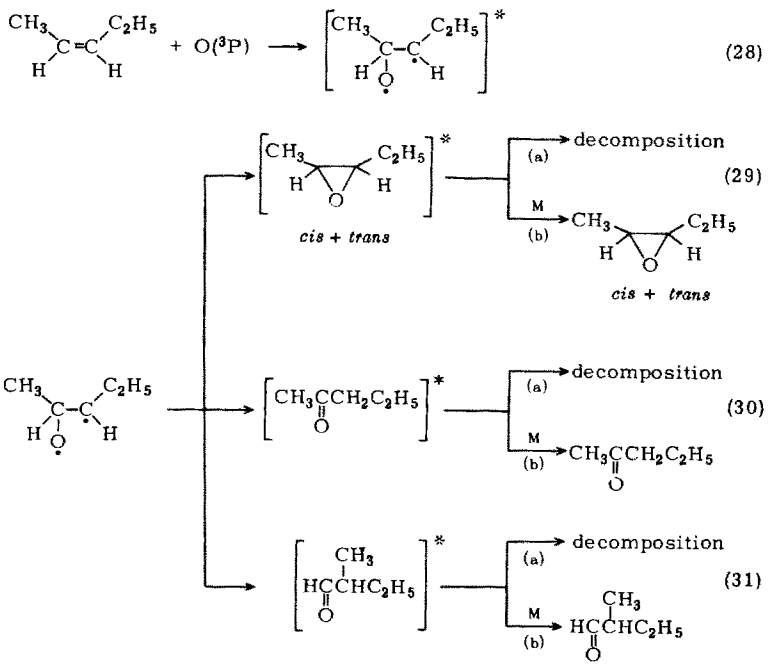
Table 2 gives the values of selected rate constants for the reactions of $O(^3P)$ with some olefins and arenes. These rates, which show an electrophilic trend[76], represent addition to the double bond. While it was suggested[78] that abstraction may occur ≈ 15 % of the time at 300 °K in the $O(^3P)$-1-butene reaction, OH was not detected[79] as an intermediate in this reaction, supporting previous assumptions that hydrogen abstraction is too slow to compete with addition at room temperature.

4.2. Mechanism of the $O(^3P)$-Olefin Reaction

The results of a definitive series of studies of the $O(^3P)$-olefin reactions led *Cvetanovic* and co-workers[76] to postulate the following reaction mechanism, illustrated by the reaction of $O(^3P)$ with *cis*-2-pentene [reactions (28)—(31)].

Table 2. Typical rate constants k at 298°K for the reaction of $O(^3P)$ with olefins [165] and arenes [77].

Olefin	$k \times 10^{-8}$ [l mol^{-1} s^{-1}]	Arene	$k \times 10^{-8}$ [l mol^{-1} s^{-1}]
Ethylene	4.3 ± 0.5	Benzene	0.144 ± 0.02
Propylene	20 ± 1.7	Toluene	0.45 ± 0.045
1-Butene	24 ± 3.7	*o*-Xylene	1.05 ± 1.11
cis-2-Butene	92 ± 15	*m*-Xylene	2.12 ± 0.21
2-Methyl-2-butene	313 ± 30	*p*-Xylene	1.09 ± 0.11
2,3-Dimethyl-2-butene	425 ± 46	1,2,3-Trimethylbenzene	6.9 ± 0.7
		1,2,4-Trimethylbenzene	6.0 ± 0.6
		1,3,5-Trimethylbenzene	16.8 ± 2.0



According to this scheme:

1) $O(^3P)$ adds to the double bond, primarily to the less substituted carbon atom, forming a triplet diradical [reaction (28)].

2) The diradical is sufficiently long-lived that some rotation about the original double bond occurs since both *cis* and *trans* epoxides are formed starting from one geometric isomer of the olefin [reaction (29)].

3) Ring closure to the epoxide must be competitive with rotation since the ratio of *cis* to *trans* epoxides formed is not the same for the reaction of the *cis* and *trans* olefins respectively.

4) The epoxide formed contains ≈90 kcal/mol excess energy and hence will decompose [reaction (29a)] unless first collisionally stabilized [reaction (29b)].

5) The diradical may also undergo an internal migration of an H atom from the carbon to which the oxygen is attached to the adjacent carbon to form methyl *n*-propyl ketone containing ≈115 kcal excess energy; the excited ketone will then decompose [reaction (30a)] if not collisionally stabilized [reaction (30b)].

6) The alkyl group attached to the carbon attacked by the $O(^3P)$ may also migrate to the neighboring carbon, ultimately forming excited 2-methylbutanal which can decompose [reaction (31a)] or be stabilized by collisions [reaction (31b)].

7) The migration of the alkyl group is partly internal and partly external in nature, as indicated by the formation of small amounts of CH_4 and C_2H_6.

8) This splitting off of an alkyl radical from the triplet diradical, its third available reaction mode, is not quenched by increasing pressures and hence is referred to as the "pressure independent fragmentation."

This reaction scheme, postulated on the basis of the observed stable products, has been confirmed recently by the detection of the intermediate radical species using photoionization mass spectrometry[80–83]. These studies have also elucidated minor reaction paths which occur in addition to those described above.

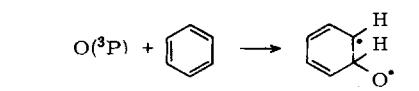
One of the major unsolved mechanistic problems of the $O(^3P)$ reaction with olefins, relevant to photochemical smog, is the effect of excess molecular oxygen at atmospheric pressure. Such studies are hampered by the possibility of ozone formation *via* reaction (2) since ozone also reacts with olefins to produce a wide variety of products including carbonyl compounds.

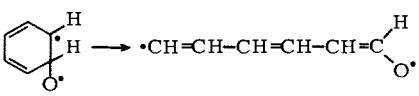
In one study[84] where NO_2 was used as the source of $O(^3P)$ and increasing amounts of O_2 were added to the *cis*-2-pentene reaction, significant quantities of acetaldehyde and propanal were formed, the epoxide yield decreased and the yields of methyl propyl ketone and 2-methylbutanal remained constant. Under these conditions O_3 formation should be negligible and it therefore appears that O_2 must interact with some of the intermediates. The triplet diradical is probably sufficiently short-lived[76] so that no collisions occur before it undergoes further reaction. Since the yields of the addition

carbonyl compounds are also unaffected by increasing pressures of O_2[84], it appears that the most likely interaction of O_2 is with the excited epoxides. However, until there is much more data available on the effect of O_2 on these reactions and on their intermediates, a detailed mechanistic discussion is not possible. Such studies are particularly important in that some monofunctional epoxides show carcinogenic activity in mice and rats[85]. Such epoxides include 3,4-epoxy-1-butene and styrene oxide which one *might* envision as being formed from oxygen atom reactions with 1,3-butadiene and styrene, respectively. It must be stressed however, that the production of such epoxides under ambient air conditions and their presence in polluted urban atmospheres at detectable levels has not been confirmed.

4.3. Mechanism of the O(^{3}P)-Arene Reaction

In 1961 *Cvetanovic* and co-workers[86,87] reported that the volatile products of the reactions of O(^{3}P) with benzene and toluene are water and CO, and phenol (from C_6H_6) and cresols (from C_7H_8), respectively, with the major product being nonvolatile polymeric compounds which deposited on the walls of the cell. This has recently been confirmed[88,92]. The polymeric material is thought to contain such functional groups as —CHO[86,89], —OH, and C—O—C[89] and to be aliphatic in nature[86]. While the formation of this "polymer" has repeatedly haunted researchers, it is interesting from the point of view of photochemical air pollution in that significant quantities of aliphatic difunctional compounds recently have been observed in ambient air particulate matter[90,91]. Many of these compounds contain five and six

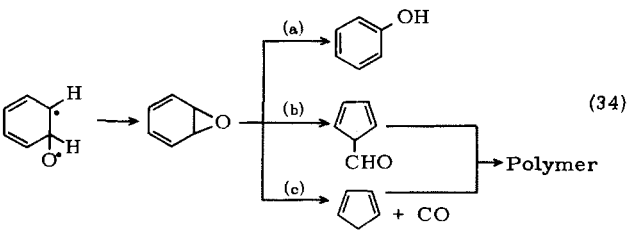

(32)


(33)

carbon atoms and hence we feel may arise from the attack of reactive radicals such as O(^{3}P) and OH on an aromatic ring, followed by ring opening and subsequent reactions with O_2, *etc.* For example, following the initial addition of O(^{3}P) to the benzene ring[86] [reaction (32)], ring opening may occur according to reaction (33)[89].

Subsequent reactions of the unsaturated diradical may then produce the nonvolatile products[86].

Alternatively, the following Scheme (34) has been proposed[86] to account for the observed products:


(34)

Such a mechanism cannot be extended to more complex arenes, as shown for example, by the lack of formation of 2,6-dimethylanisole in the 1,2,3-trimethylbenzene reaction[92].

It is obvious that the reaction of O(^{3}P) with arenes is very complex and will require the use of highly sophisticated techniques such as photoionization mass spectrometry in order to clarify the reaction mechanisms. However, with the increasing arene content of gasoline as lead is removed, even higher levels of these compounds in ambient air are anticipated. Hence, these reactions may become increasingly important, particularly if it can be conclusively demonstrated that ring opening to produce unsaturated aliphatic compounds is a major reaction pathway.

Although highly speculative at the present time, another possible route to ring opening in photochemical smog may involve the oxygen-enhanced absorption of light by arenes followed by their photooxidation to difunctional unsaturated compounds. Thus, in solution the irradiation of oxygen-saturated benzene led to the formation of both six and twelve-carbon conjugated dialdehydes[93].

5. Reactions of Electronically Excited O(^{1}D) Atoms

Electronically excited O(^{1}D) atoms containing 45.4 kcal/mol excitation[94] are produced in polluted urban atmospheres by the photolysis of O_3 at wavelengths less than 308 nm[95]. While the major tropospheric removal process of O(^{1}D) is physical quenching to O(^{3}P) primarily by O_2 and N_2, water is typically present at concentrations of ≈ 1—3% and hence can account for chemical quenching of $\approx 9\%$ of the O(^{1}D) atoms formed[96,97]:

$$O(^1D) + H_2O \xrightarrow{(a)} 2OH$$
$$\xrightarrow{(b)} H_2O + O(^3P)$$
$$\xrightarrow{(c)} H_2O_2$$
$$\xrightarrow{(d)} H_2 + O_2 \qquad (35)$$

It is estimated that more than 90% of the reaction produces hydroxyl radicals (path a)[98]. Hence, at high ozone concentrations in severe photochemical smog, this reaction may be an important source of OH radicals (see Section 7.1).

Recently, it has been shown that, in contrast to O(^{3}P) whose rates of reaction with chlorofluoroalkanes are very low[99], O(^{1}D) atoms react at almost collision frequency with a variety of these compounds[100,101]. Thus, the rate constants for its reactions with $CFCl_3$, CF_2Cl_2, CHF_2Cl, and CF_2ClCF_2Cl are 3.5×10^{11}, 3.2×10^{11}, 2.1×10^{11}, and 2.0×10^{11} l mol^{-1} s^{-1}, respectively. Major products with $CFCl_3$ and CF_2Cl_2 are COFCl and COF_2, respectively. Probably, chlorine is also formed either as Cl_2 in a molecular elimination process or as a recombination product of Cl atoms. This is currently being investigated.

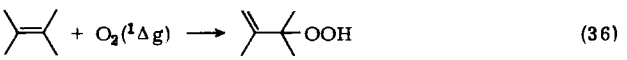
Since chlorofluoroalkanes are commonly used as aerosol propellants and are released into the atmosphere in great quantities, their atmospheric sinks are of considerable interest. In the troposphere, the concentration of O(^{1}D) is sufficiently low that reaction with chlorofluoroalkanes is not a significant loss process, and, as indicated above, other tropospheric reactions of these compounds are slow. In the stratosphere, however, the O(^{1}D) concentrations are much higher[102] and reaction with chlorofluoroalkanes that may have undergone vertical transport from the troposphere could prove to be signifi-

cant[100, 101]. This is especially true if either Cl_2 or Cl are formed in the primary attack of $O(^1D)$ or if COFCl (arising from $CFCl_3$) is photolyzed to produce Cl, as seems likely. Thus *Molina* and *Rowland* have recently proposed that chlorine atoms from the photodissociation of chlorofluoroalkanes by short wavelength solar radiation in the stratosphere[103] could lead to a chain destruction of stratospheric O_3[103, 104] in a manner similar to that suggested for nitric oxide.

Whether or not either of these proposed mechanisms for degradation of chlorofluoroalkanes, direct photodissociation or attack by $O(^1D)$ atoms, actually poses a problem depends upon several factors: (i) validation of these mechanisms under simulated stratospheric conditions; (ii) establishment of present and predicted future chlorofluoroalkane concentrations in the stratosphere; and (iii) their importance as chlorine atom sources relative to other precursors to Cl already existing in the stratosphere. Clearly, research in these areas is vitally needed.

6. Singlet Molecular Oxygen, $O_2(^1\Delta_g)$

Leighton[3] first considered the electronically excited states of O_2 as potential atmospheric oxidants, but he concluded that their production by the direct absorption of sunlight was too small to be significant. *Bayes*[105] then showed that if the O_2 absorption coefficients are corrected for collisional line broadening, excited $O_2(^1\Delta_g)$ may be formed in high enough concentrations and have a sufficiently long lifetime to react with simple olefins in the atmosphere, for example, according to reaction (36)[106, 107].



(36)

Subsequently, it was proposed[108, 109] that energy transfer from triplet excited organic pollutants to ground state oxygen might yield significant concentrations of $O_2(^1\Delta_g)$. Additional sources of $O_2(^1\Delta_g)$ in polluted urban atmospheres[110, 111] include energy transfer to O_2 from NO_2[31–34] (see Section 2), photolysis of O_3[112–114], exothermic chemical reactions producing O_2[115], oxygen-enhanced absorption by organics[116], and the hydrolysis of peracetyl nitrate[164].

Quantitative estimates of the yields of $O_2(^1\Delta_g)$ from each of these processes are difficult. However, a recent estimate[31] of the $O_2(^1\Delta_g)$ concentration due to the sum of direct absorption, energy transfer from NO_2^*, and photolysis of O_3 is $\approx 10^{-5}$ ppm.

It was thought[108–111] that $O_2(^1\Delta_g)$ might in part be responsible for the excess rate of consumption of olefins (Fig. 2) and the conversion of NO to NO_2 if its rate constants for reactions with olefins were sufficiently high, a point that was at that time unknown. Subsequently, these rate constants were found to be comparable to those of ozone-olefin reactions, *i.e.*, approximately five orders of magnitude lower than those of the corresponding $O(^3P)$ reactions[111, 117–119]. Since the $O(^3P)$ concentration is estimated[3] to be $\approx 10^{-8}$ ppm and if the $O_2(^1\Delta_g)$ concentration is $\approx 10^{-5}$ ppm[31] the oxidation of olefins by $O_2(^1\Delta_g)$ will not contribute significantly to the bulk consumption of olefins in polluted urban atmosphere [111, 120, 121] (see Table 5).

Recent calculations by *Firestone* and *Calvert*[122], however, indicate that we should be cognizant of possible health problems associated with $O_2(^1\Delta_g)$. They calculate that the half-life for quenching of $O_2(^1\Delta_g)$ by O_2 is sufficiently great (9.0×10^{-4} min) compared to the period for the inhalation cycle (3.5×10^{-2} min), that $O_2(^1\Delta_g)$ may reach the lung unquenched a significant portion of the time. Depending on the nature of the products formed by the interaction of $O_2(^1\Delta_g)$ with the lung tissue, some adverse health effects may arise.

Hence the presence of $O_2(^1\Delta_g)$ in polluted atmospheres is of concern for several reasons: (i) its calculated lifetime is sufficiently great that significant quantities may penetrate into the lung and react to form toxic compounds; (ii) it may react with a variety of olefins and arenes[123–129] and in ambient air form such known toxins as hydroperoxides[85, 129–131] which may then be inhaled; and (iii) it may be formed *in situ* by hydrolysis of air pollutants such as peracetyl nitrate[164].

Further work seems warranted to establish the ambient levels of $O_2(^1\Delta_g)$, to clarify its reactions with organics in ambient air and with biological components, and to establish the effects of the products of these reactions on human organisms.

7. The Hydroxyl Radical (OH): Kinetics and Mechanisms

The suggestion that the OH radical is an important chain carrier in photochemical smog formation[3, 15, 16] has sparked much interest in both its kinetics and reaction mechanisms. This emphasis has been given added impetus recently by the detection of OH in ambient air at daytime concentrations of the order of $10^8/cm^3$ using a tunable UV laser[132].

7.1. Sources of the OH Radical

As mentioned above, $O(^1D)$ atoms formed during ozone photolysis react with water to produce 2 OH radicals [reaction (35a)]. The reaction of HO_2 with NO [reaction (8)], and the photolysis of nitrous acid[133] are also sources of OH in the polluted troposphere.

$$HONO + h\nu \xrightarrow{\lambda < 400\,nm} OH + NO \quad \Phi \approx 1\ [133] \tag{37}$$

The HONO is formed in the reverse of reaction (37) as well as by reaction (38), which may be homogeneous or heterogeneous, or both (see discussion in references [21] and [138]),

$$NO + NO_2 + H_2O \rightarrow 2\,HONO \tag{38}$$

and possibly by reaction (39)[134]:

$$HO_2 + NO_2 \rightarrow HONO + O_2 \tag{39}$$

While HONO has not yet been detected in ambient air, it has been tentatively identified in smog chamber experiments on propylene-NO_x mixtures in moist air using *in situ* analysis by Fourier transform infrared spectroscopy[135]. The reactant concentrations in these experiments were, however, somewhat higher than ambient (7.8 ppm C_3H_6, 6.2 ppm NO, and 3.8 ppm NO_2).

The photolysis of hydrogen peroxide[3, 68, 114] also produces OH:

$$H_2O_2 + h\nu \xrightarrow{\lambda < 370\,nm} 2\,OH \qquad (40)$$

The first detection and measurement of H_2O_2 in ambient air by a wet chemical method was reported several years ago[136] when concentrations as high as 0.18 ppm in Riverside, California, were measured during a severe smog episode. Subsequent studies on a very smoggy day in July 1973 in Pasadena, California, located approximately 40 miles west and upwind of Riverside, using Fourier transform infrared spectroscopy[137], gave inconclusive results on the presence of H_2O_2. Hence further studies on the ambient concentrations and diurnal variations of H_2O_2 are important.

The relative importance of each of the OH-forming reactions changes during the day as discussed in detail by *Demerjian, Kerr,* and *Calvert*[138].

7.2. Kinetics of the Reactions of the OH Radical

Kinetic studies of the reactions of OH with both organics and inorganics indicate that its reaction rates are very fast, as shown in Table 3, and in some cases, *e.g.*, reaction with the higher olefins, are essentially diffusion controlled.

Table 3. Typical rate constants k for some reactions of the OH radical at 300°K.

Compound	Reaction	k[1 mol^{-1} s^{-1}]	Ref.
CO	$OH + CO \rightarrow H + CO_2$	9.8×10^7	[139]
O_3	$OH + O_3 \rightarrow HO_2 + O_2$	$(3.3 \pm 0.9) \times 10^7$	[140]
NO	$OH + NO \xrightarrow{(M)} HONO$	$(\approx 6\text{—}12) \times 10^9$	[141] [a]
NO_2	$OH + NO_2 \xrightarrow{(M)} HNO_3$	7.2×10^9	[141, 142] [a]
CH_4	$OH + CH_4 \rightarrow H_2O + CH_3$	6.2×10^6	[143]
HCHO	$OH + HCHO \rightarrow H_2O + HCO$	$(8.4 \pm 2.1) \times 10^9$	[22]
Ethylene	[c]	$(1.8 + 0.6) \times 10^9$	[144]
Propylene	[c]	$(8.7 \pm 1.3) \times 10^9$	[144]
trans-2-butene	[c]	4.5×10^{10} [b]	[145]
$(CH_3)_2C{=}C(CH_3)_2$	[c]	9.9×10^{10} [b]	[145]
Xylene [d]	[c]	1.1×10^{10} [b]	[145]

[a] Most rate studies done at low pressure; this is the recommended value based on extrapolation of rate data into the second order regime.
[b] Rates measured relative to that for propylene for which $k = 1.0 \times 10^{10}$ l mol^{-1} s^{-1} [146].
[c] See discussion.
[d] Mixture of isomers.

7.3. Mechanism of the Reaction of OH with Alkanes and Aldehydes

The reaction of OH with alkanes and aldehydes proceeds by abstraction to produce H_2O and a reactive radical species such as CH_3• in the case of methane, or HCO• on reaction with formaldehyde. Its rate of reaction with aldehydes is as fast as that with the smaller olefins[22, 144–146] and hence is anticipated to be significant in the atmosphere. The subsequent reactions of the radicals produced may then oxidize NO to NO_2:

$$CH_3 + O_2 \xrightarrow{(M)} CH_3O_2 \qquad (41)$$
$$CH_3O_2 + NO \rightarrow CH_3O + NO_2 \qquad (42)$$
$$CH_3O + O_2 \rightarrow HCHO + HO_2 \qquad (43)$$
$$HO_2 + NO \rightarrow OH + NO_2 \qquad (8)$$
$$HCO + O_2 \rightarrow HO_2 + CO \qquad (10)$$

Recently, there has been some controversy over the products of the important reaction between NO and CH_3O_2, which for many years had been presumed to yield NO_2 and methoxy radicals [reaction (42)]. Thus, recent studies[147] indicated that the reaction of NO with CH_3O_2 occurred by addition rather than as written in equation (42). However, subsequent work[148] has established reaction (42) as the exclusive reaction path. The absolute rate of this reaction has not yet been determined and that of reaction (43)[149] needs further definition.

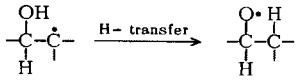
7.4. Mechanism of Reaction of OH with Olefins

The mechanism of the OH-olefin reaction is not known. In principle either abstraction of a hydrogen atom or addition to the double bond may occur. However, since activation energies for abstraction are commonly much higher than those for addition, one anticipates that at room temperature addition is the primary mode of reaction, particularly in view of the very high rate constants (Table 3). This is supported by the absence of a kinetic isotope effect on the rate of reaction of C_3D_6 as compared to C_3H_6[144, 145]. In addition, a mass peak corresponding to the OH-olefin adduct has been observed in the reactions of ethylene and propylene at total pressures of 1—4 torr[146]. These peaks increased with pressure[146] suggesting that collisional stabilization of the excited adduct is competitive with its decomposition under these conditions. The thermochemistry of the addition reaction (44) dictates that the adduct will have ≈ 35 kcal/mol excess energy.

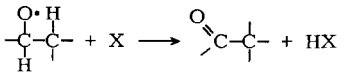
$$OH + \rangle C{=}C\langle \longrightarrow -\overset{OH}{\overset{|}{C}}-\overset{\bullet}{C}- \qquad (44)$$

The corresponding aldehydes are the major stable products, *i.e.*, CH_3CHO and C_2H_5CHO from the C_2H_4 and C_3H_6 reactions, respectively[146]. Isotope studies indicate that the H atom from the OH is retained in the product aldehyde[146], suggesting a series of reactions such as (45) and (46). Our speculations emphasize the need for much more detailed investigations of these reactions under a variety of conditions of total pressure, oxygen concentration, *etc.*

Essentially nothing is known about the kinetics and mechanism of the reactions of OH with arenes, partly because



(45)



(46)

$X = O_2$ etc.

such studies are experimentally difficult. However, this area is also one which is essential to our understanding of the detailed course of the complex reaction sequences in polluted urban air.

8. The Hydroperoxyl (HO_2) Free Radical

8.1. Sources of the HO_2 Radical

The recognized sources of HO_2 in photochemical smog[138] include any sources of H or HCO radicals as in aldehyde photolysis or alkoxy radical oxidations [reaction (43)].

While there have been regrettably few detailed analyses of the concentrations and types of aldehydes in ambient air, formaldehyde appears to constitute a significant portion ($\approx 40\,\%$) of the total aldehydes present[150]. This will of course vary with location and nature of the photochemical smog. For example, *Hanst* and co-workers[137] found in Pasadena, California, on July 25, 1973, a peak O_3 concentration of 0.68 ppm and, remarkably, no formaldehyde (≤ 0.01 ppm) but large quantities (0.05 ppm) of formic acid.

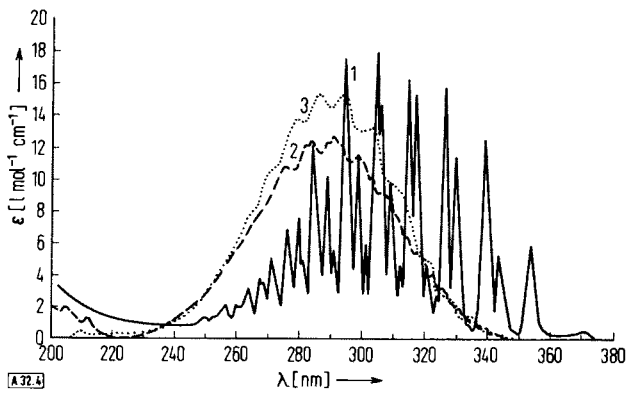


Fig. 4. Absorption spectra [68] for (1) HCHO (≈ 75 °C); (2) CH_3CHO (25 °C); and (3) C_2H_5CHO (25 °C) (after [68]).

The photochemistry of HCHO is particularly important because it absorbs radiation well into the actinic ultraviolet region (Fig. 4) and because the primary process I [reaction (47a)]

$$HCHO + h\nu \rightarrow H + HCO \qquad \text{(I) (47a)}$$

gives two precursors to HO_2 radicals per photon absorbed *via* reactions (7) and (10). Higher aldehydes are also important but they yield only one *direct* precursor of HO_2 in the primary photodissociative act I′ [reaction (48)]

$$RCHO + h\nu \rightarrow R + HCO \qquad \text{(I′) (48)}$$

and do not absorb as far into the actinic UV as does formaldehyde (Fig. 4). The alkyl radicals may also act as a source of HO_2 through a more complex reaction sequence [*e.g.* reactions (41)—(43)].

The importance of aldehyde photolysis in photochemical smog[3, 151, 152] was recently placed on a more quantitative basis by *Calvert* and co-workers[153] who estimated the rates of HO_2 generation from HCHO photolysis as a function of solar zenith angle using the wavelength dependence[154] of the quantum yields, Φ_I and Φ_{II} where process II [reaction (47b)] is

$$HCHO + h\nu \rightarrow H_2 + CO \qquad \text{(II) (47b)}$$

There is presently some controversy about the wavelength dependence of the absolute and relative values of Φ_I and Φ_{II}[155] and clearly, further quantitative photochemical studies on the system are urgently needed.

8.2. Kinetics of the Reactions of HO_2 Radicals

HO_2 reacts with a variety of compounds at rates which are generally several orders of magnitude slower than the corresponding OH reactions. Table 4 gives some typical values of rate constants recommended by *Lloyd*[156]. The errors quoted for these measurements are in many cases quite large due to the paucity of reliable data.

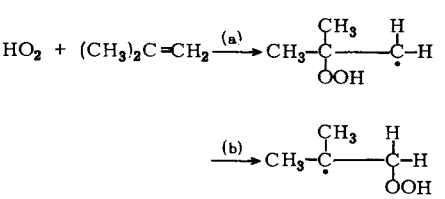
Table 4. Recommended [156] values of the rate constants (300 °K) for some gas phase reactions of the HO_2 radical.

Compound	Reaction	k [l mol^{-1} s^{-1}]
CO	$HO_2 + CO \rightarrow OH + CO_2$	6 ± 2
O_3	$HO_2 + O_3 \rightarrow OH + 2O_2$	$(9 \pm 100\,\%) \times 10^5$
NO	$HO_2 + NO \rightarrow OH + NO_2$	$(2 \pm$ factor of 3$) \times 10^8$ [19]
SO_2	$HO_2 + SO_2 \rightarrow OH + SO_3$	$(5.2 \pm 1.1) \times 10^5$ [19]
C_2H_6	$HO_2 + C_2H_6 \rightarrow H_2O_2 + C_2H_5$	$(0.08 \pm$ factor of 10)
HCHO	$HO_2 + HCHO \rightarrow H_2O_2 + HCO$	$(1.7 \pm$ factor of 10$) \times 10^3$
C_2H_4	$HO_2 + C_2H_4 \rightarrow$? [a]	$\approx 10^4$
i-C_4H_8	$HO_2 + i$-$C_4H_8 \rightarrow$? [a]	$\approx 10^5$

[a] See following discussion.

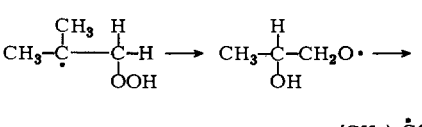
8.3. HO_2-Organic Reaction Mechanisms

If little is known about the kinetics of HO_2 reactions, even less is known about its reaction mechanisms, particularly with olefins and aromatics. *Avramenko* and co-workers[157] have proposed, from their product studies of the C_2H_4, C_3H_6, and i-C_4H_8 reactions with HO_2 in a flow-discharge system at a total pressure of ≈ 60 torr, that the first step involves addition to the double bond [reaction (49)].



(49)

These additions are much less exothermic than the corresponding OH-olefin reactions, with ≈ 10—14 kcal/mol excess energy residing in the adduct. The isomerization and decomposition



(50)

of the adduct [(reaction (50)] and subsequent reactions of the radical fragments were postulated to give the major observed products. However, the authors detected O atoms in the flow system and suggested[157] that the source of the O atoms may be the wall reaction

$$H + O_2 \xrightarrow{\text{wall}} O + OH \qquad (51)$$

Lloyd[156] suggests reaction (52b) may be responsible:

$$\begin{aligned} H + HO_2 &\xrightarrow{(a)} H_2 + O_2 \\ &\xrightarrow{(b)} H_2O + O \\ &\xrightarrow{(c)} 2OH \end{aligned} \qquad (52)$$

In either case, one anticipates that OH will also be produced. Since both $O(^3P)$ and OH react with olefins at rates which exceed that for HO_2 by 4—5 orders of magnitude, very small concentrations of these species may drastically affect the observed products and product distribution.

It is evident that the entire area of HO_2 reaction kinetics and mechanisms warrants extensive investigation. Experiments are most hampered by the problem of producing HO_2 in a manner which is free from interferences by other reactive species such as OH[156]. Wall reactions may also be important and these are often difficult to factor out. One interesting approach is that of *Hendry* and co-workers[158] who have used the radical initiated gas phase oxidation of 1,4-cyclohexadiene at $\approx 100\,^\circ C$ as their source of HO_2 for kinetic studies. This method, however, suffers from the disadvantage that studies must be carried out well above room temperature.

9. Computer and Smog Chamber Simulations of Photochemical Smog

9.1. Computer Kinetic Models

Despite this lack of critical data in many areas, several groups of researchers have made substantial inroads into computer simulation of the complex reaction sequences typified by Figure 1. Ideally, this requires both the detailed reaction mechanisms and accurate rate constants. For those elementary reactions whose rate constants are not known, one can estimate the value by standard methods[159] or else use it as an adjustable parameter which can be varied to give the best fit to time-concentration profiles (Fig. 1). As pointed out by *Calvert* and co-workers[160], the latter approach is "a sophisticated effort in curve fitting", whereas the former is a more demanding test of the validity of the proposed mechanism.

It should be recognized, however, that a good computer fit of the experimental data may be fortuitous and arise from compensating errors in various parts of the overall scheme, or from the insensitivity of the total mechanism to that particular elementary reaction.

A detailed computer simulation by *Calvert* and colleagues[138] illustrates both the utility of this approach and the chemical insights which can be gained. For example, the predicted rates of attack (rate = rate constant × concentration of reactive species) of various reactive species on *trans*-2-butene in a "typical" polluted urban atmosphere are given in Table 5. Using their mechanism and rate constants, it is evident that at short reaction times the rate of attack by OH far exceeds that by all other species combined and hence OH is primarily responsible for the excess rate of olefin consumption (Fig. 2) in the early stages of the reaction. At longer reaction times, O_3 and HO_2 become important. It should be stressed, however, that the validity of these predictions depend on the rate constants and mechanistic details chosen.

Table 5. Rate of attack (ppm min^{-1}) × 10^4 on *trans*-3-butene of some reactive intermediates as predicted by computer simulation of a sunlight irradiated, auto-exhaust polluted atmosphere [138]. Initial reactant mixture contains 0.075 ppm NO; 0.025 ppm NO_2; 0.10 ppm *trans*-2-butene; 10 ppm CO; 0.10 ppm CH_2O; 0.06 ppm CH_3CHO; and 1.5 ppm CH_4; relative humidity 50% at 25 °C; zenith solar angle, 40°.

Time [min]	Reactive species				
	$O(^3P)$	O_3	HO_2	HO	$O_2(^1\Delta_g)$
2	0.13	0.26	1.69	18.1	2.9×10^{-5}
30	0.17	1.58	1.49	5.9	2.0×10^{-5}
90	0.03	1.00	0.49	1.2	0.7×10^{-5}
120	0.01	0.65	0.28	0.7	0.4×10^{-5}

9.2. Airshed Models

Research on the detailed kinetic and mechanistic aspects of photochemical smog such as we have been discussing can be viewed as simply another "academic exercise" unless the results can be translated into a form that can be effectively utilized by public officials charged with the responsibility of actually *controlling* air pollution. Happily this challenge is currently being met by atmospheric scientists, many of whom have been cited earlier in this article, who not only are conducting basic research but also are involved with the development of reliable and operationally useful airshed models. These models can be utilized, for example, to assess the most cost-effective control strategies as well as to predict well in advance severe smog episodes which may threaten the health of the public.

Such total airshed models require as input[161]: (i) a detailed emission inventory for fixed and mobile sources; (ii) an assessment of the meteorological and topographical features of the area and an evaluation of the land use; and (iii) a reliable description of the chemical and physical processes occurring in the polluted atmosphere. Because of the complexity of the smog system in the real world, it is generally considered not feasible to include in (iii) all possible reactions as is done in the so-called "specific mechanism" approach[10, 138, 162] exemplified above by the work of *Calvert* and co-workers[138]. Hence in airshed models, a "lumped parameter"[161, 162] approach to the chemistry is often used, *i.e.*, the reaction of a whole class of compounds, *e.g.* olefins, with one reactive species, *e.g.* OH, is represented by one equation, one rate constant and stoichiometric coefficients for the amounts of products in each step. In these "lumped mechanism" models, some of the rate constants and stoichiometric coefficients are then treated as adjustable parameters. However, this approach suffers from the criticism cited above, *i.e.*, given enough parameters, curves can be drawn to fit any set of experimental data. Hence, a model which accurately reproduces one set of data may not be applicable to ambient air, or indeed, to another smog chamber.

9.3. Smog Chamber Studies

A major problem encountered in validating the chemistry portion of these computer models is the paucity of reliable data taken over a wide range of carefully controlled experimental conditions in the ppm-ppb concentration range of reactants typical of polluted ambient air. This gap is understandable since the technical (and financial) difficulties involved in conducting quantitative mechanistic photochemistry in such complex systems are not inconsiderable[10, 138, 161, 162]. They include, for example, (i) quantitative sampling and analysis of specific trace contaminants in complex and often heterogeneous mixtures in air, (ii) understanding and dealing with the important effects of the surface-to-volume ratio and the nature of the walls of the chamber, (iii) availability of an ample supply of highly purified air (volumes of some chambers run into thousands of liters), and (iv) careful control over a wide range of reaction conditions including temperature, relative humidity and the intensity and spectral distribution of the ultraviolet light to which the synthetic smog is actually exposed.

In order to overcome some of these problems, the chamber shown in Figures 5 and 6 was constructed[166]. Its features include (1) FEP Teflon lining to minimize wall reactions, (2) 20 mm thick fused silica windows which pass $\approx 90\%$ of the 240 nm radiation, (3) the capability of evacuation to 10^{-6} torr by a hydrocarbon-free pumping system, (4) a temperature operation range of $-35°$ to $+100\,°C$, (5) faithful reproduction in both absolute intensity and spectral distribution of the sun's ultraviolet radiation by means of a solar simulator powered by a 25-kilowatt high pressure xenon arc, and (6) an optical system that generates a collimated light beam that fills the cylindrical chamber without touching the walls. With appropriate filters the solar simulator can mimic tropospheric *or* stratospheric radiation. Especially important is the match in intensity in the region 295—330 nm where many important processes occur, such as the photolyses of ozone, aldehydes, and hydrogen peroxide. Previous "conventional" chambers were usually "intensity poor" in this region by virtue of their light sources (usually fluorescent black lamps emitting primarily 366 nm radiation) and the wavelength transmission cutoff of the chamber walls.

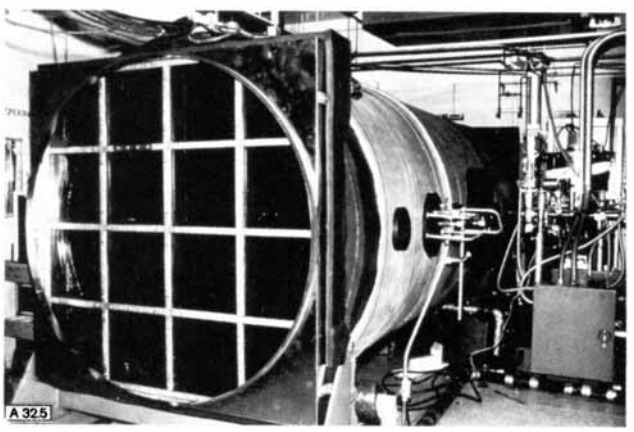


Fig. 5. Evacuable smog chamber at the Statewide Air Pollution Research Center, University of California, Riverside. Length: 3.96 m, diam. 1.52 m, vol. 5500 l.

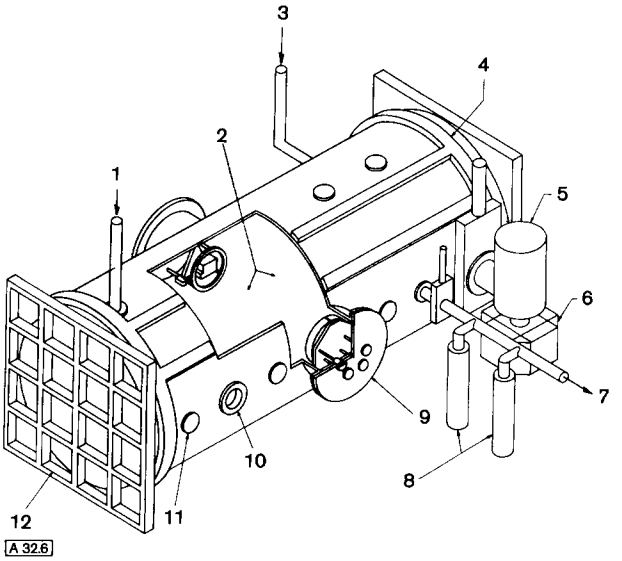


Fig. 6. Schematic diagram of the evacuable smog chamber. 1, ambient air inlet; 2, Teflon coated inner surfaces; 3, pure air inlet; 4, temperature control manifold (partial); 5, titanium sublimation pump; 6, ion pump; 7, liquid ring pump; 8, cryogenic sorption pumps; 9, multiple reflection infrared device; 10, light scattering experiment port; 11, sampling ports; 12, quartz windows.

An additional important feature of this chamber is the incorporation of a White cell multiple pass optical system capable of pathlengths up to 200 meters. When mated to an ultra high resolution ($0.06\,cm^{-1}$) and rapid scan (2.5—15 μm in six seconds) Fourier multiplex infrared spectrometer, one can carry out *in-situ* analysis of highly reactive pollutants down to 10 ppb or less.

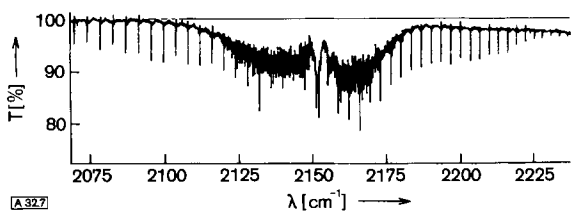


Fig. 7. Infrared spectrum, recorded using Fourier interferometry, of ketene from the reaction of *cis*-2-butene (50 ppm) with O_3 (10 ppm) at a total pressure of 2 torr and a pathlength of 50 m, in the evacuable smog chambers depicted in Figs. 5 and 6. The evenly spaced lines are the rotational lines of CO.

For example, Figure 7 shows the high resolution infrared spectrum of ketene (generated by the reaction of O_3 with *cis*-2-butene)[170] superimposed on the rotational structure of the 4.7 μm band of CO. Ketene has not been detected in ambient air to date perhaps because of the lack of suitable analytical methods. If present in smog, however, it may be amenable to identification by this technique.

10. Concluding Remarks

We hope that this rather brief and necessarily selective discussion has given the chemist who is not an expert in the field some feeling for the problems the air pollution chemist confronts and some of the areas to which he himself can make a significant contribution. The outcome and utility of air pollution simulation studies ultimately rest on the accuracy of the input data generated by a diverse group of scientists and in the long run the validity of the kinetic models reflects

what essentially amounts to the old adage often applied to computer studies, "garbage in ... garbage out". It is the task of we scientists to minimize the "garbage in!"

The authors gratefully acknowledge the generous financial assistance of the following agencies: California Air Resources Board, Grant No. ARB-3-017 and Project Clean Air 122; U. S. Environmental Protection Agency, Grant No. R-800649; Manufacturing Chemists' Association, Grant No. 73/74-1; National Aeronautics and Space Administration, Ames Research Center, Grant No. NGR 05-008-029; National Science Foundation, Grant No. GP-34524 and GP-38053 X, NSF-RANN, No. GI-41051, and the Office of Naval Research, Themis Contract No. N00014-69-A-0200-5001. The contents do not necessarily reflect the views and policies of the above agencies, nor does the mention of tradenames or commercial products constitute endorsement or recommendation for use.—We wish to thank the EOCOM Corporation and Finnigan Corporation for the loan of a Fourier Multiplex Spectrometer and a GC-MS respectively, which were used in portions of the work described above, and our colleagues at UCR in the Department of Chemistry and the Statewide Air Pollution Research Center for helpful discussions.

Received: July 9, 1974 [A 32 IE]
German version: Angew. Chem. *87*, 18 (1975)

[1] *J. T. Middleton, J. B. Kendrick,* and *H. W. Schalm,* Plant. Dis. Rep. *34*, 245 (1950).

[2] Third Interim Report on the Smog Problem in Los Angeles County. Stanford Research Institute, 1950.

[3] *P. A. Leighton:* Photochemistry of Air Pollution. Academic Press, New York, N. Y. 1961, and references therein.

[4] *A. J. Haagen-Smit, E. F. Darley, M. Zaitlin, H. Hull,* and *W. Noble,* Plant. Physiol. 27, 18 (1951).

[5] *A. J. Haagen-Smit,* Ind. Eng. Chem. *44*, 1342 (1952).

[6] *A. J. Haagen-Smit, C. E. Bradley,* and *M. M. Fox,* Ind. Eng. Chem. *45*, 2086 (1953).

[7] *A. J. Haagen-Smit* and *M. M. Fox,* J. Air Pollut. Contr. Ass. *4*, 105 (1954).

[8] *A. P. Altshuller, S. L. Kopczynski, W. A. Lonneman, T. L. Becker,* and *R. Slater,* Environ. Sci. Technol. *1*, 899 (1967).

[9] *A. P. Altshuller,* personal communication to *H. Niki,* July 1969.

[10] *H. Niki, E. E. Daby,* and *W. Weinstock,* Advan. Chem. Ser. *113*, 16 (1972), and references therein.

[11] *F. E. Blacet,* Ind. Eng. Chem. *44*, 1339 (1952).

[12] *R. E. Huie, J. T. Herron,* and *D. D. Davis,* J. Phys. Chem. *76*, 2653 (1972).

[13] *M. J. Ball* and *F. S. Larkin,* Nature (Phys. Sci.) *245*, 63 (1973), and references therein.

[14] *H. Niki,* Can. J. Chem. *52*, 1397 (1974), and references therein.

[15] *J. Heicklen, K. Westberg,* and *N. Cohen,* Center for Air Environmental Studies, Report No. 115—69 (1969).

[16] *D. H. Stedman, E. D. Norris, Jr., E. E. Daby, H. Niki,* and *B. Weinstock:* The Role of OH Radicals in Photochemical Smog Reactions. 160th Nat. Meeting of the Amer. Chem. Soc., Chicago, IL, Sept. 14—18, 1970.

[17] *D. D. Davis,* Can. J. Chem. *52*, 1405 (1974).

[18] *W. Wong* and *D. D. Davis,* Int. J. Chem. Kinet. *6*, 401 (1974), and references therein.

[19] *W. A. Payne, L. J. Stief,* and *D. D. Davis,* J. Amer. Chem. Soc. *95*, 7614 (1973).

[20] *G. Dixon-Lewis, W. E. Wilson, Jr.,* and *A. A. Westenberg,* J. Chem. Phys. *44*, 2877 (1966).

[21] *J. G. Calvert:* Proceedings of the Conference on Health Effects of Air Pollutants. National Academy of Sciences, National Research Council, Oct. 3—5, 1973, pp. 19ff.

[22] *E. D. Morris, Jr.* and *H. Niki,* J. Chem. Phys. *55*, 1992 (1971).

[23] *N. Washida, R. I. Martinez,* and *K. D. Bayes,* Z. Naturforsch. *29a*, 251 (1974).

[24] *G. Herzberg:* Molecular Spectra and Molecular Structures. III. Electronic Spectra and Electronic Structure of Polyatomic Molecules. Van Nostrand, Princeton 1967, p. 483.

[25] *H. W. Ford* and *S. Jaffe,* J. Chem. Phys. *38*, 2935 (1963).

[26] *J. N. Pitts, Jr., J. H. Sharp,* and *S. I. Chan,* J. Chem. Phys. *40*, 3655 (1964).

[27] *K. F. Preston* and *R. J. Cvetanovic,* Can. J. Chem. *44*, 2445 (1966).

[28] *I. T. N. Jones* and *K. D. Bayes,* J. Chem. Phys. *59*, 4836 (1973).

[29] *J. N. Pitts, Jr., J. H. Sharp,* and *S. I. Chan,* J. Chem. Phys. *39*, 238 (1963).

[30] *I. T. N. Jones* and *K. D. Bayes,* Proc. Roy. Soc. (London) *A 335*, 547 (1973), and references therein.

[31] *I. T. N. Jones* and *K. D. Bayes,* Chem. Phys. Lett. *11*, 163 (1971).

[32] *I. T. N. Jones* and *K. D. Bayes,* J. Chem. Phys. *59*, 3119 (1973), and references therein.

[33] *T. C. Frankiewicz* and *R. S. Berry,* Environ. Sci. Technol. *6*, 365 (1972).

[34] *T. C. Frankiewicz* and *R. S. Berry,* J. Chem. Phys. *58*, 1787 (1973).

[35] *E. K. C. Lee* and *W. M. Uselman,* Disc. Faraday Soc. *53*, 125 (1972).

[36] *A. P. Altshuller* and *J. J. Bufalini,* Photochem. Photobiol. *4*, 97 (1965).

[37] *D. H. Stedman, C. H. Wu,* and *H. Niki,* J. Phys. Chem. *77*, 2511 (1973).

[38] *H. Niki,* personal communication 1974.

[39] *D. H. Stedman* and *H. Niki,* Environ. Lett. *4*, 303 (1973).

[40] *J. A. Ghormley, R. L. Ellsworth,* and *C. J. Hochanadel,* J. Phys. Chem. 77, 1341 (1973).

[41] Air Pollution in California. Annual Report 1973. California Air Resources Board, January 1974.

[42] *J. N. Pitts, Jr., A. C. Lloyd,* and *J. L. Sprung:* Chemical Reactions in Urban Atmospheres and their Application to Air Pollution Control Strategies. Proc. Int. Symp. on Environ. Measurements, Geneva, Switzerland, Oct. 2—4, 1973, and references therein.

[43] *L. N. Pitts, Jr., A. C. Lloyd,* and *J. L. Sprung,* Chem. in Brit., in press.

[44] *B. J. Finlayson, J. N. Pitts, Jr.,* and *R. Atkinson,* J. Amer. Chem. Soc. *96*, 5356 (1974), and references therein.

[45] *R. A. Cox* and *S. A. Penkett,* J. C. S. Faraday Trans. I *68*, 1735 (1972), and references therein.

[46] *P. S. Bailey,* Chem. Rev. *58*, 925 (1958).

[47] *R. W. Murray,* Accounts Chem. Res. *1*, 313 (1968).

[48] *P. S. Bailey,* Symposium on Ozone Reactions with Organic Compounds. 161st Meeting of the Amer. Chem. Soc., Div. Petrol. Chem., Los Angeles, Calif., March 29—30, 1971; Adv. Chem. Ser. *112*, 1 (1972).

[49] *W. E. Scott, E. R. Stephens, P. L. Hanst,* and *R. C. Doerr,* Proc. Amer. Petrol. Instit. *3*, 171 (1957).

[50] *P. L. Hanst, E. R. Stephens, W. E. Scott,* and *R. C. Doerr:* Atmospheric Ozone-Olefin Reactions. The Franklin Institute, 1958.

[51] *T. Vrbaski* and *R. J. Cvetanovic,* Can. J. Chem. *38*, 1053, 1063 (1960).

[52] *Y. K. Wei* and *R. J. Cvetanovic,* Can. J. Chem. *41*, 913 (1963).

[53] *E. Briner* and *P. Schnorf,* Helv. Chim. Acta *12*, 154, 181 (1929).

[54] *E. Briner* and *R. Meier,* Helv. Chim. Acta *12*, 529 (1929).

[55] *J. J. Bufalini* and *A. P. Altshuller,* Can. J. Chem. *43*, 2243 (1965).

[56] *R. D. Cadle* and *C. Schadt,* J. Amer. Chem. Soc. *74*, 6002 (1952).

[57] *B. J. Finlayson, J. N. Pitts, Jr.,* and *H. Akimoto,* Chem. Phys. Lett. *12*, 495 (1972).

[58] *R. Atkinson, B. J. Finlayson,* and *J. N. Pitts, Jr.,* J. Amer. Chem. Soc. *95*, 7592 (1973).

[59] *D. A. Hansen* and *J. N. Pitts, Jr.,* unpublished results.

[60] *W. A. Kummer, J. N. Pitts, Jr.,* and *R. P. Steer,* Environ. Sci. Technol. *5*, 1045 (1971).

[61] *J. N. Pitts, Jr., B. J. Finlayson, H. Akimoto, W. A. Kummer,* and *R. P. Steer,* Proc. Inter. Symp. Ident. Measure. Environ. Pollutants, Ottawa, Canada, June 14—17, 1971, pp. 32ff.

[62] *J. N. Pitts, Jr., W. A. Kummer, R. P. Steer,* and *B. J. Finlayson,* Advan. Chem. Ser. *113*, 246 (1972).

[63] *S. Toby,* J. Luminescence *8*, 94 (1973).

[64] *H. E. O'Neal* and *C. Blumstein,* Int. J. Chem. Kinet. *5*, 397 (1973).

[65] *T. R. Darling* and *C. S. Foote,* J. Amer. Chem. Soc. *96*, 1625 (1974), and references therein.

[66] *R. Hiatt* in *D. Swern:* Organic Peroxides. Wiley Interscience, New York, N. Y. 1971, pp. 1ff.

[67] *H. E. O'Neal,* personal communication 1973.

[68] *J. G. Calvert* and *J. N. Pitts, Jr.:* Photochemistry. Wiley, New York, N. Y. 1966, and references therein.

[69] *P. G. Blake* and *G. E. Jackson,* J. Chem. Soc. *B 1969*, 94, and references therein.

[70] *J. M. McAfee, A. M. Winer,* and *J. N. Pitts, Jr.:* An Infrared Product Analysis of Ozone-Olefin Reactions by Fourier Interferometry. Paper pre-

sented at CODATA Symposium on Chemical Kinetics Data for the Lower and Upper Atmosphere, Warrenton, VA (USA), Sept. 16—18, 1974.

[71] *E. F. Darley, E. R. Stephens, J. T. Middleton*, and *P. L. Hanst*, Int. J. Air Pollut. 155 (1959).

[72] *W. N. Arnold*, Intern. J. Air Pollut. *2*, 167 (1959).

[73] *E. A. Schuck, H. W. Ford*, and *E. R. Stephens:* Air Pollution Effects of Irradiated Automobile Exhaust as Related to Fuel Composition. Rept. No. 26, Air Pollution Foundation, San Marino, CA (USA) 1958.

[74] *E. A. Schuck* and *G. J. Doyle:* Photooxidation of Hydrocarbons in Mixtures Containing Oxides of Nitrogen and Sulfur Dioxide. Rept. No. 29, Air Pollution Foundation, San Marino, CA (USA) 1959.

[75] *N. A. Renzetti* and *G. J. Doyle*, J. Air Pollut. Contr. Ass. *8*, 293 (1959).

[76] *R. J. Cvetanovic*, Advan. Photochem. *1*, 115 (1963), and references therein.

[77] *R. Atkinson* and *J. N. Pitts, Jr.*, J. Phys. Chem. *78*, 1780 (1974).

[78] *R. E. Huie, J. T. Herron*, and *D. D. Davis*, J. Phys. Chem. *76*, 3311 (1972).

[79] *M. Luria, R. Simonaitis*, and *J. Heicklen*, Int. J. Chem. Kinet. *5*, 715 (1973).

[80] *I. T. N. Jones* and *K. D. Bayes*, J. Amer. Chem. Soc. *94*, 6869 (1972).

[81] *J. R. Kanofsky* and *D. Gutman*, Chem. Phys. Lett. *15*, 236 (1972).

[82] *J. R. Kanofsky, D. Lucas*, and *D. Gutman*, Fourteenth Symp. (Intern.) on Combustion. The Combustion Institute, 1973, p. 285.

[83] *F. J. Pruss, Jr., I. R. Slagle*, and *D. Gutman*, J. Phys. Chem. *78*, 663 (1974).

[84] *S. Sato* and *R. J. Cvetanovic*, Can. J. Chem. *37*, 953 (1959).

[85] *B. L. Van Duuren*, Ann. N. Y. Acad. Sci. *163*, 633 (1969).

[86] *G. Boocock* and *R. J. Cvetanovic*, Can. J. Chem. *39*, 2436 (1961).

[87] *G. R. H. Jones* and *R. J. Cvetanovic*, Can. J. Chem. *39*, 2444 (1961).

[88] *J. S. Gaffney* and *J. N. Pitts, Jr.*, unpublished data, 1974.

[89] *R. A. Bonanno, P. Kim, J. Lee*, and *R. B. Timmons*, J. Chem. Phys. *57*, 1377 (1972).

[90] *D. Schuetzle, D. R. Cronn, A. L. Crittenden*, and *R. J. Charlson:* Molecular Composition of Secondary Aerosol and Its Origin. Paper presented at 166th Nat. Meeting of the Amer. Chem. Soc., Chicago, IL, August 26—31, 1973.

[91] *R. J. O'Brien, J. R. Holmes*, and *A. H. Bockian*, Environ. Sci. Technol., in press.

[92] *E. Grovenstein, Jr.*, and *A. J. Mosher*, J. Amer. Chem. Soc. *92*, 3810 (1970).

[93] *K. Wei, J. C. Mani*, and *J. N. Pitts, Jr.*, J. Amer. Chem. Soc. *89*, 4275 (1967).

[94] *C. E. Moore:* Atomic Energy Levels. Vol. I—III, Nat. Bur. Stand. Circular 4.67, U. S. Government Printing Office, Washington, DC, 1958.

[95] *C.-L. Lin* and *W. B. DeMore*, J. Photochem. *2*, 161 (1973/74), and references therein.

[96] *R. J. Cvetanovic*, Can. J. Chem. *52*, 1452 (1974).

[97] *R. F. Heidner III, D. Husain*, and *J. R. Wiesenfeld*, J. C. S. Faraday Trans. II *69*, 927 (1973).

[98] *R. Simonaitis* and *J. Heicklen*, Int. J. Chem. Kinet. *5*, 231 (1973).

[99] *J. N. Pitts, Jr., R. Atkinson, J. S. Gaffney, S. Japar, C. T. Pate, H. L. Sandoval*, and *A. M. Winer*, unpublished data.

[100] *H. L. Sandoval, R. Atkinson*, and *J. N. Pitts, Jr.*, J. Photochem., in press.

[101] *J. N. Pitts, Jr., H. L. Sandoval*, and *R. Atkinson*, Chem. Phys. Lett., in press.

[102] *M. B. McElroy, S. C. Wolfsy, J. E. Penner*, and *J. C. McConnell*, J. Atmos. Sci. *31*, 287 (1974), and references therein.

[103] *M. J. Molina* and *F. S. Rowland*, Nature *249*, 810 (1974).

[104] *R. S. Stolarski* and *R. J. Cicerone*, Can. J. Chem. *52*, 1610 (1974).

[105] *K. D. Bayes*, Sixth Informal Photochemistry Conference. University of California, Davis, June, 1974, Abstracts, p. 4.

[106] *A. M. Winer* and *K. D. Bayes*, J. Phys. Chem. *70*, 302 (1966).

[107] *C. S. Foote* and *S. Wexler*, J. Amer. Chem. Soc. *86*, 3879 (1964).

[108] *A. U. Khan, J. N. Pitts, Jr.*, and *E. B. Smith*, Environ. Sci. Technol. *1*, 656 (1967).

[109] *J. N. Pitts, Jr., A. U. Khan, E. B. Smith*, and *R. P. Wayne*, Environ. Sci. Technol. *3*, 241 (1969).

[110] *J. N. Pitts, Jr.* in *C. S. Tuesday:* Chemical Reactions in Urban Atmospheres. American Elsevier, New York, N. Y., 1971, pp. 3ff.

[111] *J. N. Pitts, Jr.*, Ann. N. Y. Acad. Sci. *171*, 239 (1970).

[112] *R. H. Kummler*, M. H. Bortner, and *T. Baurer*, Environ. Sci. Technol. *3*, 248 (1969).

[113] *R. P. Wayne*, Advan. Photochem. *7*, 311 (1969).

[114] *K. H. Welge*, Can. J. Chem. *52*, 1424 (1974), and references therein.

[115] *R. W. Murray, J. Lin*, and *M. L. Kaplan*, Ann. N. Y. Acad. Sci. *171*, 121 (1970), and references therein.

[116] *J. W. Coomber, D. M. Hebert, W. A. Kummer, D. G. Marsh*, and *J. N. Pitts, Jr.*, Environ. Sci. Technol. *4*, 1141 (1970).

[117] *W. S. Gleason, A. D. Broadbent, E. Whittle*, and *J. N. Pitts, Jr.*, J. Amer. Chem. Soc. *92*, 2068 (1970).

[118] *R. A. Ackerman, J. N. Pitts, Jr.*, and *R. P. Steer*, J. Chem. Phys. *52*, 1603 (1970).

[119] *R. E. Huie* and *J. T. Herron*, Int. J. Chem. Kinet. *5*, 197 (1973), and references therein.

[120] *J. T. Herron* and *R. E. Huie*, Environ. Sci. Technol. *4*, 685 (1970).

[121] *J. J. Bufalini*, Environ. Sci. Technol. *6*, 837 (1972).

[122] *R. F. Firestone* and *J. G. Calvert*, to be published.

[123] *C. S. Foote*, Science *162*, 963 (1968).

[124] *C. S. Foote*, Accounts Chem. Res. *1*, 104 (1968).

[125] *K. Gollnick*, Adv. Chem. Ser. *77*, 78 (1968).

[126] *K. Gollnick*, Advan. Photochem. *6*, 1 (1968).

[127] *D. R. Kearns*, Chem. Rev. *71*, 395 (1971).

[128] *I. R. Politzer, G. W. Griffin*, and *J. L. Laseter*, Chem. Biol. Interactions *3*, 73 (1971).

[129] *B. Dowty, J. L. Laseter, G. W. Griffin, I. R. Politzer*, and *C. H. Walkinshaw*, Science *181*, 659 (1973).

[130] *R. T. Holman* and *S. I. Greenberg*, J. Amer. Oil Chem. Soc. *35*, 707 (1958).

[131] *R. Cortesi* and *O. S. Privett*, Lipids *7*, 715 (1972).

[132] *C. C. Wang* and *L. I. Davis, Jr.*, Phys. Rev. Lett. *32*, 349 (1974).

[133] *H. S. Johnston* and *R. Graham*, Can. J. Chem. *52*, 1415 (1974), and references therein.

[134] *R. Simonaitis* and *J. Heicklen*, J. Phys. Chem. *78*, 653 (1974).

[135] *J. M. McAfee, J. N. Pitts, Jr.*, and *A. M. Winer:* In-Situ Long Path Infrared Spectroscopy of Photochemical Air Pollutants in an Environmental Chamber. Paper presented at the Pacific Conference on Chemistry and Spectroscopy, San Francisco, CA, Oct. 16—18, 1974.

[136] *J. J. Bufalini, B. W. Gay, Jr.*, and *K. L. Brubaker*, Environ. Sci. Technol. *6*, 816 (1972).

[137] *P. L. Hanst, W. E. Wilson, Jr., R. K. Patterson, B. W. Gay*, and *L. W. Chaney:* A Spectroscopic Study of Pasadena Smog. 167th Nat. Meeeting of the Amer. Chem. Soc., Los Angeles, CA, March 31—April 5, 1974.

[138] *K. L. Demerjian, J. A. Kerr*, and *J. G. Calvert*, Advan. Environ. Sci. Technol. *4*, 1 (1974), and references therein.

[139] *D. D. Davis, R. Schiff*, and *S. Fischer*, unpublished results, as quoted in ref. [17].

[140] *J. G. Anderson* and *F. Kaufman*, Chem. Phys. Lett. *19*, 483 (1973).

[141] *J. G. Anderson, J. J. Margitan*, and *F. Kaufman*, J. Chem. Phys. *60*, 3310 (1974).

[142] *C. Morley* and *I. W. M. Smith*, J. C. S. Faraday Trans. II *68*, 1016 (1972).

[143] *W. E. Wilson, Jr.*, J. Phys. Chem. Ref. Data *1*, 535 (1972).

[144] *F. Stuhl*, Ber. Bunsenges. Phys. Chem. *77*, 674 (1973).

[145] *E. D. Morris, Jr.* and *H. Niki*, J. Phys. Chem. *75*, 3640 (1971).

[146] *E. D. Morris, Jr., D. H. Stedman*, and *H. Niki*, J. Amer. Chem. Soc. *93*, 3570 (1971).

[147] *C. W. Spicer, A. Villa, H. A. Wiebe*, and *J. Heicklen*, J. Amer. Chem. Soc. *95*, 13 (1973).

[148] *C. T. Pate, B. J. Finlayson*, and *J. N. Pitts, Jr.*, J. Amer. Chem. Soc. *96*, 6554 (1974), and references therein.

[149] *J. Heicklen*, Advan. Chem. Ser. *76*, 23 (1968).

[150] *A. P. Altshuller* and *S. P. McPherson*, J. Air. Pollut. Contr. Ass. *13*, 109 (1963).

[151] *A. P. Altshuller, I. R. Cohen*, and *T. C. Purcell*, Science *156*, 937 (1967).

[152] *J. N. Pitts, Jr.*, J. Air Pollut. Contr. Ass. *19*, 658 (1969).

[153] *J. G. Calvert, J. A. Kerr, K. L. Demerjian*, and *R. D. McQuigg*, Science *175*, 751 (1972).

[154] *R. D. McQuigg* and *J. G. Calvert*, J. Amer. Chem. Soc. *91*, 1590 (1969).

[155] *H. P. Sperling* and *S. Toby*, Can. J. Chem. *51*, 471 (1973), and references therein.

[156] *A. C. Lloyd*, Int. J. Chem. Kinet. *6*, 169 (1974).

[157] *L. I. Avramenko, L. M. Evlashkina*, and *R. V. Kolesnikova*, Bull. Acad. Sci. USSR, Div. Chem. Sci. (Transl. of Izv. Akad. Nauk SSSR, Ser. Khim.) *1965*, 1306.

[158] *D. G. Hendry* and *W. R. Mabey:* A New System for Determining Rate Constants for HO_2 Reactions. 167th Nat. Meeting of the Amer. Chem. Soc., Los Angeles, CA, March 31—April 5, 1974.

[159] *S. W. Benson*: Thermochemical Kinetics. Wiley, New York, N. Y., 1968.

[160] *J. G. Calvert, K. L. Demerjian*, and *J. A. Kerr*, Proc. Int. Symp. Air Pollut., Tokyo, Oct. 17—19, 1972, pp. 465ff.

[161] *A. Q. Eschenroeder* and *J. R. Martinez*, Advan. Chem. Ser. *113*, 101 (1972).

[162] *T. A. Hecht, J. H. Seinfeld*, and *M. C. Dodge*, Environ. Sci. Technol. *8*, 327 (1974), and references therein.

[163] *C. M. Shy* and *J. F. Finklea*, Environ. Sci. Technol. 7, 205 (1973).

[164] *R. P. Steer, K. R. Darnall*, and *J. N. Pitts, Jr.*, Tetrahedron Lett. *1969*, 3765.

[165] *S. Furuyama, R. Atkinson, A. J. Colussi*, and *R. J. Cvetanovic*, Int. J. Chem. Kinet. *6*, 741 (1974).

[166] *J. N. Pitts, Jr., P. G. Bekowies, G. J. Doyle, J. M. McAfee*, and *A. M. Winer*, to be published.

Umpolung of Amine Reactivity. Nucleophilic α-(Secondary Amino)-alkylation *via* Metalated Nitrosamines[**][***]

New synthetic methods (7)

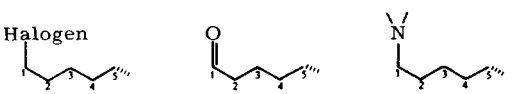
By Dieter Seebach and Dieter Enders[*]

There are basically two kinds of hetero atoms in organic molecules: one kind confers electrophilic character upon the carbon atom to which it is bound, and the other kind turns it into a nucleophilic site. The development of methods permitting transitions between the two resulting categories of reagents has become an important task of modern organic synthesis. The scope of such umpolung of the reactivity of functional groups is discussed for the case of amines as an example. A method of preparing masked α-secondary amino carbanions consists in nitrosation of the secondary amine, followed by metalation of the resulting nitrosamine α to the nitrogen, reaction with electrophiles, and subsequent denitrosation. Many examples are given for each of these steps which illustrate the wide scope of the overall synthetic operation (electrophilic substitution at the α-C atom of the secondary amine). Preliminary applications and a method for avoiding the handling of nitrosamines are presented, and the report concludes with a brief account of the significance of nitrosamines in the study of carcinogenesis and mutagenesis.

1. Introduction

1.1. Concept of Umpolung

We chemists are obliged to conform to certain simple rules dictated by Nature. Thus from the very beginning of our education in organic chemistry we learn—just how explicitly depends on the quality of our teacher—that heteroatoms such as halogen, oxygen, and nitrogen produce a certain reactivity pattern in a carbon skeleton: their electronegativity, being greater than that of carbon (−I effect), and their ability to stabilize an adjacent positive charge (+M effect) lead to the sites shown in Scheme 1 which are susceptible to attack by



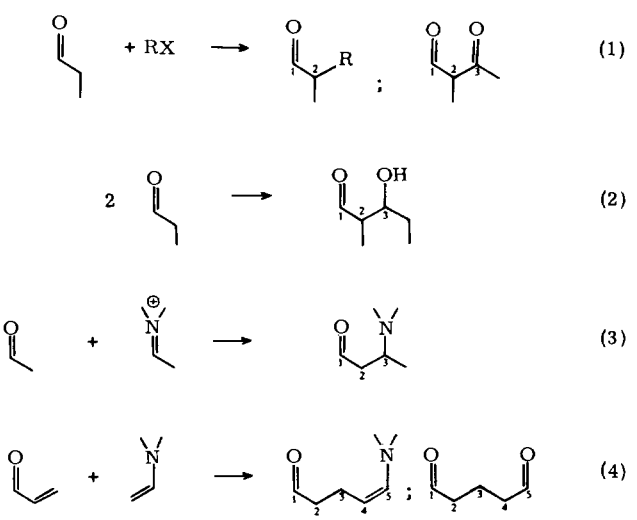
sites of $\frac{\text{electrophilic}}{\text{nucleophilic}}$ reactivity are C atoms $\quad \frac{1, 3, 5, \ldots}{2, 4, 6, \ldots}$

attack by $\frac{\text{nucleophiles}}{\text{electrophiles}}$ occurs at C atoms

Scheme 1. Polarity pattern in hetero-substituted carbon chains.

reagents possessing a given "philicity". Nucleophiles attack the odd C atoms ($N^{1,3,\cdots}$ attack)[*] whereas electrophiles attack the even C atoms ($E^{2,4,\cdots}$ attack) of the chain (for examples see Table 1).

In C—C linking reactions of two or more heterosubstituted carbon compounds it is thus established what synthetic opera-



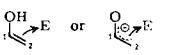
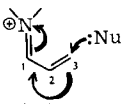
[*] Prof. Dr. D. Seebach and Dr. D. Enders [**]
Institut für Organische Chemie der Universität
63 Giessen, Ludwigstrasse 21 (Germany)

[**] This report draws extensively on the Dissertation of *D. E.*

[***] Attempts to find an English equivalent of the term "*Umpolung*" have yielded none so concise as the original German word. Its general adoption into English has therefore been proposed (see Chem. Ind. (London) *1974*, 910).

[*] Wherever there is a danger of confusion with a nitrogen atom the nucleophile will be designated "Nu".

Table 1. Examples for the typical reactivity of halogen compounds, carbonyl compounds, and amines with nucleophiles and electrophiles.

Attack by Nu or E at atom *n*	Halogen compound	Carbonyl compound	Amine
N^1			
	S_N substitution	addition or substitution at carbonyl C	aminoalkylation
E^2			
	HX′ addition	substitution at α-carbonyl C	enamine reactions
N^3			
	$S_{N'}$ substitution	1,4- or Michael addition	vinylogous Mannich reaction

tions are possible and the *distance* between the functional groups in the product is predetermined. A carbonyl compound is alkylated at position 2 by a halide [eq. (1)]; acylation, the aldol reaction, and the Mannich reaction [eqs. (1)—(3)] afford products having the heteroatoms in a 1,3 arrangement; additions of enamines to α,β-unsaturated carbonyl compounds furnish 1,5-bifunctional compounds [eq. (4)] (*odd* distance!). Any "trick" by which the polarity pattern shown in Scheme 1 is contravened will be termed umpolung of the normal reactivity in the broadest sense. The price to be paid for an umpolung invariably involves a synthetic detour, *i.e.* we must reckon with additional steps such as introduction and removal of protecting and masking groups or with having to perform rearrangements. On the other hand, we are then able to attach a synthon possessing a given reactivity, E or N, at atypical sites of a carbon chain and to synthesize molecules having *even* instead of *odd* distances between the functional groups.

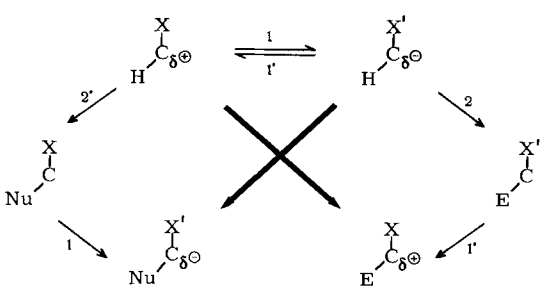
Table 2. Examples for umpolung of carbonyl compounds and amines. Newly formed bonds are shown in bold print.

Attack	Reagent	Equivalent	Product type	Ref.
E^1				[3, 4]
E^1	*(9)*			[4–6]
E^1				[3, 6]
E^1	*(8)*			[3, 6]
N^2				[3–5]
N^2				[5, 6]
E^1				[7]
E^1				[1–3]
N^2				[8]
E^3				[1–3, 8–11]
N^4				[3, 12]

Umpolung is as old as organic synthesis itself, as is apparent from the first examples listed in Table 2. However, a systematic search for umpolung methods was only initiated by the enormous advances made in carbanion and carbocation chemistry during the past twenty years. Another contributing factor has been the full realization of the advantages offered by reagents of reversed charge affinity. The lower part of Table 2 gives some examples of carbonyl umpolung which we have described in detail elsewhere[1–3].

1.2. Reversible Umpolung

Of greatest synthetic value is *reversible umpolung*. The concept is shown for a simple $E^1 \rightleftharpoons N^1$ example in Scheme 2. A compound having a C atom rendered positive is transformed,



Scheme 2. General principle of reversible umpolung.

by modification of the heteroatom from X to X′ in step 1, into a derivative in which the originally electrophilic C atom has now become nucleophilic. Reaction with an electrophile in step 2 is followed by reversal of step 1, *i.e.* by reinstitution of the original reactivity in step 1′. The net result (bold arrow from upper left to lower right) is introduction of an *electrophile* at a *positively* charged C atom.

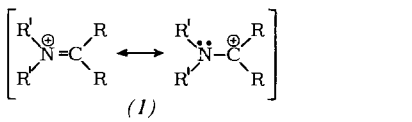
Attack by a nucleophile on a nucleophilic C atom (bold arrow from upper right to lower left) is feasible *via* the sequence 1′, 2′, 1. After temporary umpolung the C atom is in both cases finally available with normal reactivity again. A fre-

quently exploited example of the former case is umpolung of carbonyl compounds with thioacetal derivatives[1-3], and the latter case is illustrated by the masking of α-carbonyl cations by means of chloronitrones[8] (see also Table 2). In the following, the methods available for umpolung of amines will by briefly considered and a new reversible umpolung for secondary amines will be described in detail.

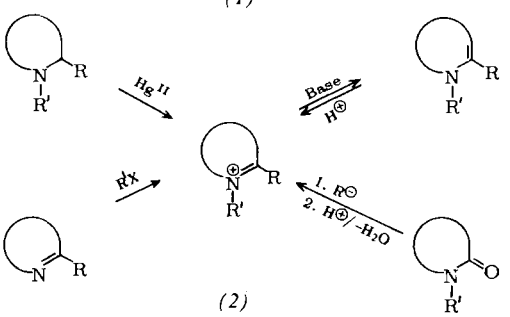
2. Possibilities of Umpolung of Amine Reactivity

2.1. α-Amino Carbocation *versus* α-Amino Carbanion

Amines display a "notorious" electrophilic reactivity at the α-C atom: the Mannich[13-15], Vilsmeier-Haak[16], Bischler-Napieralski, and Pictet-Spengler[17] reactions proceed *via* immonium ions of type *(1)*; salts of *(1)* are isolable[18-21],



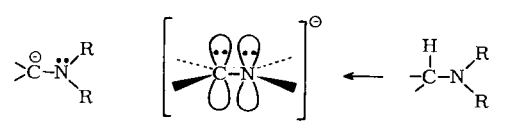
(1)



(2)

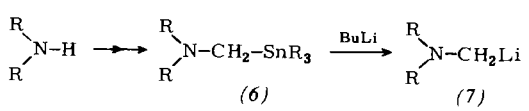
and even commercially available[22], and the dichloro derivative *(1)*, R=Cl[16] and a vinylimmonium ion *(1)*, R—R= $=C(CH_3)_2$[23] have recently been introduced into organic synthesis. Just how easy it is to come by immonium ions is obvious from the four routes shown for formation of the cyclic derivatives *(2)*. *Electrophilic* α-aminoalkylations are thus common events in organic synthesis and in biochemistry.

The situation is completely different with *nucleophilic* α-aminoalkylations, *i.e.* regarding the availability of α-amino carbanionic derivatives *(3)—(5)*; neither the relatively small electronegativity of the amino nitrogen nor the electronic configuration comparable with that in a ketyl[24] or ethylene



(3) *(3a)*

(4) *(5)*



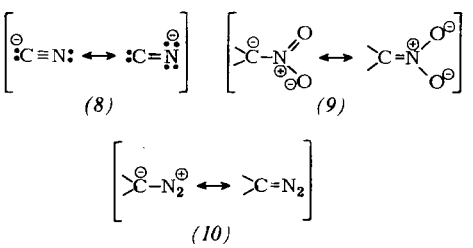
(6) *(7)*

dianion [see *(3a)*] favor the formation of a carbanion derivative, as may be seen from the extremely slow H/D[25] and H/Li exchange[26-28] in tertiary aliphatic amines. Once they have been formed, *e.g.* by transmetalation of the tin compounds *(6)*, α-aminomethyllithium compounds *(7)* display sufficient thermodynamic stability—*e.g.* toward Wittig rearrangement[29]—at 0 °C in hydrocarbons or ethers to act as reagents for nucleophilic α-*tertiary*-aminomethylation[26, 27]. Anions *(4)* and *(5)* of *secondary* and *primary* amines can be envisaged only if strong anion-stabilizing groups are bound to the carbon since tautomerization affording an amide anion would otherwise occur.

Since amines number among the most important classes of substances in organic chemistry and since at most *tertiary* α-aminoalkylating agents such as *(7)* are directly accessible, the use of *masked* synthons of anions *(3)—(5)* with reversed reactivity at the α-N-carbon atom is highly significant. Thus the question arising is: (a) what factors favor formation of a negative charge adjacent to nitrogen? and (b) which of these factors can be exploited in the sense of Scheme 2 for temporary umpolung of reactivity?

2.2. Dipolar and/or Resonance-Stabilized α-N-Carbanions

As is obvious from the "classical" α-N-carbanions *(8)* and *(9)* listed in Table 2, and from the diazo compounds *(10)*, which are likewise nucleophilic at the carbon, there exist bonding states of the nitrogen in which adjacent C atoms bear a negative charge, owing to endowment of the nitrogen



(8) *(9)*

(10)

with a positive charge (inductive effect), hybridization effects at the carbon (stability series $sp\text{-}C^{\ominus} > sp^2\text{-}C^{\ominus} > sp^3\text{-}C^{\ominus}$, increase in electronegativity of the carbon with increasing s character), and/or resonance stabilization of the negative charge.

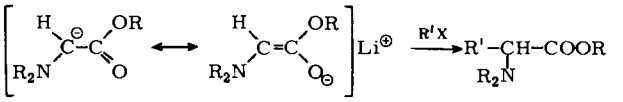
A literature search reveals that the generation of negative charges on C atoms adjacent to nitrogen in derivatives of types *(11)—(17)* is favored, as can be deduced from H/D exchange, condensation, or metalation reactions. Remarks on the various types and references are given under the relevant formulas in Table 3. It is trivial that any substitution at the negative C atom leading to additional delocalization, such as incorporation of allyl ($\overset{\ominus}{C}$—C=C), benzyl ($\overset{\ominus}{C}$—C_6—H_5, in general $\overset{\ominus}{C}$-aryl or $\overset{\ominus}{C}$-heteroaryl), enolate ($\overset{\ominus}{C}$—C=O), or iminoenolate resonance ($\overset{\ominus}{C}$—C=N, $\overset{\ominus}{C}$—C≡N) will further enhance the stability, and in the ultimate case will suffice to generate an ambident, fully masked α-N anion. Lithiated α-amino ester derivatives *(18)* represent an example[127] which should be termed lithium enolates rather than nucleophilic

Table 3. Structures *(11)*—*(17)* with negative charges on the C atoms adjacent to nitrogen.

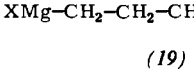
(11)	
X=C:	isocyanides [7]
X=C<	Schiff bases [30—34], imines of pyridoxal phosphate [35]
X=C=S	isothiocyanates [36]
X=NR	azo compounds [37]; anion with R=C_6H_5 reacts with carbonyl compounds at C, and with alkyl halides at N
$X=N_2$	azides [38]
X=O	oximes; oximates react with electrophiles at O or N, not at C [39], exception in intramolecular reactions [40]
(12)	
X=C<, X'=C<	azomethine ylides [41, 42], pyridinium ylides [43]
X=C<, X'=O	nitrones [38]
X=NR, X'=O	azoxy compounds [44, 45]
X=X'=O	nitro compounds [4, 39]; anions do not react with alkylating agents at C
(13)	
unstabilized [46—49], allyl- [50, 51], benzyl- [52], and enolate stabilized [53—56] nitrogen ylides [57]; cf. Stevens-Sommelet-Hauser rearrangement [58]; metalated amine oxides [38, 59—61]	
(14)	
X=⊖	dianions of Schiff bases [62]
$X=C_6H_5$	benzylic and/or allylic stabilization of anions necessary [29, 63, 64]
X=COR	R should not contain [65] α-carbonyl hydrogens [66], anion stabilization necessary, *e.g.*, by C_6H_5 [67, 68] or C≡N [69, 70], Reissert compounds; cyanamines cannot be metalated to *(14)*, X=C≡N [71]
X=N=C<	hydrazones [38], 1-methylpyrazole [72], 1-methylindazole [103]
X=N=NR	triazenes (not yet accomplished [73])
X=N=O	nitrosamines [71, 74—90]
$X=NO_2$	nitramines [89, 91]
$X=POR_2$	phosphonic amides [26, 92]
(15)	
X=C<	imidazoles, 2-methylindazole [103], 1,3-dimethylpyrazole [104], nitroolefins [125, 126]
X=O	formamides [3, 93—97]
X=S	thioformamides [71, 93, 97, 98]
(16)	
aldimines [99—102], heteroaromatics like pyrazoles, imidazoles [103, 105—108], triazoles [106—109], thiazoles [103, 110, 111], and pyridines [112—114]	
(17)	
X=X'=C<	pyridinium, quinolinium ylides [115—117]
X=C<, X'=O	nitrones [118], pyridine *N*-oxides [119—121]
X/X'=N	diazomethanes [122—124]

α-aminoalkylating agents. Although they possess considerable preparative significance, these cases will be excluded from the present discussion, as will reagents with E^3-umpolung of the amine skeleton (see Scheme 1 and Tables 1 and 2), such as *(19)*[128-130] and *(20)*[131].

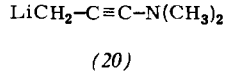
Among the numerous α-N anion systems *(11)*—*(17)* there are several which cannot be utilized as masked amino carb-



(18)



(19)



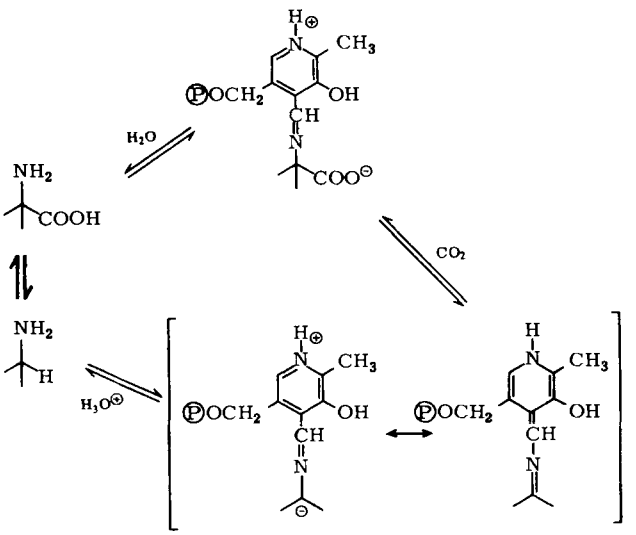
(20)

anions *(3)*—*(5)*; some have long been employed for the umpolung of amines[132] [Table 2 and Systems *(8)*—*(10)*], while others have only recently been exploited for the purpose. However, only very few of them are suitable for reversible umpolung according to the general Scheme 2.

2.3. Reversible Umpolung at the α-Position of Primary, Secondary, and Tertiary Amines

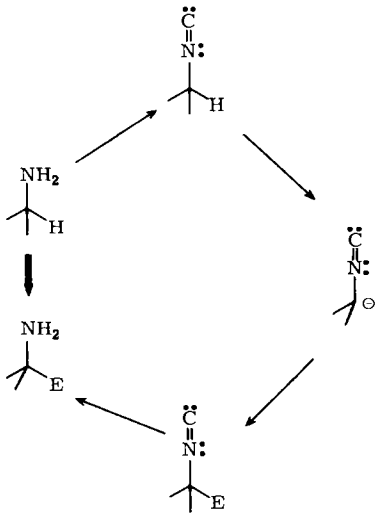
As may be seen from Scheme 2, reversible umpolung essentially involves the following three steps: Masking of the compound exhibiting normal reactivity with umpolung; reaction with "opposite sign"; "demasking".

The elegant way in which Nature has solved this problem for *primary amines* is apparent from Scheme 3 which outlines the interconversion of amino acids and biogenetic amines with the aid of a pyridoxal phosphate derivative[35]; the electrophiles $H^{\oplus}$ and CO_2 undergo mutual exchange at the α-amino C atom.



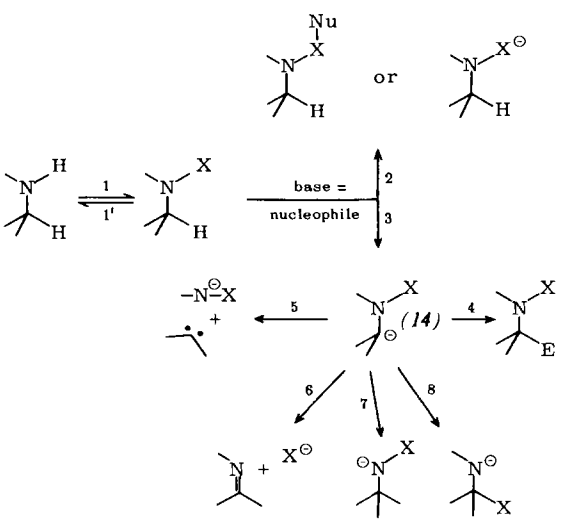
Scheme 3. Reversible umpolung of primary amines in Nature. Ⓟ = phosphate.

Those derivatives *(11)*, which can readily be prepared from primary amines, and nitro compounds of type *(12)* appear to be most suitable for imitation of this process *in vitro*. So far the best solution having a broad scope is probably the isocyanide method developed by *Schöllkopf* and his group[7] (Scheme 4): A variety of mild methods is available for conversion of primary amines into isocyanides; subsequent metalation and reaction with electrophiles proceed excellently and demasking is a hydrolytic step. In comparison, masking *via* nitro compounds (>CH—NH_2 → >CH—NO_2) requires an oxidation[133], the nitro anions (>$\overset{\ominus}{C}$—NO_2) only react with certain electrophiles at the C atom[4, 39, 134], and reductive demasking succeeds only under quite drastic conditions[135].



Scheme 4. Reversible umpolung of primary amines *via* isocyanides.

The derivatives *(14)* suggest themselves for reversible umpolung of *secondary amines*. The following conditions must be



Scheme 5. Conditions for reversible umpolung of secondary amines *via* anions of type *(14)*.

fulfilled (see Scheme 5):

a) X must be readily attached (masking, step 1);

b) X must be removable under mild conditions, *i. e.* replaceable by H (eventual "demasking", step 1');

c) X should neither contain CH acidic groups nor be subject to easy attack by a nucleophile (step 2);

d) X must impart sufficient acidity to the α-amino CH group [step 3, →*(14)*];

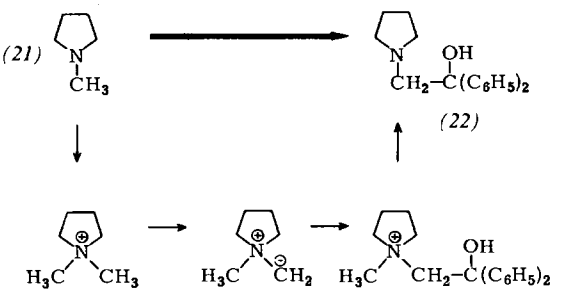
e) *(14)* must be strongly nucleophilic at the $C^{\ominus}$ atom (step 4);

f) *(14)* should not decompose by α- or β-elimination (steps 5 and 6); and

g) *(14)* should not rearrange (steps 7 and 8).

In the course of the last three years we have found only one substituent X which satisfies these requirements: the nitroso group[71, 79–81, 83, 88–90]. Thus we have used it to develop the first practicable method for reversible umpolung of secondary amines. The remaining sections of this progress report are devoted to its detailed description.

No general procedure for reversible α-anionization of *tertiary amines* has yet been developed. Ammonium ylides[46, 47] and amine oxides *(13)*[59, 60] should prove suitable for this purpose, as demonstrated by the—conceptual—conversion of 1-meth-



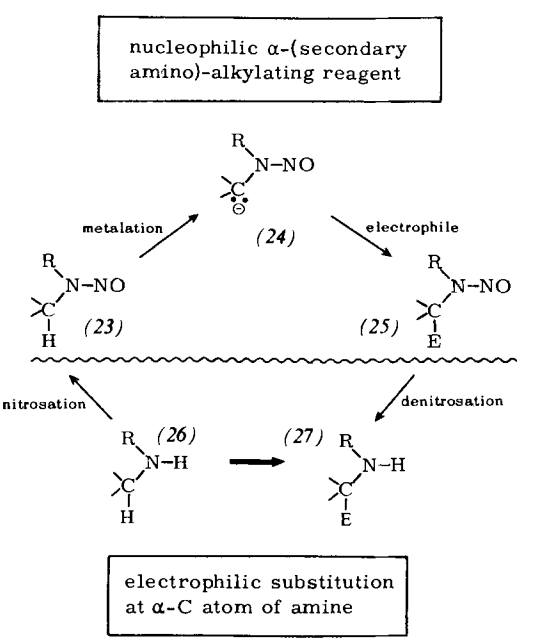
ylpyrrolidine *(21)* into the amino alcohol *(22)*. Of the steps involved, quaternization is trivial, hydroxyalkylation of the ammonium ion with benzophenone *via* the ylide is possible in 52% yield according to *Wittig*[46, 47], and mild and selective methods are nowadays available for removal of the methyl group to give *(22)*[136, 137].

Amines can also be functionalized by free-radical processes[138].

3. Metalated Nitrosamines as Masked Nucleophilic α-(Secondary Amino)alkylating Reagents

3.1. Concept

If it proves possible to convert nitrosamines *(23)* having at least one α-hydrogen atom into metal derivatives of the anion *(24)*, and if *(24)* is stable and sufficiently reactive to give good yields of the substituted nitrosamines *(25)* with



electrophiles, then a secondary amine *(26)* has effectively been subjected to electrophilic substitution at the α-C atom to form *(27)*. Nitrosation of amines, *(26)*→*(23)*, and the denitrosation of nitrosamines, *(25)*→*(27)*, are actually well-

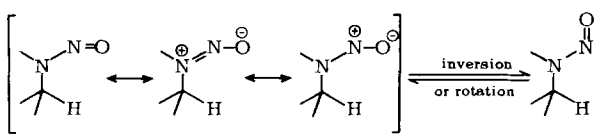
proven methods of organic synthesis. We cannot go into details of these steps here; mention should however be made of the extensive literature on this topic[139-146] and of the fact that we have performed the nitrosations[139, 140] primarily in glacial acetic acid and found either hydrogen chloride in inert solvents (benzene, ether[141]), or Raney nickel[143] in THF, most suitable for removal of the nitroso group[140-146]. In many cases both steps proceed in yields of more than 95%.

The wavy line in the reaction scheme is intended not only to separate the net electrophilic substitution from the individual steps but also to signalize an area of hazard: it is hoped that nitrosamines are generally known to be *carcinogens*. This aspect and the precautions they demand are considered in Section 3.7.

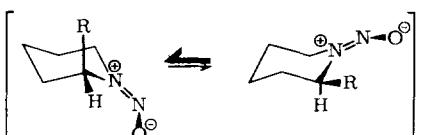
The following sections are devoted to the metalation of nitrosamines, the stability of lithionitrosamines and their reactions with electrophiles, as well as a number of examples of overall reactions *(26)*→*(27)*.

3.2. Metalation of Nitrosamines [Step *(23)*→*(24)*]

On consideration of the three resonance formulas of a nitrosamine *(23a)*↔*(23b)*↔*(23c)*, several analogies with carbonyl compounds become apparent. Besides the "neutral" formula *(23a)*, the dipolar electronic configurations *(23b)* and *(23c)* are very important. This may be deduced form the coplanarity of the nitrosated nitrogen[147], which is compatible with *(23b)*, and from the high ON—N rotational or O—N inversional



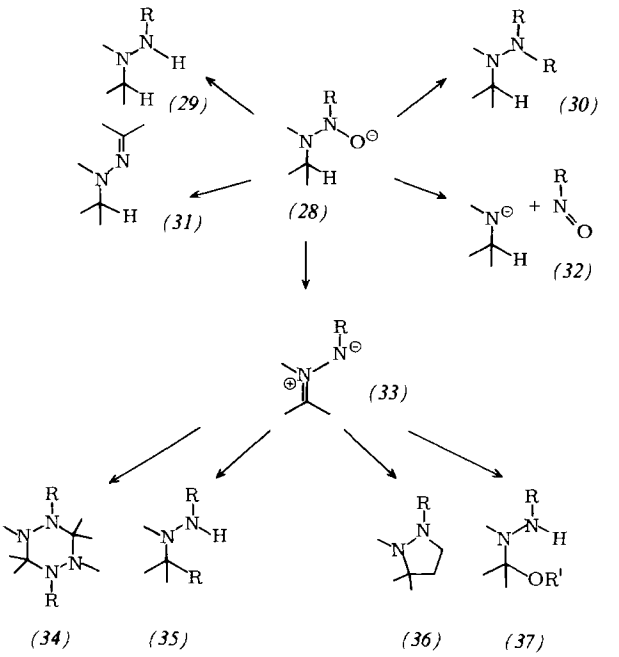
(23a) *(23b)* *(23c)* *(23')*



(23")

barrier *(23)*⇌*(23')*, which amounts to about 23 kcal/mol in dialkylnitrosamines[139, 148-150]. The marked axial preference of the substituent R in 1-nitrosopiperidines *(23")* can also be interpreted in the same way[151-156]. Electron-withdrawing groups or those that can engage in conjugation, such as CF_3 or C_6H_5, considerably lower the N—N rotational barrier when attached to the nitrosated nitrogen[157, 158]. CNDO calculations show the nitroso-N atom to bear a partial positive charge[159]. Hence this atom will be attacked readily by nucleophiles (see also pathway 2 in Scheme 5). Since the H atom adjacent to the positively charged nitrogen can be acidified, as in a carbonyl derivative [cf. *(23b)*], however, each Lewis base reacting with a nitrosamine therefore has a choice of attacking the nitroso nitrogen as a nucleophile or the α-CH group as a base.

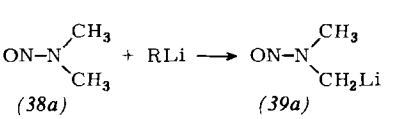
Until recently only the former reaction type was known. The primary adduct *(28)* has an unusually large range of secondary reactions from which to choose. All the products isolated



(29) *(30)* *(31)* *(28)* *(32)* *(33)* *(34)* *(35)* *(36)* *(37)*

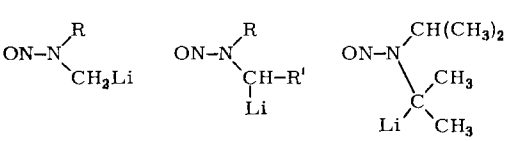
(29)—*(32)* and *(34)*—*(37)* can be explained in terms of *(28)*. Depending upon the nature of the group R and the conditions of reaction and work-up complicated mixtures[71, 79, 160-163] of these products are sometimes formed in reactions with RMgX and RLi (R=alkyl, aryl, R_2N). The hydrazines *(29)* and *(30)* apparently arise from attack of a second mol of $R^{\ominus}$ with loss or replacement of the oxygen[160-162]. Hydrazones *(31)* can result [160, 161] if R contains an α-hydrogen atom. A transnitrosation product *(32)* may be released by β-elimination[71, 79, 161]. Finally an azomethinimine *(33)*[42, 164] may be formed, either in the reaction mixture or during work-up; this species can dimerize to hexahydrotetrazine *(34)*[79, 161], react with a second $R^{\ominus}$ to yield *(35)*[161], be trapped by dipolarophiles to form *(36)*[162] or be "neutralized" on work-up with alcohols, yielding *(37)*[161, 162].

Unequivocal proof of the acidity of nitrosamines *(23)* not bearing an additional acidifying group[74, 165] was probably first established by *Rademacher* and *Lüttke*[75, 77] by base-cata-

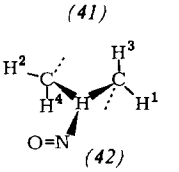


(38a) *(39a)*

R = CH_3	60%
R = n-C_4H_9	45%
R = t-C_4H_9	10%
R = C_6H_5	80%
R = $N[CH(CH_3)_2]_2$	>95%



(39) *(40)* *(41)*

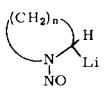
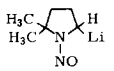
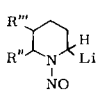
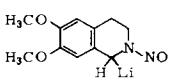
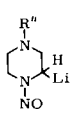
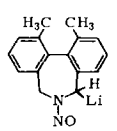


(42)

lyzed perdeuteration of dimethylnitrosamine. In 1970, *Keefer* and *Fodor* succeeded in methylating dimethylnitrosamine *(38a)* with sodium hydride/methyl iodide to give a low yield of ethylmethylnitrosamine. Two years later we reported[79] the quantitative metalation of the same nitrosamine to *(39a)* with lithium diisopropylamide (LDA) in tetrahydrofuran at $-80\,^{\circ}C$ and reactions with various electrophiles. Other metalating agents generally gave poorer yields of *(39a)* owing to competing attack at the nitroso group.

Since metalation of dimethylnitrosamine *(38a)* also succeeds in the presence of excess dimethyl sulfoxide, the pK_a value of *(38a)* must lie below 34[167]. Meanwhile, we have been able to show that other primary, as well as secondary and tertiary, Li derivatives *(39)*, *(40)*, and *(41)* can be produced from nitrosamines and LDA and reacted with a variety of electrophiles (see Sections 3.4 and 3.5). Table 4 reveals the broad scope of metalation of nitrosamines! The examples *(39b)*, *(39c)*, *(39e)*, *(39f)*, and *(40m)* show the acidity to follow the usual series $-CH_3 > -CH_2- > \geqslant CH$. Owing to the enhanced thermodynamic stability of the benzylic Li derivative the series is violated in the case of benzylmethylnitrosamine [*(39g)*, *(40d)*, Table 4].

Table 4. Primary and secondary lithium derivatives *(39)* and *(40)* of nitrosamines [71, 79—81, 83, 88—90] prepared with lithium diisopropylamide (LDA) at $-80\,^{\circ}C$.

Nr.	Li derivative R	R′	Yield [a] [%] of type *(25)*
primary			
(39a)	CH_3		100
(39b)	C_2H_5		90
(39c)	$(CH_3)_2CH$		95
(39d)	$(CH_3)_3C$		100
(39e)	cyclohexyl		95
(39f)	menthyl		90
(39g)	$C_6H_5CH_2$		60 [b]
(39h)	C_6H_5		58 [c]
secondary			
(40a)	C_2H_5	CH_3	90
(40b)	n-C_6H_{13}	n-C_5H_{11}	100
(40c)	$(CH_3)_3C$	$C_6H_5CH_2$	70
(40d)	CH_3	C_6H_5	65 [b]
(40e)	$C_6H_5CH_2$	C_6H_5	99 [78]
(40f)	$(CH_3)_3C$	SCH_3	95
(40g)	$(CH_3)_3C$	$Si(CH_3)_3$	95
(40h)		n = 2	75
(40i)		n = 3	90
(40j)		n = 4	90
(40k)		n = 5	90
(40l) [87]			
(40m)		R″ = n-C_5H_{11}, R‴ = H	70
(40n)		R″ = H, R‴ = OLi	50
(40o)			50
(40p)			60
(40q)		R″ = CH_3	45
(40r)		R″ = C_6H_5	73 [78]
(40s)			98 [78]

[a] The yields given are the highest yet obtained with the Li derivatives *(39)* and *(40)* on reaction with electrophiles (see Tables 5—8). In most cases they have not been optimized.

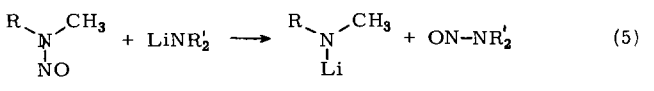
[b] Kinetically controlled metalation (5 min) at CH_3, thermodynamically controlled metalation (> 60 min) at CH_2.

[c] Metalated with cyclohexylisopropylamide at $-110\,^{\circ}C$.

The rate at which the nitrosamines are metalated by LDA at $-80\,^{\circ}C$ is extremely fast: with methylnitrosamines the electrophile can be added a few minutes after the metalating agent; hexamethylphosphoric triamide (HMPA) further accelerates this step, as we were able to show for 1-nitrosopiperidine[88]. According to our experience, its Li derivative *(40j)* is formed the most slowly of all the compounds listed in Table 4; 3—4 h are required. In the presence of four equivalents of HMPA this time can be reduced to 1 h. At the same time HMPA enhances the stability of lithionitrosamines[88] (see Section 3.3).

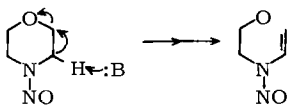
The stereochemistry of nitrosamine deprotonation was established by *Fraser et al.*[78] for the dibenzoazepine derivative *(40s)*: of the four hydrogens present in the precursor, of which two are quasi-axial and two are quasi-equatorial as indicated in *(42)*, the *syn*-axial one, H^4, is preferentially replaced by D on treatment with bases. This is in accord with our findings[88] in the metalation of nitrosopiperidines to yield *(40j)*, *(40m)*, *(40n)*, and *(40o)* (Table 4).

Difficulties arising from the side- and secondary reactions discussed in Scheme 5 occur only in special cases when our metalation procedure is employed. Transnitrosation according to eq. (5) becomes the principal reaction if R has a pronounced anion-stabilizing effect[71], as in nitrosamides and nitrososul-

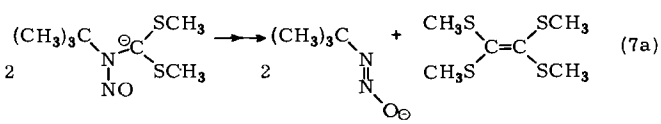


(5)

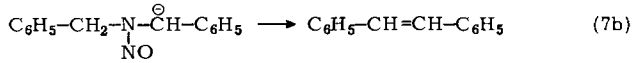
R = Ar, COR, COOR, Tos



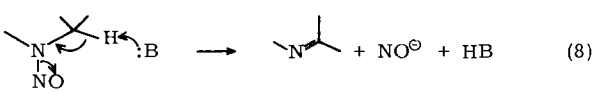
(6)



(7a)



(7b)

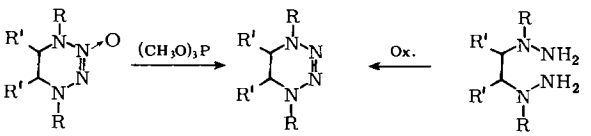


(8)

fonamides; with nitrosomorpholine, elimination according to eq. (6) takes place[71]; and the thioacetal derivative[90] shown in eq. (7a) undergoes α-elimination, which is presumably also responsible for the formation of stilbene from metalated dibenzylnitrosamine [eq. (7b)][89]. So far, in our metalation experiments with dialkylnitrosamines, we have not obtained unequivocal evidence for the $NO^{\ominus}$ elimination, described in eq. (8) and also observed with other bases[74, 165].

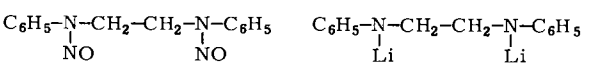
3.3. Dimerization of Lithionitrosamines to Tetrahydro-*v*-tetrazine Derivatives[71, 79, 83, 88, 89]

Even at −80 °C the lithium derivatives *(39)*—*(41)* are only short-lived reagents. Thus the lithiated dimethylnitrosamine *(39a)* decomposes with a half-life of two hours in HMPA-free THF solution (8 h in the presence of four equivalents of the



(43) *(44)* *(45)*

(a), R = CH_3, R' = H [from *(39a)*]
(b), R = Cyclohexyl, R' = H [from *(39e)*]
(c), R-R' = -$(CH_2)_3$- [from *(40i)*]
(d), R-R' = -$(CH_2)_4$- [from *(40j)*]
(e), R-R' = -$(CH_2)_5$- [from *(40k)*]
(f), R-R' = -CH_2-CH_2-N(CH_3)-CH_2- [from *(40q)*]



(46) *(47)*

amide), as we have shown by trapping with benzaldehyde as electrophile. So far we have isolated up to 55% yields of the tetrazine oxide *(43a)* as the sole decomposition product. Other derivatives *(39)* and *(40)* correspondingly afford compounds *(43b)*—*(43f)*. The structure of these novel heterocycles was confirmed by spectroscopy and by reduction to the oxygen-free tetrahydro-*v*-tetrazines *(44)*, which are meanwhile also accessible in low yield, by oxidation of bis-hydrazines *(45)*[168, 169]. After decomposition of lithiated methylphenylnitrosamine *(39h)* (see Table 4) we isolated the dinitroso derivative *(46)* (15%) and secondary products of the dianilide *(47)* (30%). The products *(43)*, *(46)*, and *(47)* are apparently formed by C—C linkage between the formerly anionic C atoms of the lithionitrosamines; *(43a)*—*(43f)* are

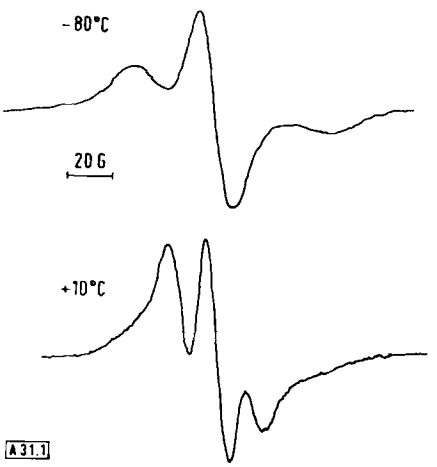
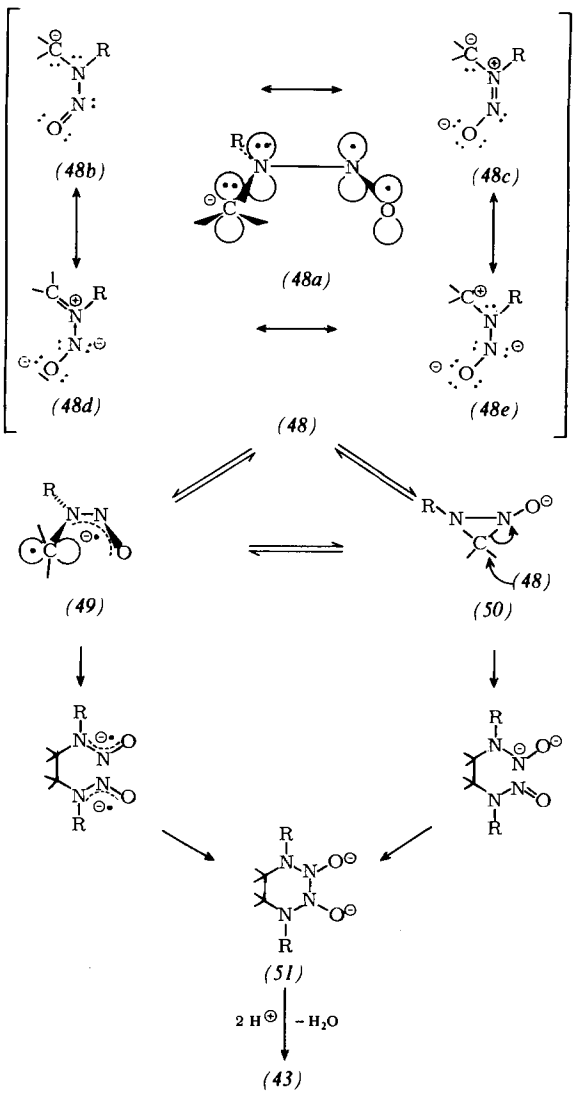


Fig. 1. ESR spectra of a lithiodimethylnitrosamine solution at −80 and +10 °C. The changes occurring on going to the higher temperature are reversible. The metalation mixture (THF/hexane/lithium diisopropylamide) does not give a signal prior to addition of the nitrosamine. Perdeuterated dimethylnitrosamine affords the same spectrum (recorded with a Varian E4 spectrometer).

dimers minus H_2O, *(46)* is a dimer minus H_2 of the original nitrosamines.

Concerning the course of this reaction one can indulge at most in interesting speculations, which are closely related to the important question of the structure of the lithionitrosamines *(39)*—*(41)*. If it is deduced from the stereochemistry of deprotonation [see *(42)*][78] that the resulting anion prefers the planar *cis* form *(48)*, then the π-system *(48a)* occupied by six electrons should be present: this system can be described by four resonance formulas *(48b)*—*(48e)*. Dimerization of *(48)* as a 1,3-dipole should not proceed *via* the head-to-head product *(51)* to the observed tetrazine *(43)*. However, a 90° rotation of the C atom with decoupling of the π-system[170]



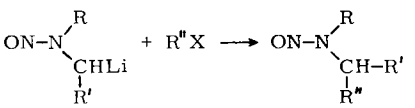
giving *(49)* or a ring closure to *(50)*, for which there is experimental evidence[165], would explain the formation of the tetrazine oxides *(43)*, as may be seen from the flow chart. Nitrosamine radical ions such as are formulated therein are formed very readily by alkali metal reduction[171]. Corroborating evidence for the presence of radicals in solutions of lithionitrosamines comes from ESR spectra of lithiodimethylnitrosamine (Fig. 1). An interpretation of the spectra and a definite mechanistic concept of *v*-triazine formation have not yet been produced.

3.4. Reactions of Lithionitrosamines with Electrophiles [Step (24)→(25)]

It is clear from the foregoing Section that all reactions of nitrosamine lithium derivatives with electrophiles must be carried out at or below −80°C. Only when the reaction of the lithium compounds with the electrophile is faster than their decomposition can good yields of products having the general structure *(25)* be expected. Hence it is hardly surprising that, for instance, epoxides, which are also relatively inert towards other lithium reagents[172], cannot be utilized as electrophiles. In contrast, additions to carbonyl groups proceed exceedingly rapidly (see Section 3.4.2, α-hydroxyalkylations and preparation of aminoethanols) and succeed even at temperatures of about 0°C under conditions of base catalysis (tBuOK)[71,85,88,89] or at even higher temperatures with α-tin-substituted nitrosamines[71] (see Section 3.4.2).

3.4.1. Alkylation

Alkylations of primary and secondary lithionitrosamines *(39)* and *(40)* accomplished so far are summarized in Table 5. The substituted derivatives *(52)* with R′=H [from *(39)*] and R′=alkyl and aryl [from *(40)*] are formed in yields ranging from 60 to 95% and higher. However, the reactions with primary alkyl iodides, especially in the case of the lithiated cyclic nitrosamines *(40i)*, *(40j)*, *(40m)*, *(40n)*, and *(40r)* give yields at the lower limit of this range, while allylation, methoxymethylation, and benzylation proceed almost quantitatively.



(39), R′ = H
(40), R′ ≠ H

(52)

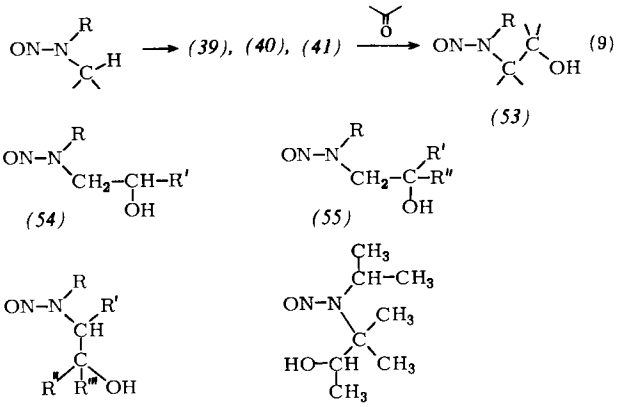
Table 5. Alkylation of lithionitrosamines *(39)* and *(40)* of Table 4 to form the products *(52)* [general type *(25)*].

No.	R″X	Yield [%] of *(52)*	Ref.
(39a)	CH_3I	75	[79]
(39a)	n-C_4H_9I	75	[79]
(39a)	$H_2C{=}CH{-}CH_2Br$	90	[88]
(39a)	$C_6H_5CH_2Br$	>95	[79]
(39c)	$C_6H_5CH_2Br$	95	[80]
(39d)	$C_6H_5CH_2Br$	>95	[71]
(39d)	$CH_3{-}O{-}CH_2Cl$	93	[71]
(40b)	$C_6H_5CH_2Br$	>95	[80]
(40c)	$C_6H_5CH_2Br$	70	[71]
(40e)	CH_3I	91	[78]
(40e)	n-C_3H_7I	85	[78]
(40f)	$C_6H_5CH_2Br$	95	[90]
(40i)	n-C_3H_7I	60	[88]
(40i)	$C_6H_5CH_2Br$	90	[80]
(40j)	n-C_3H_7I	60	[88]
(40j)	n-$C_5H_{11}I$	60	[88]
(40j)	$CH_2{=}CH{-}CH_2Br$	60	[88]
(40j)	$C_6H_5CH_2Br$	60	[80]
(40m)	n-$C_5H_{11}I$	60	[88]
(40p)	$C_6H_5CH_2Br$	60	[89]
(40n)	n-C_3H_7I	40	[88]
(40r)	CH_3I	46	[78]
(40s)	CH_3I	98	[78]

Cyclizations are also possible *via* alkylation with dihaloalkanes and are mentioned in Section 3.5.4.

3.4.2. Reactions with Aldehydes and Ketones (α-Hydroxyalkylation)

There are about 50 examples of this reaction, which corresponds to the aldol addition: it is formulated in general terms in eq. (9). Depending upon the nitrosamine and carbonyl



(53)

(54)

(55)

(56a), R/R′ not linked
(56b), R-R′ cyclic

(57)

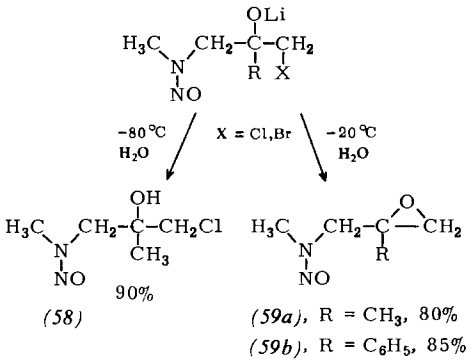
components employed, the structure of the products of type *(53)* can vary within wide limits. The primary and secondary lithionitrosamines *(39)* and *(40)* react with aliphatic and aromatic aldehydes, and with aliphatic, cycloaliphatic, and aromatic ketones to give adducts of types *(54)*, *(55)*, and *(56)* listed in Tables 6 and 7 (Section 3.5.3). The α-branched

Table 6. Reactions of primary and secondary lithionitrosamines *(39)* and *(40)* with aldehydes and ketones involving hydroxyalkylation to the products *(54)*—*(56)* [71, 79, 80, 88—90] (further examples will be found in Table 7, Section 3.5.3). The yields refer to distilled or recrystallized products [general type *(25)*].

No.	Carbonyl derivative	Product type	Yield [%]
(39a)	n-butanal	*(54)*	80
(39a)	benzylaldehyde	*(54)*	>95
(39a)	acetone	*(55)*	70
(39a)	3β-hydroxy-16α,17α-epoxy-5-pregnen-20-one	*(55)*	80 [a]
(39a)	cyclohexanone	*(55)*	95
(39a)	cyclohexenone	*(55)*	85
(39a)	*d,l*-camphor	*(55)*	70
(39a)	(−)-fenchone	*(55)*	80 [b]
(39b)	acetaldehyde	*(54)*	75
(39c)	acetaldehyde	*(54)*	85
(39d)	acetaldehyde	*(54)*	95
(39d)	diphenylacetaldehyde	*(54)*	80
(39d)	3,4-methylenedioxy-benzaldehyde	*(54)*	95
(39d)	acetone	*(55)*	90
(39e)	benzophenone	*(55)*	95
(39g)	acetaldehyde	*(54)*	60 [c]
(39h)	acetaldehyde	*(54)*	60
(40d)	acetaldehyde	*(56a)*	65 [c]
(40e)	benzaldehyde	*(56a)*	62 [78]
(40f)	benzaldehyde	*(56a)*	90
(40f)	cyclohexenone	*(56a)*	80
(40j)	acetaldehyde	*(56b)*	90
(40j)	propionaldehyde	*(56b)*	90
(40j)	benzaldehyde	*(56b)*	70
(40j)	acetone	*(56b)*	78
(40n)	benzophenone	*(56b)*	50
(40n)	acetone	*(56b)*	50
(40o)	benzophenone	*(56b)*	50
(40p)	3,4-dimethoxybenzaldehyde	*(56b)*	60
(40q)	acetaldehyde	*(56b)*	45

[a] Mixture of diastereoisomers exhibiting an unsharp melting point; no evidence for epoxide ring shift from the NMR spectrum.
[b] Optical purity of starting fenchone 82%.
[c] See Table 4, footnote [b].

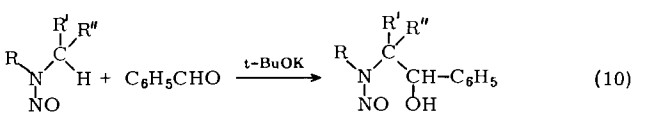
derivatives *(56)* having two chiral centers are obtained as mixtures of diastereomers. Linkage to a methine carbon atom in the nitrosamine moiety leads to the product shown in formula *(57)* [from *(41)* and acetaldehyde]. Enolate formation plays a subordinate role to carbonyl addition, even on reaction with readily enolizable carbonyl compounds like diphenylacetaldehyde, acetone, cyclohexanone, 3β-hydroxy-16α,17α-epoxy-5-pregnen-20-one, and camphor. Carbonyl groups subject to pronounced steric hindrance, such as that of fenchone, react with ease. Halo ketones like chloroacetone and bromoacetophenone are attacked exclusively at the carbonyl; if the initially formed lithium alkoxides are protonated at the reaction temperatures then nitrosaminohalohydrins like *(58)* are obtained. On warming lithium halide elimination occurs, furnishing the epoxynitrosamines *(59)*. Thus the lithionitrosamines can be described as powerful *carbonylophiles* (cf. also acylation, Section 3.4.4).



(58)

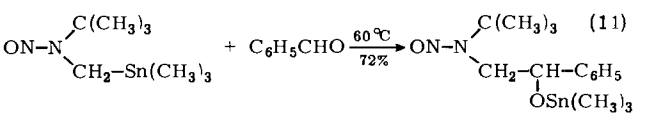
(59a), R = CH_3, 80%
(59b), R = C_6H_5, 85%

Examples[85, 88] of *in-situ* generation of nitrosamine anions and addition to a non-enolizable aldehyde are given in eq. (10). The comparison between nitrosamines and carbonyl compounds already mentioned above (see Section 3.2) comes once



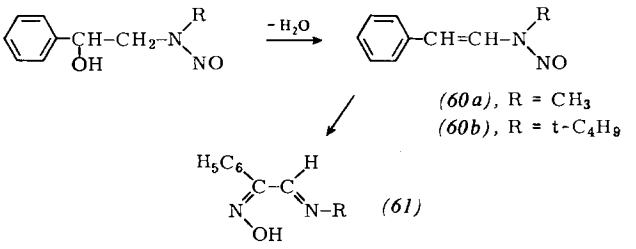
(10)

R = CH_3, R' = R'' = H >95%
R = p-Cl-C_6H_4, R' = R'' = H 69%
R-R' = -$(CH_2)_4$-, R'' = H 80%



(11)

more to mind on consideration of the carbonyl addition [eq. (11)] accomplished by merely mixing the components and warming to 60 °C[71]. This reaction type has long been known in the case of α-silyl[173] and α-stannyl[174] carbonyl derivatives[175]. Use of this modification should permit nucleophilic aminoalkylation [see *(26)* → *(27)* and Section 3.5] of carbonyl derivatives that are sensitive to aggressive organolithium compounds; moreover, the reactivity of aldehydes, ketones, and esters towards α-stannylnitrosamines should vary widely, thus rendering *selective* reaction with polyfunctional molecules possible.

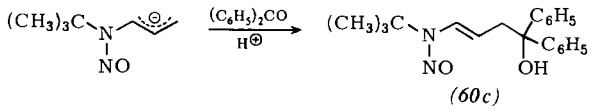


(60a), R = CH_3
(60b), R = t-C_4H_9

(61)

Adducts of type *(54)* with aromatic aldehydes can be dehydrated to the interesting but scarcely known[176, 177] enenitrosamines *(60)*. Compounds *(60a)* and *(60b)*, formed almost quantitatively in the *trans* form, undergo 1,3-nitroso shift to give iminooximes *(61)* on heating, irradiation, or treatment with gaseous hydrogen chloride in benzene[71].

An enenitrosamine *(60c)* is also obtained on reaction of metalated allyl-*tert*-butylnitrosamine with benzophenone. All

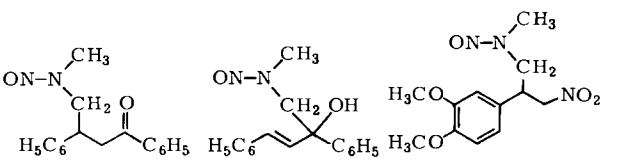


(60c)

other electrophiles we have used so far add to this allyl anion α to the heteroatom[88].

3.4.3. Reaction with α,β-Unsaturated Ketones and with Nitroolefins (Michael Addition)

As can be seen from Table 6, reaction of the lithionitrosamines *(39a)* and *(40f)* with cyclohexenone affords 85 and 80%, respectively, of the 1,2-adduct after hydrolysis[79, 90]. NMR and IR analytical comparison of the starting materials and the crude and pure products rules out the formation of more than traces of the 1,4-adduct. The situation is different with benylideneacetophenone which is even found to yield somewhat more Michael product *(62)* than allyl alcohol *(63)* on reaction with lithiodimethylnitrosamine; the overall yield is almost quantitative. From β-nitro-3,4-dimethoxystyrene and

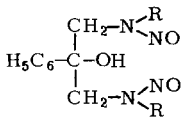


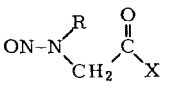
(62), 55% *(63)*, 45% *(64)*

the same nitrosamine we could finally isolate the product *(64)* of conjugated addition in 75% yield[89].

3.4.4. Acylation and Carboxylation (Nitrosated α-Amino Ketones and Amino Acid Derivatives)

The pronounced *carbonylophilic* nature of lithiated nitrosamines can interfere when they are to be acylated with acyl chlorides: 1:1 reaction of benzoyl chloride with lithiodimethylnitrosamine furnished an 80% yield (based on the latter) of the bisadduct *(65a)*[79] [similarly, *(39d)* afforded *(65b)* in 45% yield[71]]. On modification of the reaction conditions

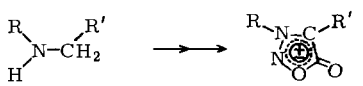




(65a), R = CH_3
(65b), R = t-C_4H_9

(66a), X = OH, R = t-C_4H_9, 80%
(66b), X = OCH_3, R = t-C_4H_9, 95%
(66c), X = NHC_6H_5, R = CH_3, 85%
(66d), X = CH_3, R = CH_3
(66e), X = C_6H_5, R = CH_3
(66f), X = C_6H_5, R = t-C_4H_9
} 40-50%

(initial excess of acyl chloride, reverse addition) and use of other acylating agents (methyl carboxylates, carbon dioxide, phenyl isocyanate, phenyl isothiocaynate), however, moderate to very good yields of α-amino acid or α-amino ketone derivatives *(66)*[71] are obtained. Carboxylation with CO_2 has been described for a further series of nitrosamine anions [*(40e)*[78], *(40i)*[80], *(40r)*[78], and *(40s)*[78]]. Removal of the nitroso group[71, 78], which is also employed as a protecting group in peptide synthesis[178], thus provides an entry to *N*-substituted amino acids. This constitutes a first example of electrophilic substitution at a secondary amine, *(26)*→*(27)*, with E=COOH, and an imitation of the biochemical interconversion of amino acids and primary amines according to Scheme 3 (see also applications, Sections 3.5). Since nitroso amino acid derivatives are readily transformed into sydnones[179, 180], the metalated nitrosamine route provides access to this class of compounds from secondary amines [eq. (12)].

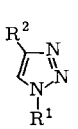


(12)

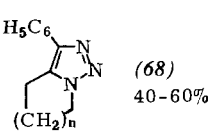
The esters and ketones *(66)* are formally analogs of 1,3-dicarbonyl compounds and should undergo base-catalyzed condensation reactions at the CH_2 group.

3.4.5. *v*-Triazoles by Reaction with Nitriles[71, 81, 89]

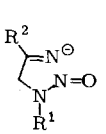
Apart from the carboxylic acid derivatives mentioned in the previous Section, nitriles also represent potential acylating agents. We were unable to react enolizable aliphatic nitriles such as acetonitrile with nitrosamine anions. In contrast, aromatic nitriles afford the *v*-triazoles *(67)* and *(68)* in the yields shown, provided that the metalated nitrosamine is employed



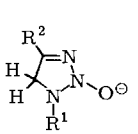
(67a), R^1 = CH_3, R^2 = C_6H_5, 83%
(67b), R^1 = CH_3, R^2 = *p*-CH_3-C_6H_4, 57%
(67c), R^1 = CH_3, R^2 = *p*-Br-C_6H_4, 84%
(67d), R^1 = CH_3, R^2 = β-Naphthyl, 80%
(67e), R^1 = $CH(CH_3)_2$, R^2 = C_6H_5, 90%
(67f), R^1 = $C(CH_3)_3$, R^2 = C_6H_5, 99%



(68)
40-60%
n = 1, 2, 3



(69)

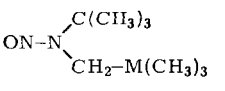


(70)

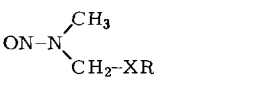
in a twofold excess. A 1:1 reaction furnishes only 35—55% of these heterocycles. By analysis of aliquot samples from the reaction mixtures we were able to show that the nitrile reacts sluggishly. If acetic acid is added at −78 °C after 30 min during the preparation of *(67a)*, 25% of triazole and 6% of the acylation product *(66e)* are isolated along with 65% of unreacted benzonitrile. After prolonged reaction only the decomposition products *(43)* and *v*-triazoles are obtained. Hence the triazoles are probably formed *via (69)* and *(70)*. It is still an open question whether the improved yields obtained from the 2:1 reaction are merely a consequence of competitive decomposition (see Section 3.3) or are due to proton abstraction at the CH_2 group of *(70)* by the excess of lithium derivative. This *v*-triazole synthesis is suitable for the preparation of novel triazoles such as *(68)*.

3.4.6. Reactions with Hetero-Electrophiles[71, 90]

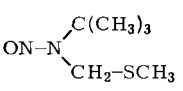
A number of hetero-substituted nitrosamines have already been mentioned [see Table 4: *(40f)*, *(40g)*; Tables 5 and 6: reactions of *(40f)*; eqs. (7) and (11)]. We obtained the derivatives *(71)*—*(73)* in high yields by reaction of the corresponding nitrosamine anions with trimethylchlorosilane, trimethylchlorostannane, disulfides, or diselenides. The sulfoxide *(74)* is accessible quantitatively by metaperiodate oxidation of *(73)*. A use of the tin derivative *(71b)* is shown in eq. (11). The sulfur- and selenium-substituted nitrosamines *(72)*—



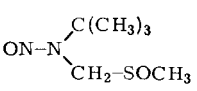
(71a), M = Si, 80%
(71b), M = Sn, > 95%



(72a), RX = SCH_3, 85%
(72b), RX = SC_6H_5, 85%
(72c), RX = SeC_6H_5, 70%



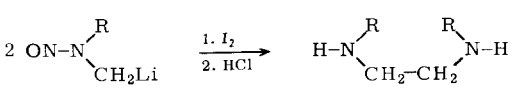
(73), 90%



(74)

(74) may be regarded as *N,S*- and *N,Se*-acetals of formaldehyde. *N,O*-Acetals of this type have recently been prepared by a completely different method[181, 184].

So far we have been unable to isolate α-halo nitrosamines on reaction of metalated nitrosamines with chlorine, bromine, and iodine[71]. Iodine leads to oxidative coupling which can be exploited in the synthesis of ethylene diamines—relevant examples are shown in eq. (13)[71, 79, 89].

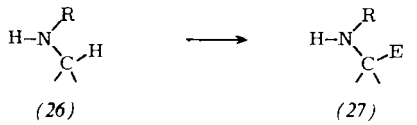


(13)

R = CH_3, 95%
R = t-C_4H_9, 50%

3.5. Applications

The two foregoing Sections (3.3 and 3.4) have demonstrated the feasibility of preparing the nitroso derivatives of higher substituted secondary amines *via* metalated nitrosamines. It has already been mentioned in Section 3.1 that secondary amines and nitrosamines can be readily interconverted. This property opens the way for a simple electrophilic substitution *(26)*→*(27)* [eq. (14)] at the α-C atom of secondary amines.

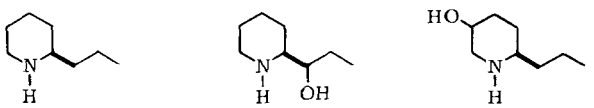


(26) (27) (14)

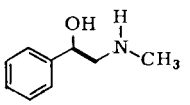
Examples of applications for the synthesis of amino acids and ethylenediamines have already been presented in Section 3.4.4 and in eq. (13).

3.5.1. Denitrosation of Products Listed in Tables 5 and 6 to Yield Simple Alkaloids

Some of the products of alkylation and hydroxyalkylation of lithionitrosamines *(39)* and *(40)* listed in Tables 5 and 6 are nitroso derivatives of simple alkaloids. We have prepared[71,88] the hemlock alkaloids *(75)*[185] and halostahine *(76)*[186] by denitrosation[140-146]. In the formulas, and also



(75a) coniine *(75b)* conhydrine *(75c)* ψ-conhydrine

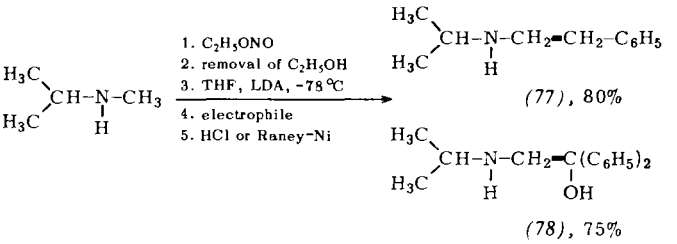


(76) halostahine

in the following discussion, the newly formed C—C bonds are emphasized by bold print. The simplicity of the new method can be demonstrated for compound *(75c)* which we have prepared from the commercially available compounds 3-hydroxypiperidine and *n*-propyl iodide[88] (40% overall yield); synthesis by "classical" methods is far more complicated and less productive[187]. Numerous applications of metalated nitrosamines can be envisaged in the field of alkaloid synthesis (see also Section 3.5.4).

3.5.2. "One-Pot" Substitution According to Equation (14)

Successful application of this method for electrophilic substitution α to the nitrogen of secondary amines requires that the handling of carcinogenic (see Section 3.7) nitrosamines is completely avoided in order to reduce the hazard to a minimum. We have therefore developed a technique by which a secondary amine is weighed into a flask and a substituted secondary amine is isolated on work-up. The method involves preparation of a standard solution of ethyl nitrite in anhydrous tetrahydrofuran, of which an aliquot is added to the amine destined for nitrosation in a flask under an inert gas. Quantitative formation of the nitrosamine is complete within 10—50 h at 20 °C. The co-product ethanol is removed together with solvent under reduced pressure. Dissolution in THF is followed by metalation in the usual manner (Section 3.2; LDA = lithium diisopropylamide), and treatment of the lithium derivative with the electrophile. After warming, the nitrosamine is denitrosated in the reaction mixture, *i.e.* without prior isolation, by gaseous hydrogen chloride or Raney nickel; only then is the product worked up[188]. In this way we have obtained phenethylisopropylamine *(77)* and the amino alcohol *(78)* in high yields from methylisopropylamine and benzyl bromide and benzophenone, respectively.



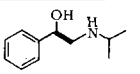
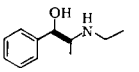
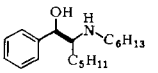
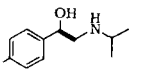
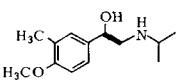
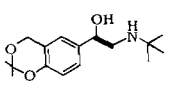
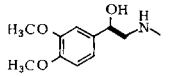
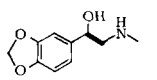
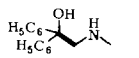
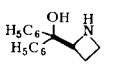
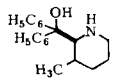
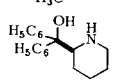
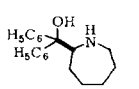
(77), 80%

(78), 75%

3.5.3. 2-Amino-1-arylethanols from Aromatic Carbonyl Compounds and Secondary Amines

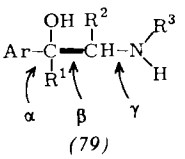
This modification can be employed for preparing numerous 2-amino-1-arylethanols, a class of compounds having an extre-

Table 7. Arylaminoethanols of types *(79)* and *(80)*. The yields given are total yields based on the original amount of carbonyl component and thus include the addition *and* denitrosation steps [71, 88].

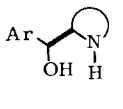
Starting components	Product	Yield [%]	M.p. [°C] [a]
benzaldehyde, isopropylmethyl-nitrosamine		74	
benzyldehyde, diethylnitrosamine		72	162–166 [b]
benzaldehyde, di-*n*-hexylnitrosamine		80	162–164 [b]
p-methylbenzaldehyde, isopropylmethyl-nitrosamine		64	157–159
4-methoxy-3-methyl-benzaldehyde, isopropylmethyl-nitrosamine		65	127–129
acetone acetal of 3-hydroxymethyl-4-hydroxybenzaldehyde, *tert*-butylmethyl-nitrosamine		88	155 [c]
3,4-dimethoxy-benzaldehyde, dimethylnitrosamine		66	118–124
3,4-methylenedioxy-benzaldehyde, dimethylnitrosamine		66	138 [c]
benzophenone, dimethylnitrosamine		70	
benzophenone, 1-nitrosoazetidine		75	195 [c]
benzophenone, 1-nitrosopiperidine		40	84 [d]
benzophenone, 1-nitroso-3-methylpiperidine		35	103 [d]
benzophenone, 1-nitrosoperhydroazepine		77	271 [c]

[a] M.p. of the hydrochloride. [b] Mixture of diastereoisomers.
[c] Decomposition point. [d] M.p. of amine.

mely wide spectrum of pharmacological activity[189]. On preparation of compounds of type *(79)*, the α-bond to the aromatic ring is normally coupled by acylation; some of the acylating agents used already contain the N-function[191,192]; however, in most cases this function is introduced subsequently by linkage of the γ-C—N bond[193-196]. Compounds of type *(79)* can be produced from metalated nitrosamines and aromatic aldehydes and ketones with formation of the β-C—C bond. Some examples and overall yields, based on the carbonyl component used, are listed in Table 7; this procedure is clearly also suitable for preparing cyclic derivatives *(80)* whose production by other methods is invariably more complicated[197,198].

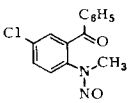
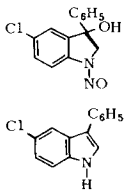
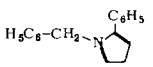
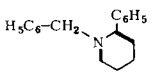
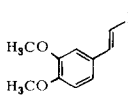
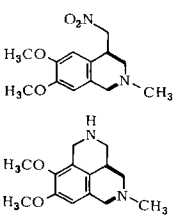
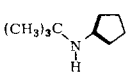


(79)

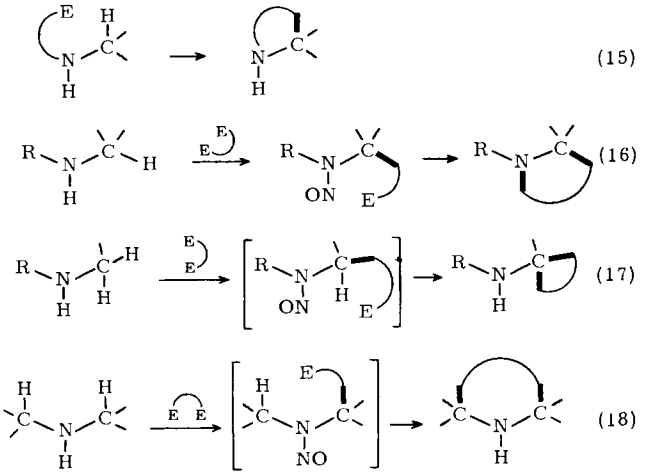


(80)

Table 8. Cyclizations *via* metalated nitrosamines according to the general equations (15)—(18).

Starting material	Eq.	Product(s)	Ref.
	(15)		[85]
dibenzylnitrosamine, 1,3-dibromopropane	(16)		[78]
dibenzylnitrosamine, 1,4-dibromobutane	(16)		[78]
1-nitrosopyrrolidine, 1-brom-3-iodopropane	(16)		[88]
1-nitrosopiperidine, 1-chloro-4-iodobutane	(16)		[88]
dimethylnitrosamine,  [see *(64)*] [a]	(16)		[89]
methyl-*tert*-butylnitrosamine, 1-chloro-4-iodobutane	(17)		[88]
dimethylnitrosamine, 1-bromo-3-iodopropane	(18)		[88]

[a] Denitrozation of *(4)* and Pictet-Spengler reaction with the resulting nitro amine initially afford the bicyclic compound, which is converted into the tricyclic compound by reduction of the nitro group and renewed Pictet-Spengler cyclization (*V. Ehrig* [89]).



(15)

(16)

(17)

(18)

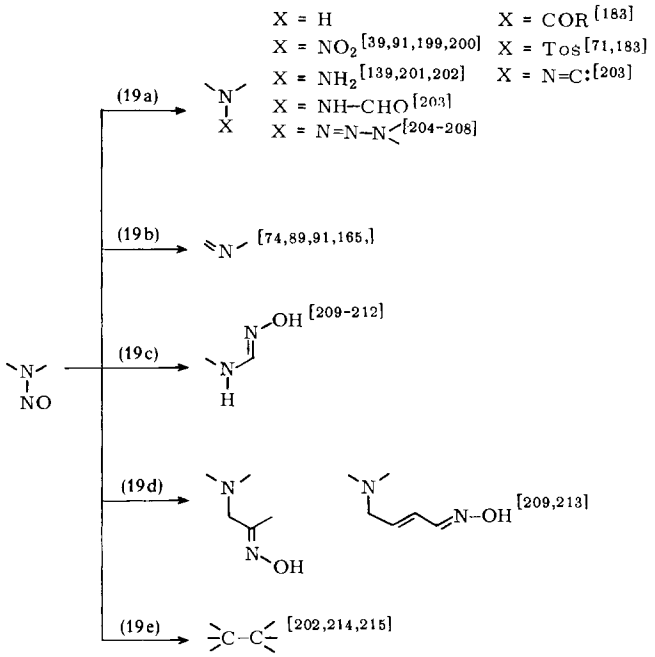
3.5.4. Cyclizations *via* Metalated Nitrosamines

In principle, heterocyclic or nitrogen-substituted carbocyclic compounds should be accessible *via* metalated nitrosamines according to the generalized equations (15)—(18). The boldly printed bonds in the rings are each newly formed. Cyclization as shown in eq. (15) is possible only with electrophilic centers E that survive the metalation conditions applied on removing the CH proton adjacent to the α-nitrogen. The same clearly applies to the cyclization steps in eqs. (17) and (18). Reactions with bifunctional electrophilic compounds according to eqs. (16)—(18) are favored if the two electrophilic centers differ in their reactivity, as for example in the case of 1-chloro-*n*-iodoalkanes or ω-halo aldehydes and ω-halo ketones. In reaction (16) the initial open-chain adduct is denitrosated, whereupon the nitrogen of the secondary amine, which has now become nucleophilic, forms a C—N bond with the electrophilic function in the incorporated side chain and thereby closes the ring.

First examples of the preparation of cyclic compounds with participation of at least one nitrosamine C—C linking step α to the nitrogen are shown in Table 8. The yields, which have not yet been optimized, lie between 30 and 80%.

3.6. Chemistry of Nitrosamines

Not only can nitrosamines be denitrosated to their parent secondary amines [eq. (19a), X=H[139,139-146]]; they also undergo many other reactions. Reactions with bases and nucleophiles have already been mentioned in Section 3.2 [products *(29)*—*(32)* and *(34)*—*(37)*]. Several other conversions of synthetic value[139] are depicted in equations (19a)—(19e). As may be seen from eq. (19a), oxidation leads to nitramines, reduction to hydrazines or their derivatives, replacement of the NO group by COR and RSO_2 gives carboxamides and sulfonamides respectively. Basic elimination of HNO or, after oxidation to the nitramine, of HNO_2 affords azomethines according to eq. (19b); photolysis according to eq. (19c) furnishes hydroximamides; photoaddition to olefins or 1,3-dienes according to eq. (19d) yields amino oximes. Finally, in certain cases it is possible to formally eliminate N_2O as shown in eq. (19e) to give compounds devoid of nitrogen. Thus substitution α to nitrogen in nitrosamines *via* the metal derivatives *(39)*—*(41)* has a preparative significance ranging well beyond the production of amines.

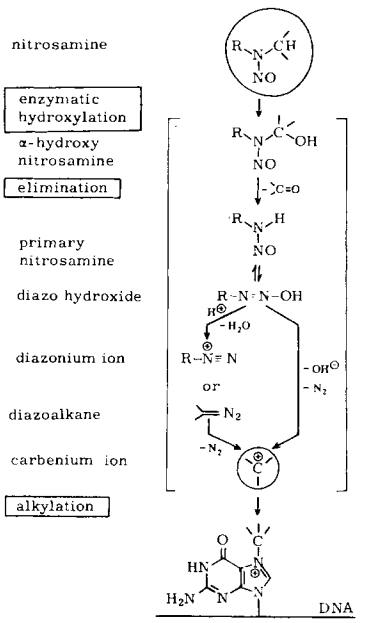


3.7. Carcinogenic and Mutagenic Action of Nitrosamines[216-222]

Most of the nitrosamines tested so far are extremely potent carcinogens and/or mutagens. Their occurrence in the environment[223], *e.g.* in cigarette smoke, in nitrite-preserved meat, and in smoked fish, is well established. Such activity is limited to those nitrosamines which bear at least one hydrogen atom on the carbon situated α to the nitrogen atom. Animal experiments show that, in contrast to other dangerous compounds encountered in everyday laboratory work, nitrosamines have a relatively low toxicity. However, these tests also reveal that in certain cases a single large dose can produce cancer. Tissue changes resulting from a single dose, or on administration over a prolonged period followed by complete cessation, become manifest only after an induction period. In experimental animals having an average life expectancy of about 800 d, the induction period can be as long as several hundred days. Treatment of pregnant animals can lead to their progeny developing carcinomas in later life without ever having been exposed to nitrosamines after birth[224].

Compared with other classes of carcinogens and mutagens, including those of similar activity, nitrosamines are characterized by showing a pronounced organospecific or organotropic effect. Depending upon its structure, a given nitrosamine will give a high "yield" (as the cancer experts say) of carcinoma in a particular organ, irrespective of how it is applied (inhalation, intravenous or subcutaneous injection, oral incorporation, or diffusion through the skin) while even closely proximate tissues remain unaffected. This structure/organ correlation places nitrosamines among the most important reagents of cancer and mutagenesis research. On the one hand they are employed for purely experimental reasons, *i.e.* for the study of morbid changes in a certain type of tissue which can also become cancerous "naturally", this work being important for the development of new methods for early diagnosis and therapy. On the other hand, it is hoped that elucidation of the mechanism underlying the organ specificity of nitrosamines might bring us one step closer to answering the question of how cancer arises. Furthermore, precisely this observed organ specificity suggests that it might be possible to find nitrosamine derivatives which specifically mutate cancerous tissue and thus exert a carcinostatic effect. In fact, nitroso derivatives, especially nitroso-amides, are presently undergoing clinical tests as anti-cancer drugs in several countries.

The currently preferred theory of carcinogenesis and mutagenesis by nitrosamines is outlined in Scheme 6.



Scheme 6. Alkylation theory of carcinogenesis by nitrosamines.

The nitrosamines are assumed to be α-hydroxylated by hydroxylases. The resulting 2-hydroxy nitrosamine decomposes to a carbonyl compound and a diazo hydroxide[225], a precursor of diazo and diazonium derivatives which like all other alkylating agents, even such "everyday" synthetic reagents as methyl iodide and dimethyl sulfate, are carcinogens.

Recent studies on the metabolism of nitrosamines *in vivo* show that the alkyl chains are also subject to ω oxidation yielding alcohols and carboxylic acids, to β-oxidation affording ketones, and to chain shortening[226-229].

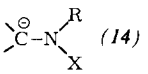
The results of animal experiments cannot be applied *a priori* to humans. After lectures on this topic we have often been approached by older colleagues who enjoy the best of health, although at one time they had worked with large amounts of nitrosamines and nitrosamides without any precautionary measures (for a time low molecular weight nitrosamines were used, *e.g.* as polar solvents on an industrial scale[230]).

What does this mean for the chemist working with nitrosamines? The chemist is accustomed to working with dangerous substances with a minimum of risk, and such work should be part of his training. He must always adapt his techniques to avoid incorporation of chemicals. We cannot even guess how many of the compounds in daily laboratory use might exert dangerous long-term effects. All our work with nitrosamines is performed in a specially reserved fume hood contain-

ing a full complement of equipment and an HBr/glacial acetic acid bath for washing all apparatus[231]. The extractors are fitted with extra-powerful motors. Disposable gloves are worn during all manipulations. Low molecular volatile nitrosamines, which possess only limited synthetic potential, are commercially available and must always be stored in a fume hood[232]. Liquids and solutions are handled with syringes. Whenever possible the "*one-pot*" procedure described above is used (Section 3.5.2).

4. Conclusions

In spite of intense searching, no other acidifying group has yet been found which permits reversible transformation of secondary amines into nucleophilic aminoalkylating agents *via* anions of type *(14)*. It requires little imagination to predict


(14)

that further searching for novel reagents with inverse reactivity will bring in a rich harvest of valuable results and additional knowledge, which might even bring us nearer to the virtuosity of analogous biochemical processes demonstrated in Scheme 3, and show us how to reach our goal in a more intelligent and less brutal way.

Generous support of our work on metalated nitrosamines by the Deutsche Forschungsgemeinschaft (Project SE 158/7), the Fonds der Chemischen Industrie, and the Schunk und Ebe Company, Giessen, is gratefully acknowledged.

Received: July 9, 1974 [A 31 IE]
German version: Angew. Chem. *87*, 1 (1975)

[1] *D. Seebach*, Angew. Chem. *81*, 690 (1969); Angew. Chem. internat. Edit. *8*, 639 (1969).

[2] *E. J. Corey* and *D. Seebach*, Angew. Chem. *77*, 1134, 1135 (1965); Angew. Chem. internat. Edit. *4*, 1075, 1077 (1965); *D. Seebach*, Synthesis *1969*, 17; *D. Seebach, E. J. Corey*, and *A. K. Beck*, Chem. Ber. *107*, 367 (1964).

[3] *D. Seebach* and *M. Kolb*, Chem. Ind. (London) *1974*, 687, and references cited therein.

[4] *J. E. McMurry et al.*, J. Org. Chem. *38*, 4367 (1973); *39*, 258, 259 (1974).

[5] Recent examples: *D. Seebach* and *H. F. Leitz*, Angew. Chem. *81*, 1047 (1969); Angew. Chem. internat. Edit. *8*, 983 (1969); Angew. Chem. *83*, 542 (1971); Angew. Chem. internat. Edit. *10*, 500 (1971); *D. Seebach* and *V. Ehrig*, Angew. Chem. *86*, 446 (1974); Angew. Chem. internat. Edit. *13*, 401 (1974); *D. Seebach et al.*, Chem. Ber. *108* (1975), in press.

[6] See textbooks of organic chemistry: Nitroaldol reactions; Kolbe synthesis of carboxylic acids; cyanohydrin synthesis; amino acid synthesis according to *Strecker*; primary amines from nitriles; aziridines as masked β-amino cations.

[7] *U. Schöllkopf*, Angew. Chem. *82*, 795 (1970); Angew. Chem. internat. Edit. *9*, 763 (1970); Chem. Ber. *106*, 3383 (1973), and previous contributions in this series.

[8] *A. Eschenmoser et al.*, Helv. Chim. Acta *55*, 2187, 2198, 2205 (1972); *56*, 2950, 2961, 2975 (1973). For an example of an E^3 reaction, see [40].

[9] *M. Braun* and *D. Seebach*, Angew. Chem. *86*, 279 (1974); Angew. Chem. internat. Edit. *13*, 277 (1974); *K.-H. Geiss, B. Seuring, R. Pieter*, and *D. Seebach*, Angew. Chem. *86*, 484 (1974); Angew. Chem. internat. Edit. *13*, 479 (1974).

[10] *B. M. Trost*, Fortschr. Chem. Forsch. *41*, 1 (1973); Accounts Chem. Res. *7*, 85 (1974).

[11] *D. A. Evans* and *G. C. Andrews*, Accounts Chem. Res. *7*, 147 (1974).

[12] *D. Seebach, M. Kolb*, and *B.-Th. Gröbel*, Angew. Chem. *85*, 42 (1973); Angew. Chem. internat. Edit. *12*, 69 (1973).

[13] *P. Reichert*: Die Mannich-Reaktion. Springer, Berlin 1960.

[14] *H. Hellmann* and *G. Opitz*: α-Aminoalkylierung. Verlag Chemie, Weinheim 1960.

[15] *M. Tramontini*, Synthesis *1973*, 703.

[16] *H. Viehe* and *Z. Janousek*, Angew. Chem. *85*, 837 (1973); Angew. Chem. internat. Edit. *12*, 806 (1973), and further references cited therein.

[17] *W. M. Whaley* and *T. R. Govindachari*, Org. React. *6*, 74, 151 (1951).

[18] *H. Böhme et al.*, Chem. Ber. *90*, 2003 (1957); *93*, 1305 (1960); *104*, 31, 2018 (1971).

[19] *A. Ahond et al.*, J. Amer. Chem. Soc. *90*, 5622 (1968).

[20] *J. Schreiber, H. Maag, N. Hashimoto*, and *A. Eschenmoser*, Angew. Chem. *83*, 355 (1971); Angew. Chem. internat. Edit. *10*, 330 (1971).

[21] *H. Volz* and *H. H. Kiltz*, Liebigs Ann. Chem. *752*, 86 (1971).

[22] Fluka AG, Chemische Fabrik, CH-9470 Buchs (Switzerland), Catalog No. 40769 (1972).

[23] *J. Marchand-Brynaert* and *L. Ghosez*, J. Amer. Chem. Soc. *94*, 2870 (1972); *L. Ghosez et al.*, Angew. Chem. *86*, 272, 273 (1974); Angew. Chem. internat. Edit. *13*, 267 (1974).

[24] *D. Seebach* and *K.-H. Geiss*, Angew. Chem. *86*, 202 (1974); Angew. Chem. internat. Edit. *13*, 202 (1974), and further references cited therein.

[25] *A. I. Shatenstein et al.*, Tetrahedron Lett. *1966*, 4161.

[26] *D. J. Peterson*, J. Organometal. Chem. *9*, 373 (1967); J. Amer. Chem. Soc. *93*, 4027 (1971); Organometal. Chem. Rev. A *7*, 295 (1972).

[27] *D. J. Peterson* and *J. F. Ward*, J. Organometal. Chem. *66*, 209 (1974).

[28] *A. R. Lepley* and *W. A. Khan*, J. Org. Chem. *31*, 2061 (1966).

[29] See, however: *J. J. Eisch* and *C. A. Kovacs*, J. Organometal. Chem. *30*, C 97 (1971).

[30] *Th. Kauffmann et al.*, Angew. Chem. *82*, 138 (1970); Angew. Chem. internat. Edit. *9*, 163 (1970); Angew. Chem. *84*, 261, 262 (1972); Angew. Chem. internat. Edit. *11*, 290, 291 (1972).

[31] *Th. Cuvigny* and *P. Hullot*, C. R. Acad. Sci. *C 272*, 862 (1971); Bull. Soc. Chim. Fr. *1973*, 2985, 2989.

[32] *T. Durst* and *M. J. Le Belle*, Can. J. Chem. *50*, 3196 (1972); *G. A. Koppel*, Tetrahedron Lett. *1973*, 4233.

[33] *D. H. Hunter* and *S. K. Sim*, Can. J. Chem. *50*, 678 (1972).

[34] *G. Dauphin et al.*, Tetrahedron *28*, 1055 (1972); *R. D. Guthrie* and *J. L. Hedrick*, J. Amer. Chem. Soc. *95*, 2973 (1973).

[35] *P. Karlson*: Kurzes Lehrbuch der Biochemie. Thieme, Stuttgart 1970; *E. Leistner* and *J. D. Spenser*, J. Amer. Chem. Soc. *95*, 4715 (1973), and further literature cited therein.

[36] *D. Hoppe*, Angew. Chem. *84*, 956 (1972); Angew. Chem. internat. Edit. *11*, 933 (1972); Angew. Chem. *85*, 909 (1973); Angew. Chem. internat. Edit. *12*, 923 (1973).

[37] *Th. Kauffmann et al.*, Angew. Chem. *82*, 987 (1970); Angew. Chem. internat. Edit. *9*, 961 (1970).

[38] To our knowledge, not yet examined from this viewpoint.

[39] a) Houben-Weyl: Methoden der Organischen Chemie. 4th Edit. Thieme, Stuttgart 1968, Vol. 10/4, p. 217; b) *H. Feuer*: The Chemistry of the Nitroso and Nitro Groups. Interscience, New York 1969, Vol. I.

[40] *A. Eschenmoser et al.*, Helv. Chim. Acta *41*, 2103 (1958); Chimia *19*, 538 (1965).

[41] *R. Huisgen*, Angew. Chem. *75*, 604, 742 (1963); Angew. Chem. internat. Edit. *2*, 565, 633 (1963).

[42] *C. G. Stuckwisch*, Synthesis *1973*, 469, and further literature cited therein.

[43] *F. Kröhnke*, Angew. Chem. *65*, 609 (1953).

[44] *R. B. Woodward* and *C. E. Wintner*, Tetrahedron Lett. *1969*, 2689.

[45] *R. A. Moss* and *G. M. Love*, Tetrahedron Lett. *1973*, 4701.

[46] *G. Wittig* and *H. Wetterling*, Liebigs Ann. Chem. *557*, 193 (1947).

[47] *G. Wittig* and *W. Tochtermann*, Chem. Ber. *94*, 1692 (1961).

[48] *W. v. E. Doering* and *A. K. Hoffmann*, J. Amer. Chem. Soc. *77*, 521 (1955).

[49] *A. C. Cope* and *A. S. Mehta*, J. Amer. Chem. Soc. *85*, 1949 (1963).

[50] *M. Saunders* and *E. H. Gold*, J. Amer. Chem. Soc. *88*, 3376 (1966).

[51] *V. Rautenstrauch*, Helv. Chim. Acta *55*, 2233 (1972).

[52] *G. Wittig* and *G. Felletschin*, Liebigs Ann. Chem. *555*, 133 (1944); *G. Wittig* and *K. Nagel*, Chem. Ber. *83*, 106 (1950); *S. H. Pine, J. Cheney, B. Catto*, and *J. D. Petersen*, J. Org. Chem. *39*, 130 (1974).

[53] *W. D. Ollis et al.*, Chem. Commun. *1971*, 1493, 1494.

[54] *N. A. Bailey et al.*, Chem. Commun. *1971*, 1429.

[55] *Y. Hata* and *M. Watanabe*, Tetrahedron Lett. *1972*, 3827.

[56] *L. M. Mauder* and *J. V. Turner*, J. Org. Chem. *38*, 2915 (1973).

[57] Reviews: *G. Wittig*, Angew. Chem. *63*, 15 (1951); *A. W. Johnson*: Ylid Chemistry. Academic Press, New York 1966, pp. 251ff.; *W. K. Musker*, Fortschr. Chem. Forsch. *14*, 295 (1970).

[58] *S. H. Pine*, Org. React. *18*, 403 (1970).

[59] *G. Wittig* and *R. Polster*, Liebigs Ann. Chem. *599*, 1 (1956).

[60] Partially successful attempts to metalate amine oxides are currently in progress in our laboratory: *D. Seebach*, *T. Hassel*, and *D. Enders*, to be published.

[61] See also the Polonovski reaction: *H. Volz* and *L. Ruchti*, Liebigs Ann. Chem. *763*, 184 (1972), and further literature cited therein.

[62] *R. E. Ludt* and *C. R. Hauser*, J. Org. Chem. *36*, 1607 (1971); *J. G. Smith* and *R. H. Turle*, *ibid. 37*, 126 (1972).

[63] *H. Ahlbrecht* and *G. Rauchschwalbe*, Synthesis *1973*, 417.

[64] *G. M. Rubottom et al.*, Tetrahedron Lett. *1972*, 3591.

[65] Except in intramolecular processes: *J. C. Sheehan* and *A. K. Bose*, J. Amer. Chem. Soc. *72*, 5158 (1950); *B. G. Chatterjee et al.*, J. Org. Chem. *30*, 4101 (1965); Tetrahedron *23*, 487 (1967); Z. Naturforsch. *24b*, 1120 (1969); *26b*, 771 (1971); cf. also *H. Greuter* and *H. Schmid*, Helv. Chim. Acta *57*, 281 (1974).

[66] *P. Beak* and *R. Farney*, J. Amer. Chem. Soc. *95*, 4771 (1973).

[67] *T. Durst*, *R. Van Den Elzen*, and *M. J. Le Belle*, J. Amer. Chem. Soc. *94*, 9261 (1972); *R. R. Fraser et al.*, Can. J. Chem. *51*, 1109 (1973).

[68] *J. G. Smith* and *G. E. F. Simpson*, Tetrahedron Lett. *1971*, 3295; *1973*, 1947.

[69] *D. W. Bayne*, *G. Tennant*, and *T. M. W. Spence*, J. C. S. Chem. Comm. *1972*, 849.

[70] *F. D. Popp*, Advan. Heterocycl. Chem. *9*, 1 (1968); *A. J. Birch*, *A. H. Jackson*, *P. V. R. Shannon*, and *P. S. P. Varma*, Tetrahedron Lett. *1972*, 4789; *M. Shamma:* The Isoquinoline Alkaloids. Organic Chemistry, Vol. 25. Academic Press, New York 1972, p. 54; *G. Stork et al.*, to be published.

[71] *D. Seebach* and *D. Enders*, hitherto unpublished experiments, 1972–1974; Chem. Ber. *108* (1975), in press; *D. Enders*, Universität Giessen, Diplomarbeit (1972), Dissertation (1974).

[72] *R. G. Micetich*, Can. J. Chem. *48*, 2006 (1970).

[73] *R. R. Fraser*, *G. Boussard*, *I. D. Postescu*, *J. J. Whiting*, and *Y. Y. Wigfield*, Can. J. Chem. *51*, 1109 (1973).

[74] *W. Kirmse* and *L. Horner*, Chem. Ber. *89*, 1674 (1956); *H. U. Daeniker*, Helv. Chim. Acta *47*, 33 (1964).

[75] *P. Rademacher*, Diplomarbeit, Universität Göttingen 1966.

[76] *L. K. Keefer* and *C. H. Fodor*, J. Amer. Chem. Soc. *92*, 5747 (1970).

[77] *P. Rademacher* and *W. Lüttke*, Spectrochim. Acta *27*, 715 (1971).

[78] *R. R. Fraser et al.*, Tetrahedron Lett. *1971*, 2515; Can. J. Chem. *51*, 1109 (1973).

[79] *D. Seebach* and *D. Enders*, Angew. Chem. *84*, 350 (1972); Angew. Chem. internat. Edit. *11*, 301 (1972).

[80] *D. Seebach* and *D. Enders*, Angew. Chem. *84*, 1186 (1972); Angew. Chem. internat. Edit. *11*, 1101 (1972).

[81] *D. Seebach* and *D. Enders*, Angew. Chem. *84*, 1187 (1972); Angew. Chem. internat. Edit. *11*, 1102 (1972).

[82] *M. I. Shevchuk*, *E. M. Volynskaya*, and *A. V. Dombrovskii*, Zh. Obshch. Khim. *41*, 1999 (1971); Chem. Abstr. *76*, 34355d (1972); J. Gen. Chem. USSR *41*, 2019 (1971).

[83] *D. Seebach*, *D. Enders*, *B. Renger*, and *W. Brügel*, Angew. Chem. *85*, 504 (1973); Angew. Chem. internat. Edit. *12*, 495 (1973).

[84] *P. S. Portoghese* and *D. L. Larson*, J. Med. Chem. *16*, 420 (1973).

[85] *A. Walser* and *G. Silverman*, J. Heterocycl. Chem. *10*, 883 (1973).

[86] *P. Thieme*, BASF, Ludwigshafen, unpublished experiments 1973.

[87] *W. T. Comer*, Mead-Johnson Co., Evansville, Indiana (USA), unpublished experiments 1973; we are indebted to Dr. *Comer* for communication of his results.

[88] *D. Seebach* and *B. Renger*, unpublished experiments 1973/74; *B. Renger*, Diplomarbeit, Universität Giessen 1973.

[89] *D. Seebach*, *A. K. Beck*, *R. Dach*, *H. Daum*, *V. Ehrig*, *T. Hassel*, *H. Hartmann*, and *R. Pieter*, unpublished experiments, 1972–1974.

[90] *D. Seebach* and *D. Enders*, J. Med. Chem. *17*, 1225 (1974).

[91] *A. H. Lamberton et al.*, J. Chem. Soc. *1954*, 2391; *1955*, 3997; *1956*, 921; *1961*, 1797.

[92] *P. Savignac* and *Y. Leroux*, J. Organometal. Chem. *57*, C 47 (1973).

[93] *U. Schöllkopf et al.*, Angew. Chem. *79*, 819, 990 (1967); *85*, 861 (1973); Angew. Chem. internat. Edit. *6*, 805, 970 (1967); *12*, 836 (1973).

[94] *E. J. Corey* and *L. S. Hegedus*, J. Amer. Chem. Soc. *91*, 1233, 4926 (1969); *S. Fukuoka et al.*, J. Org. Chem. *36*, 2721 (1971).

[95] *P. Jutzi* and *F. W. Schröder*, Angew. Chem. *83*, 334 (1971); Angew. Chem. internat. Edit. *10*, 339 (1971).

[96] *R. R. Fraser* and *P. R. Hubert*, Can. J. Chem. *52*, 185 (1974).

[97] *D. Enders* and *D. Seebach*, Angew. Chem. *85*, 1104 (1973); Angew. Chem. internat. Edit. *12*, 1014 (1973), and references cited therein.

[98] *W. Lubosch*, Diplomarbeit, Universität Giessen 1974.

[99] *H. M. Walborsky et al.*, J. Amer. Chem. Soc. *91*, 7778 (1969); *92*, 6675 (1970); Tetrahedron Lett. *1971*, 4965.

[100] *N. Koga*, *G. Koga*, and *J. S. Anselme*, Tetrahedron Lett. *1970*, 3309.

[101] *F. Millic*, Chem. Rev. *72*, 101 (1972).

[102] *E. Müller* and *V. Nespital*, Chem.-Ztg. *96*, 529 (1972); *Y. Yamamoto*, *K. Kondo*, and *I. Moritani*, Tetrahedron Lett. *1974*, 793.

[103] *B. A. Tertov et al.*, Khim. Geterotsikl. Soedin. *1969*, 560; *1970*, 1435, 1554; *1971*, 1238; *1972*, 1552; Chem. Abstr. *71*, 124328y (1969); *75*, 5785t (1971); *76*, 34326v (1972); *78*, 58308h (1973); Zh. Org. Khim. *9*, 2207 (1973); Chem. Abstr. *80*, 48065d (1974).

[104] *D. E. Butler* and *S. M. Alexander*, J. Org. Chem. *37*, 215 (1972).

[105] *W. W. Paudler*, *C. I. P. Chao*, and *L. S. Helmick*, J. Heterocycl. Chem. *9*, 1157 (1972).

[106] *Th. Kauffmann et al.*, Angew. Chem. *84*, 828 (1972); Angew. Chem. internat. Edit. *11*, 846 (1972).

[107] *T. Ogawa*, *M. Yasui*, and *M. Matsui*, Agr. Biol. Chem. *36*, 1441 (1972).

[108] *W. Döpke* and *U. Mücke*, Z. Chem. *13*, 104 (1973).

[109] *H. Reimlinger et al.*, Chem. Ber. *104*, 3940, 3965 (1971); *E. M. Burgess* and *J. P. Sanchez*, J. Org. Chem. *39*, 940 (1974).

[110] *H. Gilman* and *J. A. Beel*, J. Amer. Chem. Soc. *71*, 2328 (1949); cf. also [7] and *A. I. Meyers* and *H. W. Adickes*, Tetrahedron Lett. *1969*, 5151.

[111] *P. Jutzi* and *H.-J. Hoffmann*, Chem. Ber. *106*, 594 (1973).

[112] *D. W. Adamson* and *J. W. Billinghurst*, J. Chem. Soc. *1950*, 1039.

[113] *W. Flitsch* and *E. Gerstmann*, Chem. Ber. *102*, 1309 (1969).

[114] *F. Marsais et al.*, C. R. Acad. Sci. *C 275*, 1535 (1972).

[115] *S. Hünig et al.*, Chem. Ber. *99*, 2017 (1966); *102*, 3176 (1969).

[116] *J. A. Zoltewicz*, *C. L. Smith*, and *G. M. Kauffmann*, J. Heterocycl. Chem. *8*, 337 (1971).

[117] Ylides of other heterocycles: *R. A. Olofson*, *W. R. Thompson*, and *J. S. Michelman*, J. Amer. Chem. Soc. *86*, 1865 (1964); *R. B. Woodward* and *D. J. Woodman*, J. Amer. Chem. Soc. *88*, 3169 (1966).

[118] *A. Todd et al.*, J. Chem. Soc. *1959*, 2116.

[119] *R. A. Abramovitch et al.*, J. Amer. Chem. Soc. *89*, 1537 (1967); J. Org. Chem. *37*, 1690, 3584 (1972); J. Heterocycl. Chem. *9*, 1367 (1972).

[120] *J. A. Zoltewicz* and *G. M. Kauffmann*, Tetrahedron Lett. *1967*, 337; *J. A. Zoltewicz* and *L. S. Helmick*, J. Amer. Chem. Soc. *92*, 7547 (1970).

[121] *S. A. Krueger* and *W. W. Pandler*, J. Org. Chem. *37*, 4188 (1972).

[122] *B. Beutler*, *B. Zeeh*, and *E. Müller*, Chem. Ber. *102*, 2636 (1969).

[123] *U. Schöllkopf* and *H. Frasnelli*, Angew. Chem. *82*, 290 (1970); Angew. Chem. internat. Edit. *9*, 301 (1970).

[124] *O. J. Scherer* and *M. Schmidt*, Z. Naturforsch. *20b*, 1009 (1965); *D. Seyferth* and *T. C. Flood*, J. Organometal. Chem. *29*, C 25 (1971).

[125] Not yet detected with certainty. Cf. *W. M. Jones* and *C. D. Broaddus*, J. Org. Chem. *26*, 2316 (1961).

[126] *D. E. Pearson* and *C. A. Buehler*, Chem. Rev. *74*, 45 (1974).

[127] *K. Rühlmann et al.*, Angew. Chem. *80*, 797 (1968); Angew. Chem. internat. Edit. *7*, 809 (1968); Z. Chem. *10*, 392, 393 (1970).

[128] *G. Maahs* and *P. Hegenberg*, Angew. Chem. *78*, 927 (1966); Angew. Chem. internat. Edit. *5*, 888 (1966).

[129] *W. Ried* and *D. P. Schäfer*, Chem. Ber. *102*, 4193 (1969).

[130] *G. Rosseels et al.*, Synthesis *1970*, 302.

[131] *E. J. Corey* and *D. E. Cane*, J. Org. Chem. *35*, 3405 (1970).

[132] Many practicable methods have been collected in an excellent book (see

$$C{-}X \rightarrow C{-}CH_2{-}N\lessdot, \text{ and } \gtrdot C{=}O \rightarrow \gtrdot C(OH){-}CH_2{-}N\lessdot):$$

J. Mathieu and *J. Weill-Raynal:* Formation of C–C-Bonds. Thieme, Stuttgart 1973, Vol. 1.

[133] Readily feasible only with tertiary amines. *N. Kornblum*, Org. React. *12*, 101 (1962); Org. Synth. *43*, 87 (1963).

[134] See also: *M. Stiles* and *H. L. Finkenbeiner*, J. Amer. Chem. Soc. *81*, 505 (1959); *N. Kornblum et al.*, *ibid. 92*, 5783, 5784 (1970); *93*, 4316 (1971).

[135] This does not detract from the utility of nitroalkanes and nitroolefins for simple umpolung as mentioned in the introduction.

[136] *T.-S. Ho*, Synthesis *1972*, 702 and further references cited therein.

[137] *R. O. Hutchins* and *F. J. Dux*, J. Org. Chem. *38*, 1961 (1973).

[138] See, *e.g.*, *J. K. Kochi:* Free Radicals. Wiley, New York 1973, Vol. I and II.

[139] Recent review of nitrosamines: *A. L. Fridman*, *F. M. Mukhametshin*, and *S. S. Novikov*, Russ. Chem. Rev. *40*, 34 (1971).

[140] Nitrosation of secondary amines and denitrosation: Houben-Weyl: Methoden der Organischen Chemie. 4th Edit., Thieme, Stuttgart 1958, Vol. 11/2, pp. 178—181; Vol. 11/1, pp. 957—959.

[141] Examples of denitrosation with gaseous HCl in benzene: *P. Quitt, R. O. Studer*, and *K. Vogler*, Helv. Chim. Acta *47*, 166 (1964); *F. H. C. Stewart*, Austr. J. Chem. *22*, 2451 (1969); *K.-F. Hebenbrock* and *K. Eiter*, Liebigs Ann. Chem. *765*, 78 (1972).

[142] Denitrosation with HBr/HOAc: *R. Preussmann* and *G. Eisenbrand*, Arzneim.-Forsch. *20*, 1513 (1970).

[143] Examples of denitrosation Raney nickel: *E. Lorz* and *R. Baltzly*, J. Amer. Chem. Soc. *73*, 93 (1951); *M. Harfenist* and *E. Magnieu, ibid. 79*, 2215 (1957).

[144] Denitrosation with transition metal carbonyl compounds: *H. Alper* and *J. T. Edward*, Can. J. Chem. *48*, 1543 (1970); *H. Alper*, Organometal. Chem. Synth. *1*, 69 (1970/71); *A. Tanaka* and *J.-P. Anselme*, Tetrahedron Lett. *1971*, 3567.

[145] Photochemical denitrosation: *Y. L. Chow*, Accounts Chem. Res. *6*, 354 (1973); see also *R. Preussmann* and *D. Daiber*, Z. Anal. Chem. *206*, 344 (1964).

[146] Electrochemical denitrosation: *H. Lund*, Acta Chem. Scand. *11*, 990 (1957).

[147] *W. Costain* and *E. G. Cox*, Nature *160*, 826 (1947); *P. Rademacher, R. Stølevik*, and *W. Lüttke*, Angew. Chem. *80*, 842 (1968); Angew. Chem. internat. Edit. *7*, 806 (1968).

[148] *G. J. Karabatsos* and *R. A. Taller*, J. Amer. Chem. Soc. *86*, 4373 (1964).

[149] *H. W. Brown* and *D. P. Hollis*, J. Mol. Spectrosc. *13*, 305 (1964).

[150] *J. T. D'Agostino* and *H. H. Jaffé*, J. Amer. Chem. Soc. *92*, 5160 (1970).

[151] *R. K. Harris* and *R. A. Spragg*, J. Mol. Spectrosc. *23*, 158 (1967).

[152] *Y. L. Chow, C. L. Colón*, and *J. N. S. Tam*, Can. J. Chem. *46*, 2821 (1968).

[153] *H. Paulsen, K. Todt*, and *H. Ripperger*, Chem. Ber. *101*, 3365 (1968).

[154] *H. C. Beyerman, S. van den Bosch, J. H. Breuker*, and *L. Maat*, Rec. Trav. Chim. Pays-Bas *90*, 755 (1971).

[155] *L. Keefer, W. Lijinsky*, and *W. Gaffield*, Tetrahedron Lett. *1972*, 779.

[156] *L. Maat* and *H. C. Beyerman*, Rec. Trav. Chim. Pays-Bas *92*, 156 (1973).

[157] *C. E. Looney, W. D. Phillips*, and *E. L. Reilly*, J. Amer. Chem. Soc. *79*, 6136 (1957).

[158] *S. Andreades*, J. Org. Chem. *27*, 4163 (1962).

[159] *C. Nagata* and *A. Imamura*, Gann *61*, 169 (1970).

[160] *H. Wieland et al.*, Ber. Deut. Chem. Ges. *44*, 898 (1911); *48*, 1112, 1117 (1915).

[161] *P. R. Farina*, Dissertation, University of New York, Buffalo 1970; Tetrahedron Lett. *1970*, 4971.

[162] *P. R. Farina* and *H. Tieckelmann*, J. Org. Chem. *38*, 4259 (1973).

[163] *C. J. Michejda* and *R. W. Schluenz*, J. Org. Chem. *38*, 2412 (1973).

[164] This dipole *(33)*, R = OAlkyl, is likewise readily formed from alkoxydiazenium salts: *S. Hünig*, Rev. Chim. (Bukarest) *7*, 935 (1962); Chem. Ber. *102*, 2093, 2109, 2889, 3159, 3176 (1969); *104*, 1088, 1104, 1118 (1971).

[165] *D. H. R. Barton et al.*, J. Chem. Soc. *C 1971*, 2184.

[166] See also *W. Lijinsky, L. Keefer*, and *J. Loo*, Tetrahedron *26*, 5137 (1970).

[167] *H. F. Ebel:* Die Acidität der CH-Säuren. Thieme, Stuttgart 1969.

[168] *S. F. Nelson* and *R. Fibiger*, J. Amer. Chem. Soc. *94*, 8497 (1972).

[169] *R. Kreher* and *H. Wissmann*, Chem. Ber. *106*, 3097 (1973).

[170] According to calculations by *R. Gleiter*, Darmstadt, the most stable arrangement of the dimethylnitrosamine anion is the planar form shown in *(48)*. We are grateful to Professor *Gleiter* for his interest in this problem and for communication of his results.

[171] *G. R. Stevenson* and *C. J. Colón*, J. Phys. Chem. *75*, 2704 (1971).

[172] *D. Seebach, E. J. Corey*, and *A. K. Beck*, Chem. Ber. *107*, 367 (1974), footnote [14].

[173] *L. Birkofer, A. Ritter*, and *H. Wieden*, Chem. Ber. *95*, 971 (1962); *P. L. Creger*, Tetrahedron Lett. *1972*, 79.

[174] *J. G. Noltes, F. Verbeek*, and *H. M. J. C. Creemers*, Organometal. Chem. Synth. *1*, 57 (1970/71); *Y. Odic* and *M. Pereyre*, J. Organometal. Chem. *55*, 273 (1973).

[175] Use of boronenolates for this purpose: *T. Mukaiyama, K. Inomata*, and *M. Muraki*, J. Amer. Chem. Soc. *95*, 967 (1973).

[176] *N. N. Ogimachi* and *H. Kruse*, J. Org. Chem. *26*, 1642 (1961).

[177] *R. Preussmann*, Dissertation, Universität Freiburg 1966; Chem. Ber. *95*, 1571 (1962).

[178] *P. Quitt, R. O. Studer*, and *K. Vogler*, Helv. Chim. Acta *47*, 166 (1964).

[179] *W. Baker* and *W. D. Ollis*, Quart. Rev. Chem. Soc. *11*, 15 (1957).

[180] *F. H. C. Stewart*, Chem. Rev. *64*, 129 (1964).

[181] *Th. Curtius* and *R. Jay*, Ber. Deut. Chem. Ges. *23*, 744 (1890).

[182] *R. Kotani et al.*, Tetrahedron *25*, 4743 (1969).

[183] *K. Eiter, K.-F. Hebenbrock*, and *H.-J. Kabbe*, Liebigs Ann. Chem. *765*, 55, 78 (1972).

[184] *D. Swern et al.*, Tetrahedron Lett. *1973*, 2671.

[185] Review: *E. Leete*, Accounts Chem. Res. *4*, 100 (1971).

[186] *G. P. Men'shikov* and *G. M. Borodina*, J. Gen. Chem. USSR *17*, 1569 (1947); Chem. Abstr. *42*, 2245a (1948); and literature cited therein.

[187] *E. Brown, J. Lavone*, and *R. Dhal*, Tetrahedron *29*, 455 (1973).

[188] Very sensitive tests are available for the detection of nitrosamines [*F. Feigl, V. Anger*, and *O. Frehden*, Mikrochemie *15*, 181, 183 (1934); *F. Feigl:* Spot Tests in Organic Analysis. Elsevier, New York 1956; *H. P. Nagasawa* and *P. S. Fraser*, J. Med. Chem. *16*, 583 (1973)], enabling the chemist to convince himself of the absence of nitrosamines in the reaction and to dispel all fear before work up.

[189] See, for example, reviews on catecholamines: *H. Blaschko* and *E. Muscholl:* Handbuch der Experimentellen Pharmakologie, Vol. 33: Catecholamine. Springer, Berlin 1972, and the special issue on catecholamines of the Brit. Med. Bull. *29*, 91 (1973).

[190] Exception: Ar—COCl + $CN^{\ominus}$ → Ar—CO—CN → reduction; see, *e.g., A. M. Z. Kazi, J. R. Merchant*, and *J. R. Patell*, J. Indian Chem. Soc. *49*, 397 (1972).

[191] From aryllithium and oxalylamides, *e.g.: C. Temple, J. D. Rose*, and *J. A. Montgomery*, J. Pharm. Sci. *61*, 1297 (1972); *E. Campaigne, G. Showronski*, and *R. B. Rogers*, Synth. Commun. *3*, 325 (1973).

[192] With aminoacetonitriles as acylating agents, *e.g.: J. van Dijk* and *H. D. Moed*, Rec. Trav. Chim. Pays-Bas *92*, 1281 (1973).

[193] By substitution on the α-halo ketone, *e.g.: S. D. Brown, J. E. Hodgkins*, and *M. G. Reinecke*, J. Org. Chem. *37*, 773 (1972); *K. Wetterlin*, J. Med. Chem. *15*, 1182 (1972); *P. Pratesi, F. Grana*, and *L. Villa*, Farm. Ed. Sci. *28*, 753 (1973); *D. Ehlers, H. Bercher*, and *A. Grisk*, J. Prakt. Chem. *315*, 1169 (1973).

[194] Regarding ring opening of epoxides with amines, see, *e.g.: W. S. Emerson*, J. Amer. Chem. Soc. *67*, 516 (1945).

[195] By oximation of the aryl ketone, see, *e.g.*, [190].

[196] Regarding aziridines, see, *e.g.: K. N. Campbell, B. Knapp-Campbell*, and *E. P. Chaput*, J. Org. Chem. *8*, 99 (1943).

[197] Concerning the use of 2-lithiopyridines, which are likewise masked α-aminoalkylating agents since the products can be reduced to piperidines, see, *e.g., K. Schreiber* and *G. Adam*, Liebigs Ann. Chem. *666*, 176 (1963).

[198] Examples of the preparation of cyclic aminoethanols *via* intramolecular ring opening of an epoxide by an amino group are given by *E. J. Corey et al.*, J. Amer. Chem. Soc. *92*, 2476, 2488 (1970); *J. W. Huffman* and *S. N. Singh*, J. Heterocycl. Chem. *10*, 463 (1973).

[199] *A. H. Lamberton*, Quart. Rev. Chem. Soc. *5*, 75 (1951).

[200] *W. D. Emmons*, J. Amer. Chem. Soc. *76*, 3468 (1954).

[201] *P. A. S. Smith:* Open Chain Nitrogen Compounds. Benjamin, New York 1965, 1966, Vol. 1 and Vol. 2 (Chap. 15).

[202] *C. G. Overberger, J. P. Anselme*, and *J. G. Lombardino:* Organic Compounds with N—N-Bonds. Ronald Press, New York 1966.

[203] *H. Bredereck, B. Föhlisch*, and *K. Walz*, Liebigs Ann. Chem. *686*, 92 (1965).

[204] *E. Fischer*, Liebigs Ann. Chem. *190*, 67 (1878).

[205] *H. Wieland* and *H. Fressel*, Liebigs Ann. Chem. *392*, 133 (1912); see also *H. Wieland:* Die Hydrazine. Enke, Stuttgart 1913.

[206] *L. Knorr*, Liebigs Ann. Chem. *221*, 297 (1883).

[207] *L. Knorr* and *H. W. Brownsdon*, Ber. Deut. Chem. Ges. *35*, 4474 (1902).

[208] *F. Effenberger* and *P. Fischer*, Tetrahedron *26*, 3029 (1970).

[209] Review of the photochemistry of nitrosamines: *Y. L. Chow*, Accounts Chem. Res. *6*, 354 (1973).

[210] *E. Burgess* and *J. L. Lavanish*, Tetrahedron Lett. *1964*, 1221.

[211] *Y. L. Chow*, Tetrahedron Lett. *1964*, 2333.

[212] *Y. L. Chow*, Can. J. Chem. *45*, 53 (1967).

[213] *Y. L. Chow et al.*, Can. J. Chem. *43*, 2711 (1965); *45*, 2559 (1967); *48*, 1664 (1970); *50*, 1065 (1972).

[214] *C. G. Overberger, M. Valentine*, and *J. P. Anselme*, J. Amer. Chem. Soc. *91*, 687 (1969).

[215] *R. W. Gleason* and *J. F. Paulin*, J. C. S. Chem. Comm. *1973*, 98.

[216] *P. N. Magee* and *J. M. Barnes*, Brit. J. Cancer *10*, 114 (1956).

[217] *R. Preussmann*, Dissertation, Universität Freiburg 1966.

[218] *H. Druckrey, R. Preussmann, S. Ivankovic*, and *D. Schmähl*, Z. Krebsforsch. *69*, 103 (1967).

[219] *P. N. Magee* and *J. M. Barnes*, Advan. Cancer Res. *10*, 163 (1967).

[220] *H. Druckrey, R. Preussmann,* and *S. Ivankovic,* Ann. N. Y. Acad. Sci. *163,* 676 (1969).

[221] See also ref. [39b].

[222] *N. P. Sen:* Toxic Constituents of Animal Foodstuffs. Academic Press, New York 1974, Vol. 5, p. 131.

[223] *K. Heyns:* Getreide, Mehl, Brot *27,* 249 (1973).

[224] *H. Druckrey:* Transplacental Carcinogenesis. International Agency for Research on Cancer, Lyon 1973, p. 45, and further literature cited therein.

[225] If oxygen is passed into solutions of lithionitrosamines at low temperature, or if peroxides [di-*tert*-butyl peroxide, bis(trimethylsilyl) peroxide] are added, then vigorous evolution of gas rapidly sets in on warming or on attempted evaporation. The structure of the decomposition products, which we are currently examining, should reveal whether the α-hydroxy nitrosamine derivatives postulated in Scheme 6 are actually formed.

[226] *M. Okada et al.,* Gann *63,* 391, 637 (1972); *65,* 13, 69 (1974).

[227] *L. Blattmann* and *R. Preussmann,* Z. Krebsforsch. *79,* 3 (1973).

[228] *F. W. Krüger et al.,* Z. Krebsforsch. *76,* 147 (1971); *79,* 90 (1973); *80,* 189 (1973).

[229] *R. Schoental,* Brit. J. Cancer *28,* 436 (1973), further references cited therein.

[230] *D. Daiber,* Med. Dissertation, Universität Freiburg 1966.

[231] *G. Eisenbrand* and *R. Preussmann,* Arzneim.-Forsch. *20,* 1513 (1970).

[232] The maximum working place concentrations of dimethylnitrosamines have been set at zero in the USA: Chem. Eng. News *51,* No. 2, p. 4 (1973).

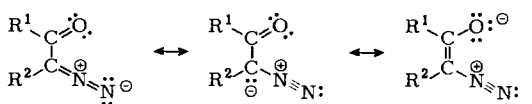
The Wolff Rearrangement of α-Diazo Carbonyl Compounds

By Herbert Meier and Klaus-Peter Zeller[*]

The readily accessible α-diazo carbonyl compounds are distinguished by their high reactivity, which opens up a variety of preparative applications under modified conditions. Wolff rearrangements of these compounds, induced thermally, photochemically, or catalytically, afford ketenes. Free and complexed carbenes, 1,3-dipoles, 1,3-diradicals, and the antiaromatic oxirenes have been considered as intermediates or transition states. The present progress report attempts to integrate preparative and theoretical aspects.

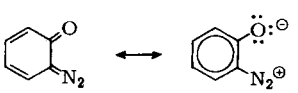
1. Introduction

α-Diazo carbonyl compounds *(1)* contain the CO—CN_2 group, which is capable of resonance, as characteristic structural unit.



(1)

The C—C bond can be part of a carbon chain or of a cyclic system. If it belongs to an aromatic ring then an inner diazonium phenoxide ("*o*-quinone diazide") *(2)* is present.

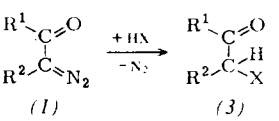


(2)

Key positions in the attached groups may also be occupied by heteroatoms. In this context, the α-diazo carboxylic acid derivatives *(1)*, R^1 = OR, NH_2, NHR, NR_2, *etc.*, warrant special attention.

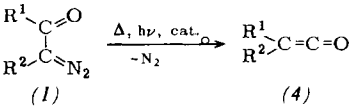
Apart from the CO stretching vibration, a simple analytical feature of the open-chain α-diazo carbonyl structure is the diazo band lying between 2090 and 2190 cm^{-1} (usually at 2130 cm^{-1}) in the IR spectrum. Mutual interaction between the diazo and the carbonyl group lowers the CO frequency and raises the N_2 frequency.

α-Diazo carbonyl compounds are particularly reactive substances. Reactions involving loss of the N_2 group are generally induced thermally, photochemically, catalytically, or by (Lewis) acids. Whereas the decomposition by acids is applic-



(1) *(3)*

able to all diazoalkanes, in the other three processes one observes a rearrangement that is specific for α-diazo carbonyl compounds and is known after its discoverer as the Wolff



(1) *(4)*

rearrangement[1, 2]. The preparative value of the Wolff rearrangement is due to the ready accessibility of the α-diazo carbonyl compounds[3] and to the wide range of reactions of the resulting ketenes *(4)*.

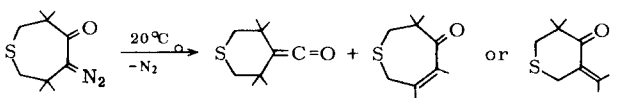
[*] Univ.-Doz. Dr. H. Meier and Dr. K. P. Zeller [**]
74 Tübingen 1, Auf der Morgenstelle (Germany)

[**] European Science Exchange Program Fellow.

2. Methods of Conducting the Reaction

2.1. Thermolysis

Thermal energy can induce α-diazo carbonyl compounds to lose nitrogen and undergo Wolff rearrangement. The decomposition temperatures range between room temperature and 750 °C in gas phase pyrolysis[4]. Although generally greater than that of common diazoalkanes, the thermal stability of α-diazo carbonyl compounds can be reduced by electronic effects[5, 6] and even more effectively by steric effects[7]. Thus the diazo ketone *(5)*, whose —CO—CN_2— is twisted owing to ring strain, decomposes on formation at room temperature[7].

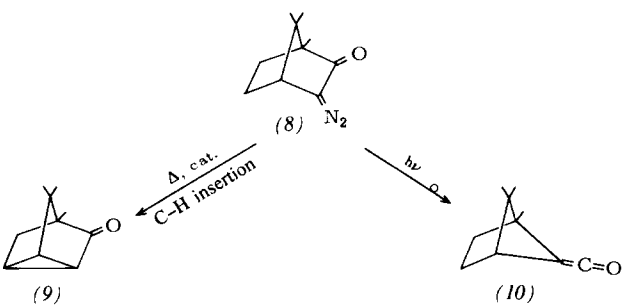


(5) *(6)* 49% *(7)*

The tendency to undergo Wolff rearrangement often shows a marked initial increase at the expense of other competing reactions as the thermolysis temperature is raised. Reaction in boiling aniline or boiling benzyl alcohol with addition of tertiary bases such as collidine, isoquinoline, or *N*,*N*-dimethylaniline has become a proven preparative method.

2.2. Photolysis

The photochemical variant of the Wolff rearrangement discovered by *Horner*[8] is frequently superior to other methods. It also succeeds when the thermal or catalytic approach merely results in a C—H insertion, as with diazocamphor *(8)*[9-11].



(9) *(10)*

The limit of the photochemical method is reached when the desired reaction product is itself photolabile under the irradiation conditions, *e.g.* with 2-diazo-1,3-indandione *(11)*.

The choice of wavelength should be guided by the common photochemical principle: as long as possible, as short as necessary. Decreasing wavelength (increasing energy) of the radiation used leads to increasing amounts of by-products. However, the lowest energy excited singlet state S_1 of diazo ketones, generated by irradiation at the wavelength of a low-intensity forbidden transition in the near UV or visible range, displays only modest reactivity (cf. Section 6).

In the presence of triplet sensitizers, Wolff rearrangement is greatly reduced or completely suppressed in favor of other carbene reactions.

2.3. Catalysis

The decomposition temperature of α-diazo carbonyl compounds can be drastically lowered by metal (ion) catalysts Ag, $Ag^{\oplus}$, Cu, $Cu^{\oplus}$, $Cu^{2\oplus}$, Pt, Pd, Rh, *etc.* Most frequently use is made of freshly precipitated Ag(I) oxide in the presence of alkaline reagents. With the exception of CuI, copper catalysts not only exert an activating effect on nitrogen elimination but also stabilize the resulting carbene (see Section 6.2) by complex formation[3]. The same applies to rhodium[12] and palladium catalysts[13]. As a consequence, Wolff rearrangement no longer occurs or becomes very difficult. Catalysts are sometimes also used during photolysis of α-diazo carbonyl compounds[14] (Table 1).

Table 1. Catalysts for Wolff rearrangement of α-diazo ketones.

Catalyst	Ref.
$Ag_2O/Na_2S_2O_3$	[1]
$Ag_2O/Na_2S_2O_3/Na_2CO_3$	[15]
$AgNO_3$	[16]
$C_6H_5—CO_2Ag$/tertiary base	[17]
$CF_3—CO_2Ag$	[17]
colloidal Ag from $Ag_2O + H_2CO$	[18]
CuO	[19]
CuI/acetonitrile	[20]
Cu/acetonitrile	[19]
platinum	[21]

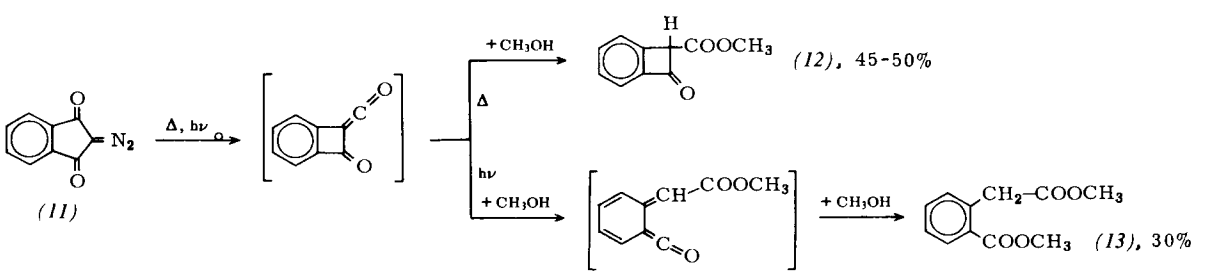
3. Secondary Reactions of Ketene Products

The ketenes *(4)* are generally not isolated after a Wolff rearrangement; instead their reaction products are obtained.

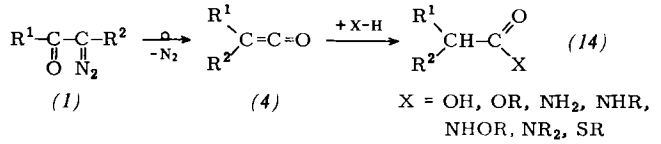
3.1. Addition of Nucleophiles

If the Wolff rearrangement is conducted in the presence of nucleophilic reagents whose proton activity is not excessively high, then the ketene intermediates yield carboxylic acids *(14)* or their derivatives[3, 22, 22a].

This synthesis represents the principal application of the Wolff rearrangement, particularly in connection with the homologization of carboxylic acids[15]. Remarkably, the photochemical



(11) *(12)*, 45-50% *(13)*, 30%



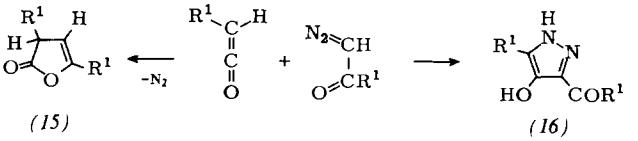
(1) (4) (14)

X = OH, OR, NH_2, NHR, NHOR, NR_2, SR

Wolff rearrangement of 2-diazo 1,3-diketones in the presence of water leads to β-keto carboxylic acids which otherwise prove to be unisolable[151, 151a] (cf. Section 4.5).

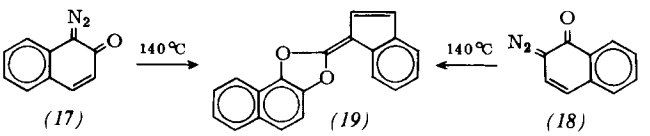
3.2. Intermolecular and Intramolecular Cycloadditions

While the relatively stable ketenes resulting from decomposition of corresponding α-diazo ketones in inert solvents are isolable, neither aldo ketenes nor their dimers can be prepared. In some cases the more labile aldo ketenes react with intact α-diazo ketone to give 3-buten-4-olides *(15)*[23-26] or pyrazoles *(16)*[27].



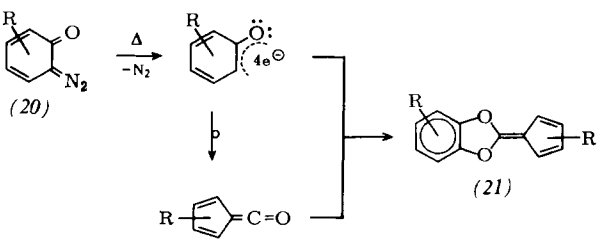
(15) (16)

On thermolysis of 1-diazo-2-oxo- *(17)* and 2-diazo-1-oxo-1,2-dihydronaphthalene *(18)*, *Yates* and *Robb* obtained the same 2-methylene-1,3-dioxole derivative *(19)*[28].



(17) (19) (18)

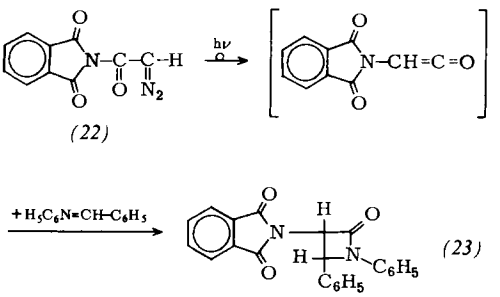
Nearly all *o*-quinone diazides behave in this manner on thermolysis[28a]. The resulting ketene reacts with unrearranged primary fragments (carbenes), yielding compounds of type *(21)*.



(20) (21)

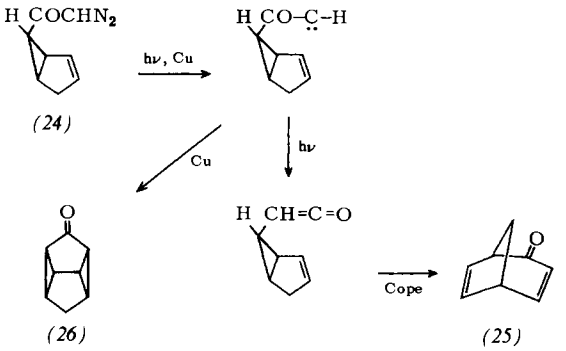
The ketenes formed "*in situ*" in the Wolff rearrangement have frequently been subjected to cycloadditions with C=C, C=N, and N=N double bonds or with *o*-quinones[29-35]. The trapping of an unstable aminoketene to give the α-amino β-lactam *(23)* should be cited as an example[36].

The scope of this cycloaddition is limited above all by reaction of the starting compound itself or its primary fragments (carbenes) prior to rearrangement. The case of the diazo ketone *(24)* is interesting because intramolecular cycloadditions



(22) (23)

occur preferentially at the ketene stage in the photochemical reaction[37] but at the carbene stage in the catalytic process[38].

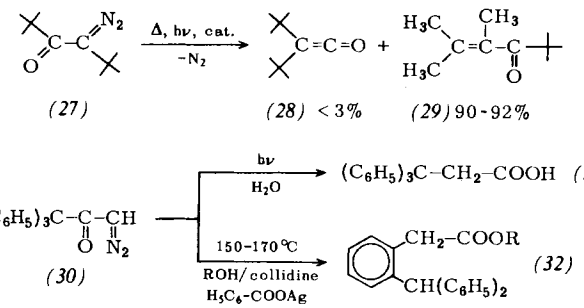


(24) (26) (25)

4. Substrates Capable of Rearrangement

4.1. Open-Chain α-Diazo Ketones

Whereas little is known about the Wolff rearrangement of α-diazo aldehydes[39-41], numerous publications have appeared on the fragmentation of open-chain α-diazo ketones[3]. In principle, alkyl, aryl, and aralkyl groups can migrate. The *tert*-butyl group in *(27)*[42] and the triphenylmethyl group in *(30)*[43] qualify as borderline cases.

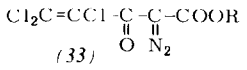


(27) (28) < 3% (29) 90-92%

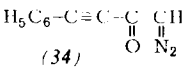
While the *tert*-butyl group of *(27)* invariably displays only a limited proclivity to migrate, the triphenylmethyl group undergoes clean photochemical reaction. In the catalytic process, however, anomalous attack at the *ortho* position of a phenyl ring occurs in compound *(30)*. 9-Diazoacetylfluorene behaves similarly to triphenyldiazoacetylmethane *(30)*[43].

The presence of additional functional groups, particularly in α position to the CO group, can interfere with the Wolff rearrangement or lead to secondary reactions. Studies on the influence of, for example, halo[44-53], substituted hydroxyl[54, 55], free and substituted amino[56-64], cyclopropyl[65],

and cyclopropenyl groups[35, 66-71] have been reported. Incorporation of double or triple bonds into the α-diazo carbonyl compounds, especially in the αβ position to the CO group[78], suppresses the Wolff rearrangement either completely or partially[34, 37, 38, 72-78]. The Wolff rearrangement is known to occur with the α,β-unsaturated diazo carbonyl compounds *(33)*[79] and *(34)*[80].



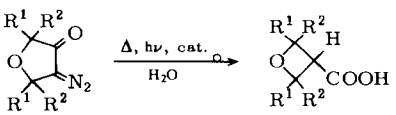
(33)



(34)

4.2. Cyclic α-Diazo Ketones

Apart from the Arndt-Eistert homologization[81, 82], ring contraction is the main application of the Wolff rearrangement. Above all the photochemical variant proves suitable for producing strained systems (bicyclics[10, 83-99], polycyclics[85, 87, 100-103], paracyclophanes[104-106], steroids[107-112]). The formation of the oxetane *(36)* can be considered as an example[113, 114].

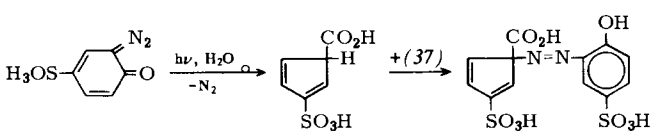


(35) *(36)*

2-Diazo-1-oxoacenaphthene is a negative example—it fails to undergo ring contraction[115].

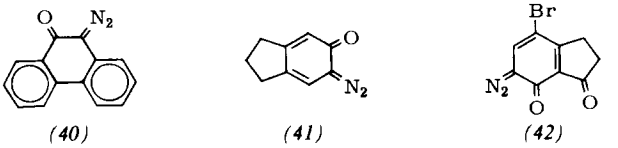
4.3. *o*-Quinone Diazides

As originally demonstrated by *O. Süs*[116, 117, 117a], the Wolff rearrangement can also be implemented with *o*-quinone diazides. In this case the rearrangement involves ring contraction, thus providing access to the cyclopentadiene series (Süs reaction). This reaction is exploited in a photocopying process (Diazotype, offset process)[116-118] in which an increase in pH promotes coupling of rearrangement products with unreacted *o*-quinone diazide, *e.g. (38)* with *(37)*, to yield the azo dye *(39)*.



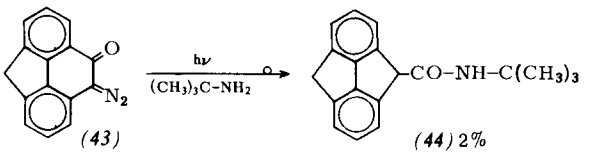
(37) *(38)* *(39)*

Coupling reactions can be avoided by working in acid media. Thus irradiation of derivatives of 1-diazo-2-oxo-1,2-dihydronaphthalene and 2-diazo-1-oxo-1,2-dihydronaphthalene leads to the corresponding derivatives of 1-indenecarboxylic acid[116, 119, 120] [see formula *(19)* in Section 3.2]. Application to the pyridine and quinoline series[119-121] permits synthesis of pyrrole- and indolecarboxylic acids. Photochemical transformation of 3-diazo-2-oxo-2,3-dihydropyridine to 2-pyrrolecarboxylic acid is a remarkable reaction because it involves migration of an sp^2 nitrogen[120]. Whereas *(40)*[122, 123], *(41)*[120], and *(42)*[124] undergo smooth Wolff rearrangement,



(40) *(41)* *(42)*

only 2% ring contraction occurs with *(43)*[125], presumably owing to an increase of *ca.* 50 kcal/mol in strain energy[123].

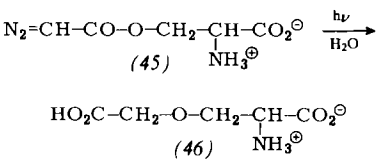


(43) *(44)* 2%

Thermal decomposition of *o*-quinone diazides in inert solvents leads to 1,3-dioxoles, only part of the keto carbene being subject to Wolff rearrangement (cf. Section 3.2).

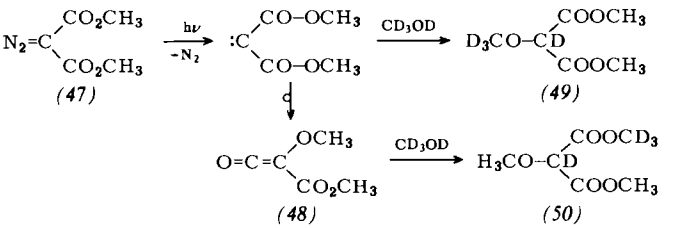
4.4. Derivatives of α-Diazo Carboxylic Acids

The first example of Wolff rearrangement of a functional group bound to a heteroatom was observed in the photolysis of *O*-diazoacetylserine *(45)* in water[126].



(45) *(46)*

Nowadays a series of examples is known for the migration of substituted hydroxyl[127-133], mercapto[134], and amino groups[127, 135-137], which are all usually induced photochemically. Formation of dimethyl methoxymalonate from

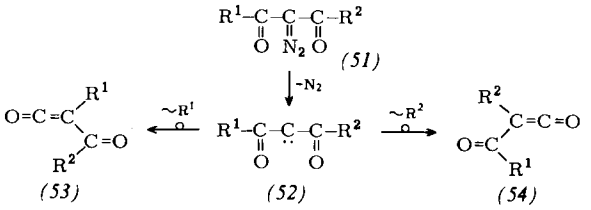


(47) *(48)* *(49)* *(50)*

dimethyl diazomalonate *(47)* involves, for example, about 30% of an intramolecular methoxy group migration since irradiation of *(47)* in perdeuteriomethanol affords an 80% overall yield of the insertion product *(49)* and the rearrangement product *(50)* in the ratio 9:4[130].

4.5. 2-Diazo 1,3-Dicarbonyl Compounds

On rearrangement of unsymmetrically substituted[138] 2-diazo 1,3-dicarbonyl compounds *(51)*, both R^1 and R^2 can migrate, since a diacylcarbene *(52)* is present after loss of N_2. Studies on compounds *(51)* (see Table 2) therefore provide an indication of the relative migration tendencies of various groups (cf. Section 6).



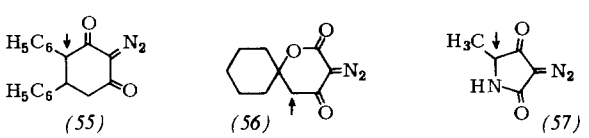
(51)

(53) (52) (54)

Table 2. Wolff rearrangement of unsymmetrically substituted open chain 2-diazo 1,3-dicarbonyl compounds of type (51).

R^1	R^2	Mode of reactions	(53) + (54) yield [%]	(53)	(54)	Ref.
C_2H_5	CH_3	*hν*	84	49	51	[151a]
$C(CH_3)_3$	CH_3	*hν*	82	13	87	[151, 151a]
C_6H_5	H	Δ	>90	0	100	[152]
		hν	>90	0	100	[152]
		$Ag^{\oplus}$-cat.		0	100	[153]
C_6H_5	CH_3	Δ	74	62	38	[152]
		Δ		60	40	[154]
		hν	64	4	96	[152]
4-CH_3O—C_6H_4	CH_3	Δ	74	76	24	[152]
		hν	53	25	75	[152]
4-NO_2—C_6H_4	CH_3	Δ	21	0	100	[152]
		hν	15	0	100	[152]
2,4,6-$Br_3C_6H_2$	CH_3	Δ	—	80	20	[154]
2,4,6-$(CH_3)_3C_6H_2$	CH_3	Δ	—	98	2	[154]
OCH_3	CH_3	Δ	44	0	100	[155]
		hν	57	0	100	[155]
OC_2H_5	CH_3	*hν*	78	0	100	[150]
OCH_3	C_6H_5	*hν*	88	0	100	[150]
OC_2H_5	C_2H_5	Δ	—	0	100	[156]
OC_2H_5	C_6H_5	Δ	—	0	100	[156]
OC_2H_5	C(O)—OC_2H_5	Δ	—	0	100	[156]
OCH_3	$CCl{=}CCl_2$	Δ	7	0	100	[79]
		hν	20—28	0	100	[79]
OCH_3	$N(CH_3)_2$	*hν*	28	40	60	[155]
OC_2H_5	$NH(C_6H_5)$	Δ	14—18	0	100	[137]
		hν	16—25	0	100	[137]

Cyclic 2-diazo 1,3-dicarbonyl compounds can also be included in these investigations. The arrows in formulas (55)[157], (56)[158] and (57)[159] indicate the centers of selective migratory aptitude.

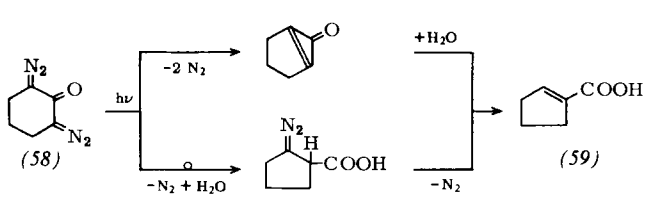


(55) (56) (57)

4.6. Other Diazo Carbonyl Compounds

Thermally[160] or photochemically induced[161, 162] Wolff rearrangement of 1-diazo 2,3-dicarbonyl compounds requires migration of an electron-impoverished carbonyl carbon to a carbenoid center, thus imparting not only preparative but also theoretical interest to the reaction.

Final confirmation of the Wolff rearrangement of 1,3-bisdiazo 2-carbonyl compounds (58)[163-166] is still outstanding.

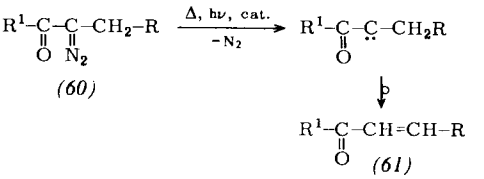


(58) (59)

5. Competing Reactions

5.1. [1.2]-Hydrogen Shifts

α-Diazo ketones of type (60) very frequently react *via* a [1.2]-H shift at the carbene stage, especially under catalytic conditions, to form α,β-unsaturated ketones (61)[167-171].

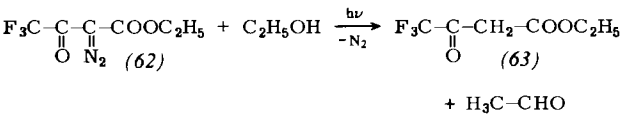


(60) (61)

A [1.2]-methyl shift is the principal reaction route of 4-diazo-2,2,5,5-tetramethyl-3-hexanone (27)[42] (cf. Section 4.1).

5.2. Hydrogen Abstraction

Saturation of the transient carbene by H abstraction from the solvent occasionally accompanies the Wolff rearrangement. In ethyl α-diazotrifluoroacetate (62)[51] it becomes the major reaction:

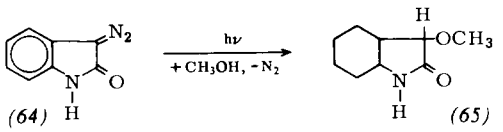


(62) (63)

In the photochemical process, the lowest triplet state (of the diazo ketone) is responsible for H abstraction[140]. The extent of this competing reaction depends upon the wavelength and solvent[140].

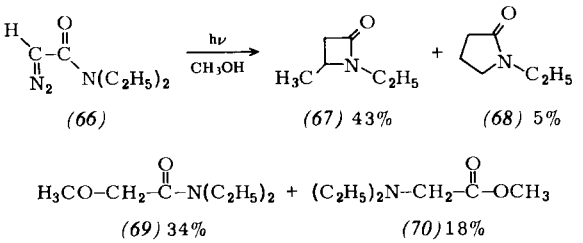
5.3. Intermolecular and Intramolecular Insertions

The α-oxo carbenes arising as intermediates in the Wolff rearrangement frequently insert into C—H, C—C, C—O, C—S, C—N, C—Hal, O—H, N—H, and S—H bonds[3]. Greatest preparative importance attaches to the insertion reactions into the O—H bonds of water, alcohols, phenols, carboxylic acids, *etc.* For instance, *(64)* does not undergo rearrangement but insertion on irradiation[172].



(64) *(65)*

An example of an intramolecular insertion should also be mentioned in this context[135]: only *(70)* is formed by Wolff rearrangement.

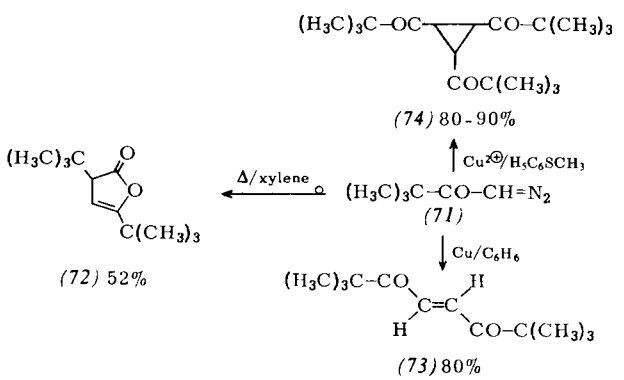


(66) *(67)* 43% *(68)* 5%

(69) 34% *(70)* 18%

5.4. Dimerization and Oligomerizations

Dimerizations and oligomerizations of the stabilized carbenes is often observed in the decomposition of α-diazo carbonyl compounds, especially when performed catalytically—as illustrated by the following example[173]:



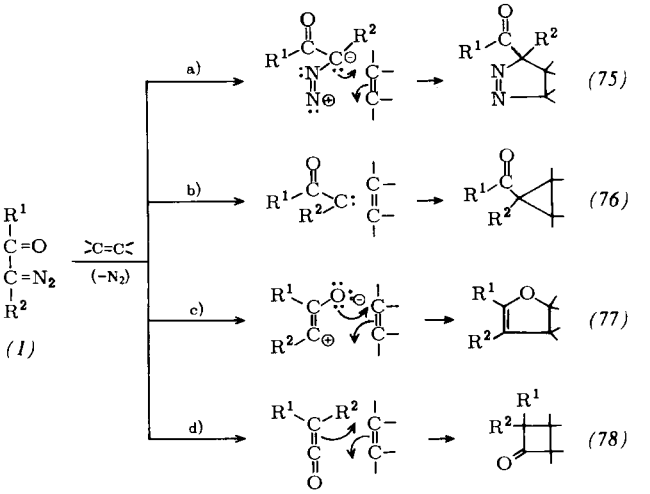
(74) 80-90%

(72) 52% *(71)* *(73)* 80%

5.5. Cycloadditions

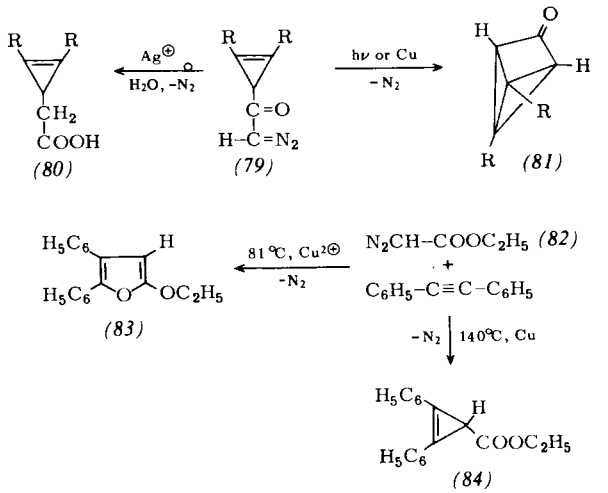
α-Diazo carbonyl compounds are capable of numerous intermolecular and intramolecular cycloadditions to double bonds (C=C, C=O, C=N, C=S, N=N) or triple bonds (C≡C, C≡N)[3]. The possible reactive species are (a) the starting compound itself, (b) a carbene intermediate, (c) a 1,3-dipolar intermediate, and (d) the ketene ensuing from Wolff rearrangement (cf. Section 3.2).

The competing processes (a) and (b) are particularly interesting with regard to the mechanism of the Wolff rearrangement.



(1) *(75)* *(76)* *(77)* *(78)*

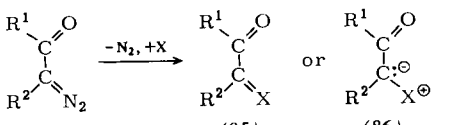
The reactions of *(79)* to give *(81)*[174-176] and of *(82)* to form *(83)*[177, 178] should illustrate this point.



(80) *(79)* *(81)* *(83)* *(84)*

5.6. Other Competing Processes

A wide range of reagents can interfere with the Wolff rearrangement owing to the pronounced reactivity of the diazo compounds and the degradation products[3]. Special mention is made here of additions to the carbene intermediate or to the starting compound itself:



(1) *(85)* *(86)*

X = O[84, 114, 185, 188]
X = N-N=CR$_2$[114, 179-185]
X = C=N-R[186]
X = SR$_2$[187]

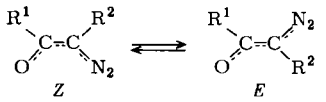
6. Reaction Mechanisms and Intermediates

6.1. Elimination of Nitrogen

6.1.1. Steric Effects

Physicochemical investigations (IR, UV, NMR data, dipole moments) demonstrate that, in solution, α-diazo carbonyl com-

pounds generally exist in *Z/E* equilibrium about the C—C bond having partial double bond character[189-193] ($\Delta G^{\ddagger}_{298} \approx 15$ kcal/mol).

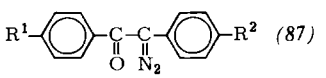


Z *E*

In view of a concerted mechanism of the Wolff rearrangement starting from the *Z*-conformation, the two rotamers have occasionally been assigned differing reactivities[189]. The behavior of compounds *(5)* (*Z*, labile) and *(27)* (*E*, 3% Wolff rearrangement) fits this concept well, but still does not prove its validity. Steric hindrance has been proposed as an alternative explanation for the inertness of *(27)*, and the lack of delocalization energy for the lability of *(5)*. Resonance of the coplanar CO—CN_2 group normally leads to a gain of about 0.7 β in delocalization energy[194]. However, resonance is impossible in the twisted heptacycle *(5)* since the CO and CN_2 are mutually orthogonal. Kinetic studies[195-199] and the finding that substituents have different effects on nitrogen elimination[196, 200] and on migratory aptitude contraindicate a concerted mechanism, regardless of the manner in which the reaction is conducted.

6.1.2. Electronic Effects

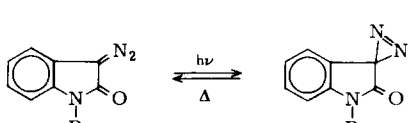
For the case of substituted azibenzils *(87)*, electronic effects occurring on thermal nitrogen elimination can be correlated with the Hammett σ constants[196].



(87)

Electron-withdrawing groups R^2 decelerate the decomposition, while their electron-repelling counterparts have an accelerating action. The effect of groups R^1 is exactly opposite, but less significant[196, 197].

In the photochemical variant, N_2 elimination can be accomplished both by direct irradiation in the entire absorption range of the α-diazo carbonyl compound and on triplet sensitization. The apparent integral quantum yield is always lower than 1[200]. Values of 0.6, 0.5, and 0.07[201] are obtained for diazoacetophenone at 250, 294, and 325 nm. The longest wavelength forbidden transition[193], which leads to the lowest energy singlet excited state S_1, is therefore not very effective. S_1 undergoes mainly radiationless deactivation. Under suitable conditions additional photochromic valence isomerization to diazirines *(89)* is possible[201, 202].



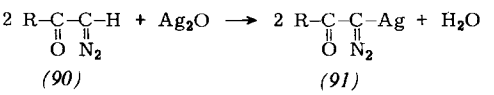
(88) *(89)*

Numerous quantum yield measurements have been performed on substituted diazoacetophenones[200]. Electron-withdrawing and electron-repelling *para* substituents lower the quantum yield. No uniform trend could be established for electronic effects in the catalytic variant[198, 199].

6.1.3. Medium Effects

Elimination of nitrogen is independent of both the rearrangement and also the presence of nucleophilic reagents[195, 196]. It obeys a first-order rate law[196]. This disproves the addition-protonation mechanism discussed by *Eistert*[203], which assumes participation of the nucleophile prior to nitrogen elimination. There remain certain medium effects[195-197, 204] arising from polarity changes and from hydrogen bonding to the carbonyl oxygen or the diazo carbon. The presence of such aggregates in mixed systems of aprotic and protic solvents has also been detected by UV spectroscopy[205]. The resulting barrier to resonance facilitates thermal elimination of N_2. However, the absence of H/D isotope effects[196] demonstrates that complete $H^{\oplus}$ transfer does not take place in the rate-determining step.

Whereas monomolecular decomposition can be assumed in the thermal and photochemical processes, transient participation of the metal or metal ion occurs in the catalytic variant. According to a hypothesis put forward by *Huisgen*[206], the electrophilic $Ag^{\oplus}$ ion adds to the diazo carbon and thus effects nitrogen elimination and migration of the group. Indeed, reaction of diazomethyl ketones *(90)* with silver(I) oxide in tetrahydrofuran at −15 °C affords silver-substituted diazo ketones *(91)*[207].

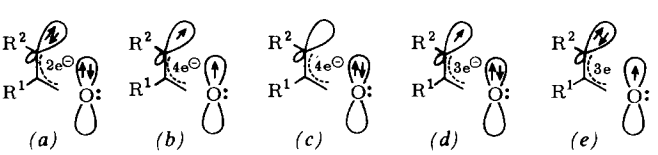


(90) *(91)*

Newman and *Beal*[17], who have developed a homogeneous medium for the $Ag^{\oplus}$ catalyzed rearrangement (methanol in the presence of silver benzoate and triethylamine) assume a radical chain process to occur under these conditions. Triethylamine has a kind of initiating effect as proton transfer agent and $Ag^{\oplus}$ likewise for electron transfer[17]. In recent kinetic studies[198] a complex between the deprotonated diazo ketone and $Ag[N(C_2H_5)_3]_n^{\oplus}$ has been proposed as crucial intermediate.

6.2. Primary Fragments

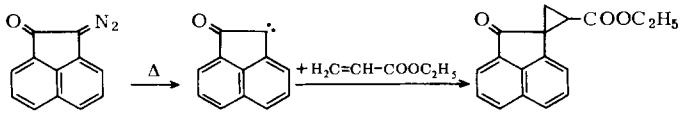
The singlet carbene *(a)*, the 1,3-diradical *(b)*, the 1,3-dipole *(c)*, and the two-spin systems *(d)* and *(e)* are reasonable possibilities for the ground state of the primary fragments left after elimination of nitrogen.



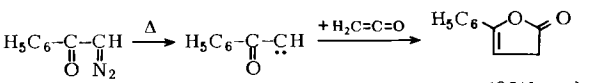
(a) *(b)* *(c)* *(d)* *(e)*

In the plane of the σ bond skeleton there is a p orbital of the oxygen and an sp^2 or p orbital of the "diazo carbon" to be populated; in a plane at right angles there are three

p orbitals comprising an allyl system. *(a)* and *(c)* are singlet states. A scalar and dipolar spin coupling can be assumed in *(b)*, and dipolar spin couplings in *(d)* and *(e)*. This leads to singlet and triplet splitting, so that a total of five singlet and three triplet states will result. If the sp^2/p alternative or antibonding levels are included, then the number of possibilities increases considerably. The energetic proximity of these states makes any theoretical decision difficult. In the thermal case [*e.g. (92), (94)*] an indication of the nature of the primary fragments is provided by trapping- and side reactions (cf. Section 5).

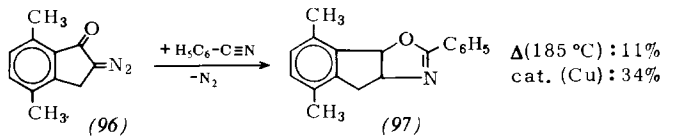


(92) *(93)*[208]



(94) *(95)*[209]

Thus a singlet carbene and 1,3-dipole participation may be assumed. However, in the numerous 1,3-dipolar cycloadditions with C=C, C=O, C=S, C=N, C≡C, and C≡N bonds[210] it is often doubtful whether the primary fragments or the original α-diazo carbonyl compound itself is involved in the reaction. With primary fragments showing a low tendency to undergo rearrangement and additional stabilization by complex formation with copper, trapping reactions, yielding *e.g. (97)* are much more likely[211].

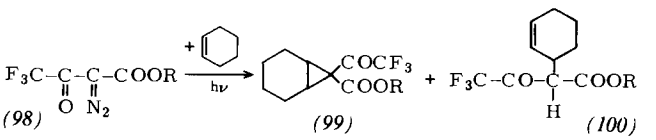


(96) *(97)*

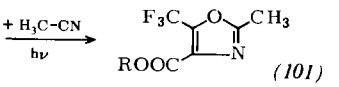
In the $Ag^{\oplus}$-catalyzed Wolff rearrangement the free keto carbene is apparently present after elimination of nitrogen.

The reaction course during direct photolysis was followed by absorption spectrometry (flash photolysis)[212] and by ESR spectroscopy[213, 214]. At 77 K, azibenzil affords a triplet carbene exhibiting hardly any Wolff rearrangement (<3%). Marked deviation from an angle of 180° can be deduced from the ratio of its zero field parameters ($D/hc = 0.3815$, $E/hc = 0.0489\ cm^{-1}$). (The triplet carbene disappears in favor of an oxygen radical when the temperature is raised[214].)

The Wolff rearrangement of azibenzil increases up to a yield of 85–90% at room temperature[214]. In the triplet-sensitized decomposition of α-diazo carbonyl compounds, Wolff rearrangement occurs at most as a minor reaction[152, 215–217]. The major processes are H abstraction and insertions. The most obvious conclusion to be drawn from all these observations is that the photochemical Wolff rearrangement takes place in a singlet state of the primary fragment. Since the relative migratory aptitudes of individual groups differ from those in the thermal variant (cf. Sections 4.7 and 6.4), the process must involve a singlet excited state. For small singlet-triplet splitting, an intersystem crossing of low activation energy in both directions can be assumed so that reactions of the triplet state are also observed on direct photolysis, and the Wolff rearrangement is found to occur in sensitized photolysis. The quantum yield for the transition $S_1 \rightarrow T_1$ increases with the temperature and the energy of the illuminating light[140].



(98) *(99)* *(100)*

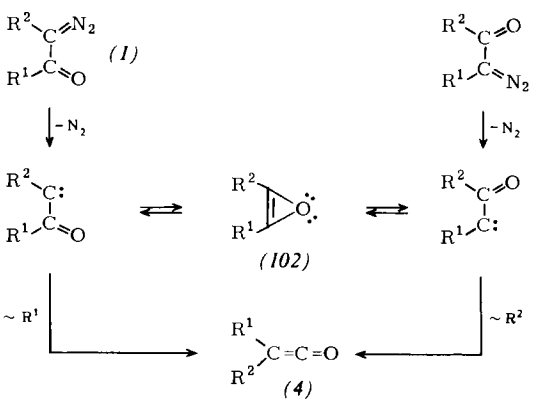


(101)

Photochemically generated primary fragments, *e.g.* from *(98)*, can also be trapped in a kind of carbene reaction or a 1,3-dipolar reaction[218–221].

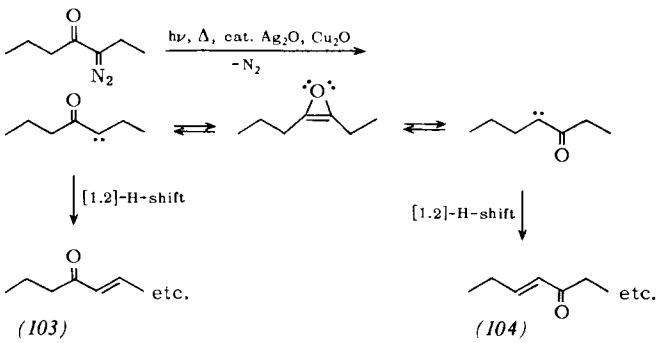
6.3. The Oxirene Intermediate

The oxirenes *(102)*, antiaromatic 4π electron systems, formed by valence isomerization of the primary fragments should possess similar energies to the α-oxo carbenes[222–224]. The true role of the oxirenes in decomposition of α-diazo carbonyl compounds long remained unclear due to a lack of experimental work[225–227]. Conclusive proof of the intermediate appearance of oxirenes during the photochemical Wolff rearrangement has been obtained with the aid of three independent methods employing isotopic labeling.



The extent of oxirene[*] formation depends upon the conditions, *e.g.* on the concentration of water[228]. The carbene-oxirene equilibrium makes it difficult to reach any conclusion regarding the migratory aptitude of the groups R^1 and R^2. In all systems investigated so far[229], however, the initial carbene formed after nitrogen elimination undergoes reaction. Oxirene participation could be ruled out on sensitized photolysis, on catalysis, and on thermolysis in solution[227–231]. Proof of oxirene formation that is completely independent of the Wolff rearrangement was obtained with unsymmetrical α-diazo dialkyl ketones[170] and a number of special aryl-substituted α-diazo ketones[232a].

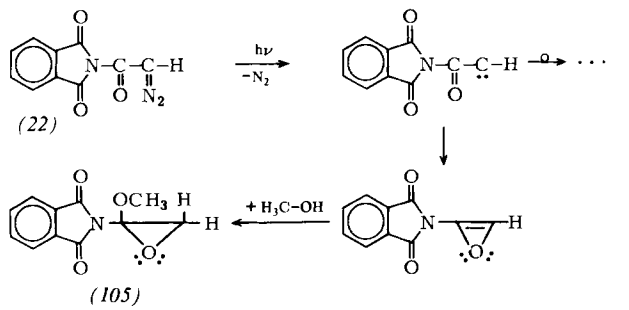
[*] No oxirene could be detected on photolysis of α-diazohomoadamantanone in the presence of water [228a].



(103) *(104)*

hν:	57%	43%
Δ(465 °C):	64%	36%
cat.:	100%	0%

The trapping reaction yielding *(105)* strongly suggests that the oxirenes are true intermediates, and not merely transition states[232].



(22) *(105)*

6.4. Rearrangement of the Primary Fragments

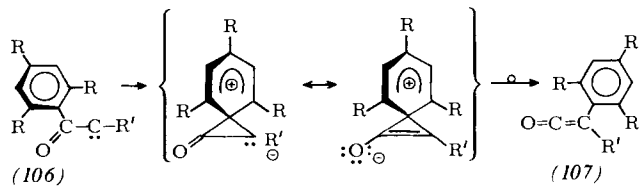
The examples cited in Section 4 demonstrate that hydrogen, alkyl, aryl, substituted hydroxyl, mercapto, and amino groups can all migrate. Thus H, C(sp^3), C(sp^2), C(sp), N(sp^3), N(sp^2), O, or S represent migrating centers. Apart from this absolute migratory disposition, the relative migratory aptitudes of individual groups established primarily with 2-diazo 1,3-dicarbonyl compounds (Section 4.5) also warrant interest. The following series is generally valid for the thermal reaction[152, 155, 156, 137]:

$$H > C_6H_5 > CH_3 > NR_3 > OR$$

In the photochemical variant, phenyl and methyl change places. The electronic effects are similar in both cases[152]:

$$p\text{-}H_3CO{-}C_6H_4 > C_6H_5 > p\text{-}O_2N{-}C_6H_4$$

The mesityl and above all the 2,4,6-tribromophenyl group migrate far more readily than purely electronic effects of methyl and bromo substituents would suggest[154]. This pronounced steric effect is most probably due to restriction of resonance in the keto carbene intermediate *(106)*.



(106) *(107)*

R = CH_3, Br

All these findings show that a high electronegativity at the migrating center and an electron-poor R^1—CO bond tend to favor the relative migratory aptitude of the group R^1 (in accord with classical ideas of an anionotropic migration). In contrast, a partial double bonding character of this bond arising from participation of the CO group in resonance of R^1 have an unfavorable effect, especially in the excited state. The group R^2 also influences the migratory disposition of R^1[233].

Regardless of the way in which the reaction is conducted, the migrating groups are not severed entirely from the molecular framework, thus largely or completely conserving all stereochemical information[234–242]. In particular all intermolecular mechanisms can therefore be discounted.

7. Conclusion

The principles of the above mechanistic and preparative investigations on the Wolff rearrangement show how fresh aspects have repeatedly come to light during the course of work on a 70-year old reaction. A considerable extension of this topic has recently been provided by electron-impact induced Wolff rearrangement[243–246], and by thermal and photolytic rearrangements of related systems such as α-diazo sulfones[247], α-diazo phosphane oxides[248, 249], β-oxo sulfonium ylides[250] and their *S*-oxides[251], 1,2,3-triazoles[252], 1,2,3-thiadiazoles[253–256], and 1,2,3-selenadiazoles[257–259].

Received: July 18, 1974 [A 36 IE]
German version: Angew. Chem. *87*, 43 (1975)

[1] *L. Wolff*, Liebigs Ann. Chem. *325*, 129 (1902); *333*, 1 (1904); *394*, 23 (1912).

[2] Work independent of *Wolff* was published almost simultaneously by *G. Schröter*, Ber. Deut. Chem. Ges. *42*, 2346 (1909); *49*, 2704 (1916).

[3] Recent surveys of general syntheses and reactions of α-diazo carbonyl compounds: *B. Eistert, M. Regitz, G. Heck*, and *H. Schwall* in Houben-Weyl-Müller: Methoden der Organischen Chemie. 4th Edit., Thieme, Stuttgart 1968, Vol. 10/4, pp. 473ff.; *F. Weygand* and *H. J. Bestmann*, Angew. Chem. *72*, 535 (1960); *W. Ried* and *H. Mengler*, Fortschr. Chem. Forsch. *5*, 1 (1965); *W. Kirmse:* Carbene Chemistry. 2nd Edit., Academic Press, New York 1971; *W. J. Baron, M. R. De Camp, M. E. Hendrick, M. Jones, Jr., R. H. Levin*, and *M. B. Sohn* in *M. Jones, Jr.* and *R. A. Moss:* Carbenes. Wiley, New York 1973, Vol. 1, pp. 2ff.; *L. L. Rodina* and *I. K. Korobitsyna*, Russ. Chem. Rev. *36*, 260 (1967); *A. Mustafa*, Advan. Photochem. *2*, 113 (1964).

[4] *M. P. Cava* and *R. J. Spangler*, J. Amer. Chem. Soc. *89*, 4550 (1967).

[5] *W. Jugelt* and *D. Schmidt*, Tetrahedron *25*, 969 (1969).

[6] *A. Melzer* and *E. F. Jenny*, Tetrahedron Lett. *1968*, 4503.

[7] *A. de Groot, J. A. Boerma, J. de Valk*, and *H. Wynberg*, J. Org. Chem. *33*, 4025 (1968).

[8] *L. Horner* and *E. Spietschka*, Chem. Ber. *85*, 225 (1952).

[9] *J. Bredt* and *W. Holz*, J. Prakt. Chem. [2] *95*, 133 (1917).

[10] *L. Horner* and *E. Spietschka*, Chem. Ber. *88*, 934 (1955).

[11] *T. Gibson* and *W. F. Erman*, J. Org. Chem. *31*, 3028 (1966).

[12] *R. Paulissen et al.*, Tetrahedron Lett. *1973*, 2233.

[13] *N. Yoshimura, S.-J. Murahashi*, and *J. Moritani*, J. Organometal. Chem. *52*, C 58 (1973).

[14] *U. R. Ghatak et al.*, J. C. S. Chem. Comm. *1973*, 548.

[15] *F. Arndt* and *B. Eistert*, Ber. Deut. Chem. Ges. *68*, 200 (1935); cf. also ref. [81].

[16] *A. Burger* and *S. Avakian*, J. Org. Chem. *5*, 606 (1940).

[17] *M. S. Newman* and *P. F. Beal*, J. Amer. Chem. Soc. *72*, 5163 (1950).

[18] *R. Casanova* and *T. Reichstein*, Helv. Chim. Acta *32*, 649 (1949).

[19] *P. Yates* and *J. Crawford*, J. Amer. Chem. Soc. *88*, 1562 (1966).

[20] *P. Yates* and *J. Fugger*, Chem. Ind. (London) *1957*, 1511.

[21] *L. Wolff*, Liebigs Ann. Chem. *394*, 23 (1912).

[22] *F. Weygand* and *H. J. Bestmann*, Chem. Ber. *92*, 528 (1959).

[22a] *M. T. W. Hearn* and *H. D. Ward*, Austral.-J. Chem. *1969*, 1731.

[23] *K. B. Wiberg* and *T. W. Hutton*, J. Amer. Chem. Soc. *76*, 5367 (1954).
[24] *J. Quintana, M. Torres*, and *F. Serratosa*, Tetrahedron *29*, 2065 (1973).
[25] *P. Yates* and *T. J. Clark*, Tetrahedron Lett. *1961*, 435.
[26] *J. E. Baldwin*, Tetrahedron *20*, 2933 (1964).
[27] *M. Takebayashi* and *T. Ibata*, Bull. Chem. Soc. Jap. *41*, 1700 (1968).
[28] *P. Yates* and *E. W. Robb*, J. Amer. Chem. Soc. *79*, 5760 (1957).
[28a] *W. Ried* and *H. Mengler*, Fortschr. Chem. Forsch. *5*, 1 (1965); *R. Clinging, F. M. Dean*, and *G. H. Mitchell*, Tetrahedron *30*, 4065 (1974).
[29] *W. Kirmse* and *L. Horner*, Chem. Ber. *89*, 2759 (1956).
[30] *L. Horner* and *E. Spietschka*, Chem. Ber. *89*, 2765 (1956).
[31] *L. Horner, E. Spietschka*, and *A. Gross*, Liebigs Ann. Chem. *573*, 17 (1951).
[32] *W. Ried* and *W. Radt*, Liebigs Ann. Chem. *676*, 110 (1964); *688*, 170 (1965).
[33] *W. Fischer* and *E. Fahr*, Tetrahedron Lett. *1966*, 5245.
[34] *P. Yates* and *A. G. Fallis*, Tetrahedron Lett. *1968*, 2493.
[35] *S. Masamune* and *K. Fukumoto*, Tetrahedron Lett. *1965*, 4647.
[36] *E. Müller* and *P. Heinrich*, Chem.-Ztg. *95*, 567 (1971); *96*, 112 (1972).
[37] *P. K. Freeman* and *D. G. Kuper*, Chem. Ind. (London) *1965*, 424.
[38] *J. Meinwald* and *G. H. Wahl*, Chem. Ind. (London) *1965*, 424.
[39] *A. Krantz*, J. C. S. Chem. Comm. *1973*, 670.
[40] *Z. Arnold*, Chem. Commun. *1967*, 299.
[41] *J. Kučera, Z. Janoušek*, and *Z. Arnold*, Collect. Czech. Chem. Commun. *35*, 3618 (1970).
[42] *M. S. Newman* and *A. Arkel*, J. Org. Chem. *24*, 385 (1959).
[43] *A. L. Wilds et al.*, Tetrahedron Lett. *1965*, 4841; J. Amer. Chem. Soc. *84*, 1503 (1962); J. Org. Chem. *34*, 2401 (1969).
[44] *J. Michalsky* and *I. Rakova*, J. Prakt. Chem. [4] *8*, 181 (1959).
[45] *J. Michalsky, M. Holik*, and *A. Podperova*, Monatsh. Chem. *90*, 814 (1959).
[46] *A. Roedig* and *H. Lunk*, Chem. Ber. *87*, 971 (1954).
[47] *A. Roedig* and *R. Maier*, Chem. Ber. *86*, 1467 (1953).
[48] *F. J. Buckle, F. L. Pattison*, and *B. C. Saunders*, J. Chem. Soc. *1949*, 1471, 2774.
[49] *F. Brown* and *W. K. R. Musgrave*, J. Chem. Soc. *1953*, 2087.
[50] *J. D. Parker et al.*, J. Org. Chem. *23*, 1166 (1958).
[51] *F. Weygand, W. Schwenke*, and *H. J. Bestmann*, Angew. Chem. *70*, 506 (1958).
[52] *B. L. Dyatkin* and *E. P. Mochalina*, Izv. Akad. Nauk SSSR, Ser. Khim. *1965*, 1035.
[53] *F. Weygand* and *K. Koch*, Angew. Chem. *73*, 531 (1961).
[54] *J. H. Looker* and *L. L. Braun*, J. Org. Chem. *23*, 1062 (1958).
[55] *F. W. Bachelor* and *G. A. Miano*, Tetrahedron Lett. *1967*, 4733.
[56] *K. Balenovic, V. Thaller*, and *L. Filipovic*, Helv. Chim. Acta *34*, 744 (1951).
[57] *K. Balenovic* and *J. Dvornik*, J. Chem. Soc. *1954*, 2976.
[58] *K. Balenovic, D. Fles*, and *I. Jambresic*, Croat. Chem. Acta *28*, 303 (1956).
[59] *K. Balenovic, I. Jambresic*, and *I. Ranogajec*, Croat. Chem. Acta *29*, 87 (1957).
[60] *K. Balenovic*, Chem. Ind. (London) *1955*, 1673.
[61] *F. Weygand*, Chem. Ber. *91*, 1037 (1958).
[62] *F. Weygand, P. Klinke*, and *I. Eigen*, Chem. Ber. *90*, 1896 (1957).
[63] *D. Fles* and *M. Markovac-Prpic*, Croat. Chem. Acta *28*, 73 (1956); *29*, 79 (1957).
[64] *K. Balenovic* and *N. Stimac*, Croat. Chem. Acta *29*, 153 (1957).
[65] *W. C. Agosta et al.*, Tetrahedron Lett. *1969*, 4517.
[66] *S. Masamune* and *M. Kato*, J. Amer. Chem. Soc. *87*, 4190 (1965).
[67] *S. Masamune*, J. Amer. Chem. Soc. *86*, 735 (1964).
[68] *W. von E. Doering* and *M. Pomerantz*, Tetrahedron Lett. *1964*, 961.
[69] *S. Masamune* and *N. T. Castellucci*, Proc. Chem. Soc. *1964*, 298.
[70] *S. Masamune* and *K. Fukumoto*, Tetrahedron Lett. *1965*, 4647.
[71] *A. S. Monahan*, J. Org. Chem. *33*, 1441 (1968).
[72] *W. von E. Doering et al.*, Tetrahedron *23*, 3943 (1967).
[73] *W. von E. Doering, E. T. Fossel*, and *R. L. Keye*, Tetrahedron *21*, 25 (1965).
[74] *M. M. Fawzi* and *C. D. Gutsche*, J. Org. Chem. *31*, 1390 (1961).
[75] *K. Mori* and *M. Matsui*, Tetrahedron Lett. *1969*, 2729.
[76] *A. A. Plente* and *M. T. Bogert*, J. Org. Chem. *6*, 669 (1941).
[77] *R. Grewe* and *A. Bokranz*, Chem. Ber. *88*, 49 (1955).
[78] *J. H. Wotiz* and *S. N. Buco*, J. Org. Chem. *20*, 210 (1955).
[79] *A. Roedig, E. Fahr*, and *H. Aman*, Chem. Ber. *97*, 77 (1964).
[80] *R. Selvarajan* and *J. H. Boyer*, J. Org. Chem. *36*, 1679 (1971).
[81] *B. Eistert* in *W. Foerst*: Neuere Methoden der präparativen organischen Chemie. 4th Edit. Verlag Chemie, Weinheim 1963, Vol. 1, p. 359.
[82] *W. E. Bachmann* and *W. S. Struve*, Org. React. *1*, 38 (1942).
[83] *K. B. Wiberg, B. R. Lowry*, and *T. H. Colby*, J. Amer. Chem. Soc. *83*, 3988 (1961).
[84] *L. Horner, W. Kirmse*, and *K. Muth*, Chem. Ber. *91*, 430 (1958).
[85] *L. Horner, K. Muth*, and *H. G. Schmelzer*, Chem. Ber. *92*, 2953 (1959).
[86] *P. R. Brook* and *B. V. Brophy*, Tetrahedron Lett. *1969*, 4187.
[87] *M. P. Cava, R. L. Litle*, and *D. R. Napier*, J. Amer. Chem. Soc. *80*, 2257 (1958).
[88] *J. Meinwald, A. Lewis*, and *P. G. Gassman*, J. Amer. Chem. Soc. *82*, 2649 (1960); *84*, 977 (1962).
[89] *J. Meinwald* and *J. K. Crandall*, J. Amer. Chem. Soc. *88*, 1292 (1966).
[90] *J. Meinwald* and *P. G. Gassman*, J. Amer. Chem. Soc. *82*, 2857 (1960).
[91] *J. Meinwald et al.*, J. Org. Chem. *33*, 99 (1968).
[92] *J. Meinwald et al.*, J. Org. Chem. *29*, 3469 (1964).
[93] *K. B. Wiberg* and *R. W. Ubersax*, Tetrahedron Lett. *1968*, 3063.
[94] *T. Gibson* and *W. F. Erman*, J. Org. Chem. *31*, 3028 (1966).
[95] *K. B. Wiberg* and *B. A. Hess*, J. Org. Chem. *31*, 2250 (1966).
[96] *K. B. Wiberg* and *A. de Meijere*, Tetrahedron Lett. *1969*, 519.
[97] *A. J. Ashe*, Tetrahedron Lett. *1969*, 519.
[98] *L. Horner* and *E. Spietschka*, Chem. Ber. *88*, 934 (1955).
[99] *A. T. Blomquist* and *C. Bottomley*, Liebigs Ann. Chem. *653*, 67 (1962).
[100] *T. Tanida* and *Y. Hata*, J. Amer. Chem. Soc. *88*, 4289 (1966); *91*, 1170 (1969).
[101] *L. Horner* and *D. W. Baston*, Chem. Ber. *98*, 1252 (1965).
[102] *W. G. Dauben* and *D. L. Whalen*, Tetrahedron Lett. *1966*, 3743.
[103] *S. Huneck*, Chem. Ber. *98*, 1837 (1965).
[104] *N. L. Allinger et al.*, J. Amer. Chem. Soc. *85*, 1171 (1963).
[105] *M. G. Newton, T. J. Walter*, and *N. L. Allinger*, J. Amer. Chem. Soc. *95*, 5652 (1973).
[106] *N. L. Allinger* and *T. J. Walter*, J. Amer. Chem. Soc. *94*, 9267 (1972).
[107] *A. Hassner, A. W. Coulter*, and *W. S. Seese*, Tetrahedron Lett. *1962*, 759.
[108] *J. L. Mateos, O. Chao*, and *H. Flores*, Tetrahedron *19*, 1051 (1963).
[109] *S. Huneck*, Tetrahedron Lett. *1963*, 375.
[110] *G. Muller, C. Huynh*, and *J. Mathieu*, Bull. Soc. Chim. Fr. *1962*, 296.
[111] *M. P. Cava* and *E. Moroz*, J. Amer. Chem. Soc. *84*, 115 (1962).
[112] *J. Meinwald, G. G. Curtis*, and *P. G. Gassman*, J. Amer. Chem. Soc. *84*, 116 (1962).
[113] *I. K. Korobitsyna* and *L. L. Rodina*, Zh. Org. Khim. *1*, 932 (1965).
[114] *I. K. Korobitsyna, L. L. Rodina*, and *L. M. Stashkova*, Khim. Geterotsikl. Soed. *2*, 843 (1966); Zh. Obshch. Khim. *33*, 3109 (1963).
[115] *W. Ried* and *H. Lohwasser*, Liebigs Ann. Chem. *683*, 118 (1965).
[116] *O. Süs*, Liebigs Ann. Chem. *556*, 65, 85 (1944); *557*, 237 (1947); *579*, 133 (1953).
[117] *O. Süs*, Z. Wiss. Photogr., Photophysik, Photochem. *50*, II, 476 (1955).
[117a] Cf. also *P. A. S. Smith* and *W. L. Berry*, J. Org. Chem. *26*, 27 (1961).
[118] *J. de Jonge* and *R. Dijkstra*, Rec. Trav. Chim. Pays-Bas *67*, 328 (1948); *69*, 1448 (1950).
[119] *O. Süs et al.*, Liebigs Ann. Chem. *583*, 150 (1953).
[120] *O. Süs* and *K. Möller*, Liebigs Ann. Chem. *593*, 91 (1955).
[121] Cf. also *O. Süs* and *K. Möller*, Liebigs Ann. Chem. *599*, 233 (1956).
[122] *O. Süs* and *R. Dietrich*, Liebigs Ann. Chem. *617*, 20 (1958); Angew. Chem. *70*, 25 (1958).
[123] *B. M. Trost* and *P. L. Kinson*, Tetrahedron Lett. *1973*, 2675.
[124] *L. Horner et al.*, Liebigs Ann. Chem. *661*, 44 (1963).
[125] *B. M. Trost* and *P. L. Kinson*, J. Amer. Chem. Soc. *92*, 2591 (1970).
[126] *J. Shafer, P. Baronowsky, R. Laursen, F. Finn*, and *F. H. Westheimer*, J. Biol. Chem. *241*, 421 (1966).
[127] *H. Chaimovich, R. J. Vaughan*, and *F. H. Westheimer*, J. Amer. Chem. Soc. *90*, 4088 (1968).
[128] *O. P. Strausz, T. Do Minh*, and *H. E. Gunning*, J. Amer. Chem. Soc. *90*, 1660 (1968); *91*, 1261 (1969); cf. also *89*, 6785 (1967).
[129] *G. O. Schenck* and *A. Ritter*, Tetrahedron Lett. *1968*, 3189.
[130] *K.-P. Zeller*, Chem. Ztg. *97*, 37 (1973); cf. also [139].
[131] *T. Do Minh* and *O. P. Strausz*, J. Amer. Chem. Soc. *92*, 1766 (1970).

[132] *I. G. Csizmadia, J. Font*, and *O. P. Strausz*, J. Amer. Chem. Soc. *90*, 7360 (1968).

[133] *D. G. Thorntan, R. K. Gosari*, and *O. P. Strausz*, J. Amer. Chem. Soc. *92*, 1768 (1970).

[134] *S. S. Hixon* and *S. H. Hixon*, J. Org. Chem. *37*, 1279 (1972).

[135] *R. R. Rando*, J. Amer. Chem. Soc. *92*, 6706 (1970).

[136] *E. Müller* and *P. Heinrich*, Chem.-Ztg. *95*, 567 (1971); *96*, 112 (1972).

[137] *N. T. Buu* and *J. T. Edward*, Can. J. Chem. *50*, 3719 (1972); cf. also *50*, 3730 (1972).

[138] Concerning the symmetrically substituted compounds, cf., *e.g.*, refs. [1, 4, 130, 139–150].

[139] *D. C. Richardson, M. E. Hendrick*, and *M. Jones*, J. Amer. Chem. Soc. *93*, 3790 (1971).

[140] *N. Baumann*, Helv. Chim. Acta *55*, 2716 (1972).

[141] *H. Stetter* and *K. Kiehs*, Chem. Ber. *98*, 1181, 2099 (1965).

[142] *H. Schwall, V. Schmidt*, and *B. Eistert*, Chem. Ber. *102*, 1731 (1969).

[143] *H. Veschambre* and *D. Vocelle*, Can. J. Chem. *47*, 1981 (1969).

[144] *B. Eistert, H. Elias, E. Kosch*, and *R. Wollheim*, Chem. Ber. *92*, 130 (1959).

[145] *B. Eistert, G. Bock, E. Kosch*, and *F. Spalink*, Chem. Ber. *93*, 1461 (1960).

[146] *B. Eistert, D. Greiber*, and *I. Caspari*, Liebigs Ann. Chem. *659*, 79 (1972).

[147] *H. Ledon, G. Linstrumelle*, and *J. Sylvestre*, Bull. Soc. Chim. Fr. *1973*, 2065.

[148] *I. Arnold* and *J. Sanliová*, Collect. Czech. Chem. Commun. *38*, 2641 (1973).

[149] *J. K. Korobitsyna* and *W. A. Nikolaev*, Zh. Org. Khim. 7, 413 (1971).

[150] *L. Horner* and *E. Spietschka*, Chem. Ber. *85*, 225 (1952).

[151] *J. K. Korobitsyna* and *W. A. Nikolaev*, Zh. Org. Khim. 7, 413 (1971).

[151a] *W. A. Nikolaev, C. D. Kotok*, and *J. K. Korobitsyna*, Zh. Org. Khim. *10*, 1335 (1974).

[152] *K.-P. Zeller, H. Meier*, and *E. Müller*, Tetrahedron *28*, 5831 (1972).

[153] *F. M. Stojanovic* and *Z. Arnold*, Collect. Czech. Chem. Commun. *32*, 2155 (1967).

[154] *G. Hayes* and *G. Holt*, J. C. S. Perkin I *1973*, 1206.

[155] *H. Meier*, unpublished.

[156] *H. Staudinger* and *H. Hirzel*, Ber. Deut. Chem. Ges. *49*, 2526 (1917).

[157] *W. D. Barker, R. Gilbert, J. P. Lapointe, H. Veschambre*, and *D. Vocelle*, Can. J. Chem. *47*, 2853 (1969).

[158] *B. Eistert* and *G. Heck*, Liebigs Ann. Chem. *681*, 138 (1965).

[159] *G. Lowe* and *D. D. Ridley*, J. C. S. Chem. Comm. *1973*, 328; J. C. S. Perkin I *1973*, 2024.

[160] *H. Staudinger, J. Becker*, and *H. Hirzel*, Ber. Deut. Chem. Ges. *49*, 2522 (1916).

[161] *W. Kirmse* and *L. Horner*, Chem. Ber. *89*, 2759 (1956).

[162] *C. W. Bird* and *C. K. Wong*, Tetrahedron Lett. *1972*, 4281.

[163] *W. Kirmse*, Angew. Chem. *71*, 539 (1959).

[164] *R. Tasovac, M. Stefanovic*, and *A. Stojiljkovic*, Tetrahedron Lett. *1967*, 2729.

[165] *R. F. Borch* and *D. L. Fields*, J. Org. Chem. *34*, 1480 (1969).

[166] *P. J. Whitman* and *B. M. Trost*, J. Amer. Chem. Soc. *91*, 7534 (1969).

[167] *V. Franzen*, Liebigs Ann. Chem. *603*, 202 (1957).

[168] *S. Hauptmann* and *K. Hirschberg*, J. Prakt. Chem. [4] *34*, 269 (1966).

[169] *M. Regitz* and *J. Rüter*, Chem. Ber. *101*, 1263 (1968).

[170] *M. Regitz* and *J. Rüter*, Chem. Ber. *102*, 3877 (1969).

[171] *S. A. Matlin* and *P. G. Sammes*, J. C. S. Perkin I *1972*, 2623.

[172] *E. Voigt* and *H. Meier*, Angew. Chem., in press.

[173] *J. Quintana, M. Torres*, and *F. Serratosa*, Tetrahedron *29*, 2065 (1973).

[174] *S. Masamune*, J. Amer. Chem. Soc. *86*, 735 (1964).

[175] *S. Masamune* and *N. Castelluci*, Proc. Chem. Soc. *1964*, 298.

[176] *W. von E. Doering* and *M. Pomerantz*, Tetrahedron Lett. *1964*, 961.

[177] *R. Breslow, R. Winter*, and *M. Battiste*, J. Org. Chem. *24*, 415 (1959).

[178] *R. Breslow* and *D. Chipman*, Chem. Ind. (London) *1960*, 1105.

[179] *W. Ried* and *K. Lohwasser*, Liebigs Ann. Chem. *683*, 118 (1965).

[180] *R. Huisgen* and *R. Fleischmann*, Liebigs Ann. Chem. *623*, 47 (1959).

[181] *C. Grundmann*, Liebigs Ann. Chem. *536*, 26 (1938).

[182] *W. Kirmse, L. Horner*, and *H. Hoffmann*, Liebigs Ann. Chem. *614*, 19 (1958).

[183] *H. Reimlinger*, Chem. Ber. *97*, 339 (1964); Angew. Chem. *74*, 153 (1962); Angew. Chem. internat. Edit. *1*, 157 (1962).

[184] *C. Oberger* and *J. Anselme*, J. Org. Chem. *29*, 1188 (1964).

[185] *M. Tanaka, T. Nagai*, and *N. Takura*, Chem. Lett. *1972*, 1207; J. Org. Chem. *38*, 1602 (1973).

[186] *E. Ciganek*, J. Org. Chem. *35*, 862 (1970).

[187] *W. Ando et al.*, J. Amer. Chem. Soc. *91*, 2786 (1969).

[188] *S. A. Matlin* and *P. G. Sammes*, J. C. S. Perkin I *1973*, 2851.

[189] *F. Kaplan* and *G. K. Meloy*, J. Amer. Chem. Soc. *88*, 950 (1966); Tetrahedron Lett. *1964*, 2427.

[190] *H. Kessler* and *D. Rosenthal*, Tetrahedron Lett. *1973*, 393.

[191] *S. Sorrisso* and *A. Foffani*, J. C. S. Perkin II *1973*, 2142.

[192] *G. Piazzo, S. Sorriso*, and *A. Foffani*, Tetrahedron *24*, 4751 (1968); J. Chem. Soc. *B 1971*, 805.

[193] *J. G. Csizmadia et al.*, Tetrahedron *25*, 2121 (1969).

[194] *P. Schuster* and *O. E. Polansky*, Monatsh. Chem. *96*, 396 (1965).

[195] *W. Bartz* and *M. Regitz*, Chem. Ber. *103*, 1463 (1970).

[196] *W. Jungelt* and *D. Schmidt*, Tetrahedron *25*, 969 (1969).

[197] *A. Melzer* and *E. F. Jenny*, Tetrahedron Lett. *1968*, 4503.

[198] *Y. Yukawa, Y. Tsuno*, and *T. Ibata*, Bull. Chem. Soc. Jap. *40*, 2613, 2618 (1967).

[199] *Y. Yukawa* and *T. Ibata*, Bull. Chem. Soc. Jap. *42*, 802 (1969).

[200] *W. Kirmes* and *L. Horner*, Liebigs Ann. Chem. *625*, 34 (1959).

[201] *H. Meier* and *E. Voigt*, unpublished.

[202] *G. Lowe* and *J. Parker*, Chem. Commun. *1971*, 1135; *R. A. Franich, G. Lowe*, and *J. Parker*, J. C. S. Perkin I *1972*, 2034.

[203] *B. Eistert*, Chem. Ber. *68*, 208 (1935); cf. also *A. L. Wilds, N. F. Woolsey, J. van den Berghe*, and *C. H. Winestock*, Tetrahedron Lett. *1965*, 4841.

[204] *U. Mazzucato, G. Canzzo*, and *A. Foffani*, Tetrahedron Lett. *1963*, 1525.

[205] *E. Fahr*, Chem. Ber. *92*, 398 (1959).

[206] *R. Huisgen*, Angew. Chem. *67*, 439 (1955).

[207] *U. Schöllkopf* and *W. Rieber*, Chem. Ber. *102*, 488 (1969).

[208] *O. Tsuge, I. Shinkai*, and *M. Koga*, J. Org. Chem. *36*, 745 (1971).

[209] *W. Ried* and *H. Mengler*, Liebigs Ann. Chem. *678*, 113 (1964).

[210] *W. Ried* and *H. Mengler*, Fortschr. Chem. Forsch. *5*, 27 (1965), and references concerning the stereospecificity of olefin addition cited therein; cf. especially *G. Binsch, R. Huisgen*, and *H. König*, Chem. Ber. *97*, 2893 (1964).

[211] *R. Huisgen, G. Binsch*, and *L. Ghosez*, Chem. Ber. *97*, 2628 (1964).

[212] *K. Nakamura, S. Udagawa*, and *K. Honda*, Chem. Lett. *1972*, 763.

[213] *A. M. Trozzolo* and *S. P. Fahrenholtz*, Abstr. 151st Meeting Amer. Chem. Soc. *1966*, K 23; *A. M. Trozzolo*, Accounts Chem. Res. *1*, 329 (1968).

[214] *H. Meier*, IV IUPAC Symp. Photochemistry *1972*, 163.

[215] *A. Padwa* and *R. Layton*, Tetrahedron Lett. *1965*, 2167.

[216] *D. O. Cowan et al.*, J. Org. Chem. *29*, 1922 (1964).

[217] *M. Jones* and *W. Ando*, J. Amer. Chem. Soc. *90*, 2200 (1968).

[218] *M. Jones*, J. Amer. Chem. Soc. *90*, 2200 (1968).

[219] *F. Weygand et al.*, Angew. Chem. *73*, 409 (1961).

[220] *E. J. Moriconi* and *J. J. Murray*, J. Org. Chem. *29*, 3577 (1964).

[221] *H. Dworschok* and *F. Weygand*, Chem. Ber. *101*, 289, 302 (1968).

[222] *M. J. S. Dewar* and *C. A. Ramsden*, J. C. S. Chem. Comm. *1973*, 688.

[223] *A. C. Hopkinson*, J. C. S. Perkin II *1973*, 794.

[224] *J. G. Csizmadia et al.*, J. Amer. Chem. Soc. *95*, 133 (1973).

[225] *C. Hugget, R. T. Arnold*, and *T. S. Taylor*, J. Amer. Chem. Soc. *64*, 3043 (1942).

[226] *V. Franzen*, Liebigs Abb. Chem. *614*, 31 (1958).

[227] *I. G. Csizmadia, J. Font*, and *O. P. Strausz*, J. Amer. Chem. Soc. *90*, 7360 (1968).

[228] *K.-P. Zeller, H. Meier, H. Kolshorn*, and *E. Müller*, Chem. Ber. *105*, 1875 (1972); cf. also ref. [231].

[228a] *Z. Majerski* and *C. S. Redvanly*, Chem. Commun. *1972*, 694.

[229] *D. E. Thornton, R. K. Gosavi*, and *O. P. Strausz*, J. Amer. Chem. Soc. *92*, 1768 (1970).

[230] *G. Frater* and *O. P. Strausz*, J. Amer. Chem. Soc. *92*, 6654 (1970).

[231] *J. Fenwick, G. Frater, K. Ogi*, and *O. P. Strausz*, J. Amer. Chem. Soc. *95*, 124 (1973).

[232] *P. Heinrich* and *H. Meier*, cf. also ref. [214].

[232a] *K. G. Nogai*, Dissertation, Technische Universität Hannover 1972.

[233] *F. M. Dean* and *A. Robertson*, J. Chem. Soc. *1948*, 1674.

[234] *J. F. Lane* and *F. S. Wallis*, J. Org. Chem. 6, 443 (1941).

[235] K. J. Sax and W. Bergmann, J. Amer. Chem. Soc. 77, 1910 (1955).
[236] N. A. Preobrashenski, A. M. Poljakowa, and W. A. Preobrashenski, Ber. Deut. Chem. Ges. 68, 850 (1935).
[237] J. F. Lane and E. S. Wallis, J. Org. Chem. 6, 443 (1941).
[238] J. F. Lane and E. S. Wallis, J. Amer. Chem. Soc. 63, 1674 (1947).
[239] K. B. Wiberg and T. W. Hutton, J. Amer. Chem. Soc. 78, 1640 (1956).
[240] C. D. Gutsche, J. Amer. Chem. Soc. 70, 4150 (1948).
[241] F. V. Brutcher and D. D. Rosenfeld, J. Org. Chem. 29, 3154 (1964).
[242] J. F. Lane et al., J. Org. Chem. 5, 276 (1940).
[243] K.-P. Zeller, H. Meier, and E. Müller, Liebigs Ann. Chem. 749, 178 (1971).
[244] K.-P. Zeller, H. Meier, and E. Müller, Tetrahedron 28, 5831 (1972).
[245] P. Kinson and B. M. Trost, Tetrahedron Lett. 1964, 1075.
[246] D. C. de Jong, R. Y. Fossen, L. R. Dussold, and M. P. Cava, Org. Mass Spectrom. 3, 31 (1970).
[247] R. J. Mulder, A. M. van Leusen, and J. Stating, Tetrahedron Lett. 1967, 3057.
[248] M. Regitz et al., Tetrahedron Lett. 1968, 3171.
[249] W. Jugelt and D. Schmidt, Tetrahedron 25, 5569 (1969).
[250] B. M. Trost, J. Amer. Chem. Soc. 88, 1587 (1966); 89, 138 (1967).
[251] E. J. Corey and M. Chaykovsky, J. Amer. Chem. Soc. 86, 1640 (1964).
[252] E. M. Burgess, R. Carithers, and L. McCullaugh, J. Amer. Chem. Soc. 90, 1923 (1968).
[253] W. Kirmse and L. Horner, Liebigs Ann. Chem. 614, 4 (1958).
[254] K.-P. Zeller, H. Meier, and E. Müller, Tetrahedron Lett. 1971, 537.
[255] P. Krauss, K.-P. Zeller, H. Meier, and E. Müller, Tetrahedron 27, 5953.
[256] K.-P. Zeller, H. Meier, and E. Müller, Liebigs Ann. Chem. 766, 32 (1972).
[257] H. Meier and I. Menzel, Tetrahedron Lett. 1972, 445.
[258] H. Meier and E. Voigt, Tetrahedron 28, 187 (1972).
[259] H. Meier and I. Menzel, J. C. S. Chem. Comm. 1971, 1059.

Isomerization Polymerization of Lactams

By H. K. Reimschuessel[*]

Isomerization polymerization affords a macromolecule whose repeating unit is derived from an isomer of the original monomer. Thus hexa- and heptacyclic β-carboxymethyllactams yield polymers containing glutarimide units, whereas penta- and hexacyclic β-carboxylactams furnish polymers containing succinimide units. Some dimethyl derivatives of β-carboxylactams isomerize or rearrange, and 5-oxopyrrolidine-3-acetic acid does not react at all. These observations can be explained in terms of a bicyclic intermediate.

1. Introduction

Isomerization polymerization is feasible with substituted lactams containing a carboxylic group capable of interacting with the amide function[1]. Whereas the ordinary ring opening polymerization of lactams yields polyamides, isomerization polymerization affords polyimides. Both processes are characterized by competition between intramolecular cyclization and intermolecular polymerization. In the ordinary ring opening polymerization of lactams the former reaction is part of a polymer-monomer equilibrium, and the product of cyclization is the particular lactam itself. The chemical structure of the repeating unit of the corresponding polymer molecule is in this case identical with that of the opened lactam ring. Of course, this also applies to any cyclic oligomers formed during polymerization. A rather different situation, however, characterizes isomerization polymerization for which no polymer-monomer equilibrium is indicated. The structures of both the propagating species entailed in this polymerization and the product of any cyclization differ from that of the starting lactam. Furthermore, no structural identity exists in this case between the lactam and the repeating unit of the polymer molecule.

[*] Dr. H. K. Reimschuessel
Chemical Research Center, Allied Chemical Corporation
Morristown, N. J. 07960 (USA)

Whether polymerization or cyclization is the dominating reaction depends for either process upon thermodynamic and kinetic factors, and upon the total molecular strain energy of the particular ring structure. This energy is directly related to the sum of all molecular deformations which are usually expressed in terms of:

1) bond stretching or bond compression (a function of the bond length, related to the motion of the bonded nuclei along the internuclear line);

2) bond angle bending (related to the radial scissoring motion of the bond angle—also known as angle strain or Baeyer strain);

3) bond torsion (refers to the rotational motion around the bond axis, related to the dihedral angle—also known as torsional strain, Pitzer strain, bond opposition force);

4) nonbonded interactions (refers to the interaction between substituents on neighboring carbon atoms and depends on the nuclear distance).

The extent to which each type of strain contributes to the total molecular strain depends upon the ring size. In the ordinary ring opening polymerization of lactams it appears that bond angle bending (2) dominates in case of the four-membered rings, whereas torsional forces (3) prevail in the five-, six-, and seven-membered rings, and both torsional forces and nonbonded interactions (4) seem to characterize the larger

rings. In general, the four-, seven-, eight-membered, and larger ring lactams polymerize readily, whereas the five- and six-membered lactams do not polymerize easily. This agrees with results reported by *Dainton et al.*[2], according to which the thermodynamic feasibility with respect to ring-opening polymerization is at a minimum for the five- and six-membered rings. In case of lactams, the six-membered δ-valerolactam (2-piperidone) is the most stable ring and exhibits the least tendency to polymerize.

Regardless of ring size, substituents generally increase both the rate of ring closure and the stability of the ring, and thus decrease the polymerizability of the particular lactam. This is due mainly to conformational effects: both the enthalpy and entropy of reaction are affected by the presence of a substituent. *Cubbon*[3] related the enthalpy of ring closure to the increase in the number of *gauche* interactions between adjacent carbon atoms in lactams. This increase becomes less when a substituent is introduced, *i.e.* the contribution to the enthalpy of ring closure is less than for the unsubstituted lactam. This is reflected in a lower heat of polymerization and a higher monomer equilibrium concentration for lactams such as methyl caprolactam and the respective equilibrium polymers[4].

A substituent has little or no influence on the entropy of the ring compound[2]; however, it has a considerable effect on the entropy of a linear polymer molecule by restricting its rotation. Consequently, introduction of a substituent increases the entropy of ring closure. The magnitude of this entropy increase seems to be directly proportional to both the size and number of the substituents. Thus ring closure of a substituted lactam is characterized by a lower enthalpy and higher entropy than that of the unsubstituted compound. Both effects shift the equilibrium toward the cyclic monomer at the expense of the extent of polymerization.

The above phenomena and rationalizations, however, pertain only to lactams containing substituents that are incapable of reacting with other functions present in the system. If the particular substituent is capable of inter- or intramolecular interaction with the amide function of the lactam such that either a cyclic transition state or a cyclic intermediate results, because the formation of such a cyclic structure is highly favored both geometrically and thermodynamically, then a drastically altered reactivity of the parent ring system could be the consequence.

It is well known that carboxyl groups can react with amide functions. Transamidation and acylation are the main reactions occurring. The present account will therefore consider lactams bearing carboxyl or carboxymethyl groups.

2. Substituted Lactams

The lactams investigated thus far may be divided into three groups: (i) carboxymethyl lactams; (ii) carboxy lactams; (iii) carboxy lactams containing non-reactive substituents. The first group contains 2-oxoperhydroazepine-3- and -4-acetic acid (α- and β-carboxymethylcaprolactam, α-CM7 and CM7 respectively), 2-oxopiperidine-4-acetic acid (4-carboxymethyl-2-piperidone, CM6), and 5-oxopyrrolidine-3-acetic acid (4-carboxymethyl-2-pyrrolidone, CM5). The second group is represented by 2-oxopiperidine-4-carboxylic acid (4-carboxy-2-piperidone, C6) and 5-oxopyrrolidine-3-carboxylic acid (4-carboxy-2-pyrrolidone, C5), and the third group comprises 2,2-dimethyl-6-oxopiperidine-4-carboxylic acid (6,6-dimethyl-4-carboxy-2-piperidone, DMC6), 2,2-dimethyl-5-oxopyrrolidine-3-carboxylic acid (5,5-dimethyl-4-carboxy-2-pyrrolidone, DMC5), 2-methyl-6-oxopiperidine-4-carboxylic acid (6-carboxy-6-methyl-2-piperidone, MC6), the ethyl derivative (EC6), 2-methyl-5-oxopyrrolidine-3-carboxylic acid (4-carboxy-5-methyl-2-pyrrolidone, MC5), and the ethyl derivative (EC5) (see Table 1).

α-CM7 was obtained from α-bromocaprolactam *via* nucleophilic substitution employing sodium diethyl sodiomalonate[5], whereas both CM7 and CM6 were synthesized *via* nucleophilic addition of the malonate anion to the corresponding α,β-unsaturated lactam[6,7]. CM5 was prepared by hydrolysis of its ethyl ester, which was synthesized according to the procedure given by *Henecka et al.*[8,7].

The synthesis of C6 entailed addition of hydrogen cyanide to dialkyl itaconate, and reductive cyclization of the resulting dialkyl cyanomethylsuccinate to alkyl 2-oxopiperidine-4-carboxylate followed by saponification[9]. C5 was obtained from its methyl ester which was synthesized *via* esterification of aminomethylsuccinic acid[10].

DMC6 was synthesized by reductive cyclization of methyl 2-(2-nitroisobutyl)succinate followed by saponification[10]. DMC5 was prepared by the same sequence of reactions[10]. The synthesis of MC6 and EC6 consisted in nucleophilic addition of nitroethane (or 1-nitropropane) to dimethyl itaconate, reductive cyclization of the resulting ester, and subsequent saponification[11]. The synthesis of MC5 and EC5 entailed Michael addition of nitromethane (or 1-nitropropane) to either diethyl maleate or fumarate, reductive cyclization of the resulting ester, and saponification[11].

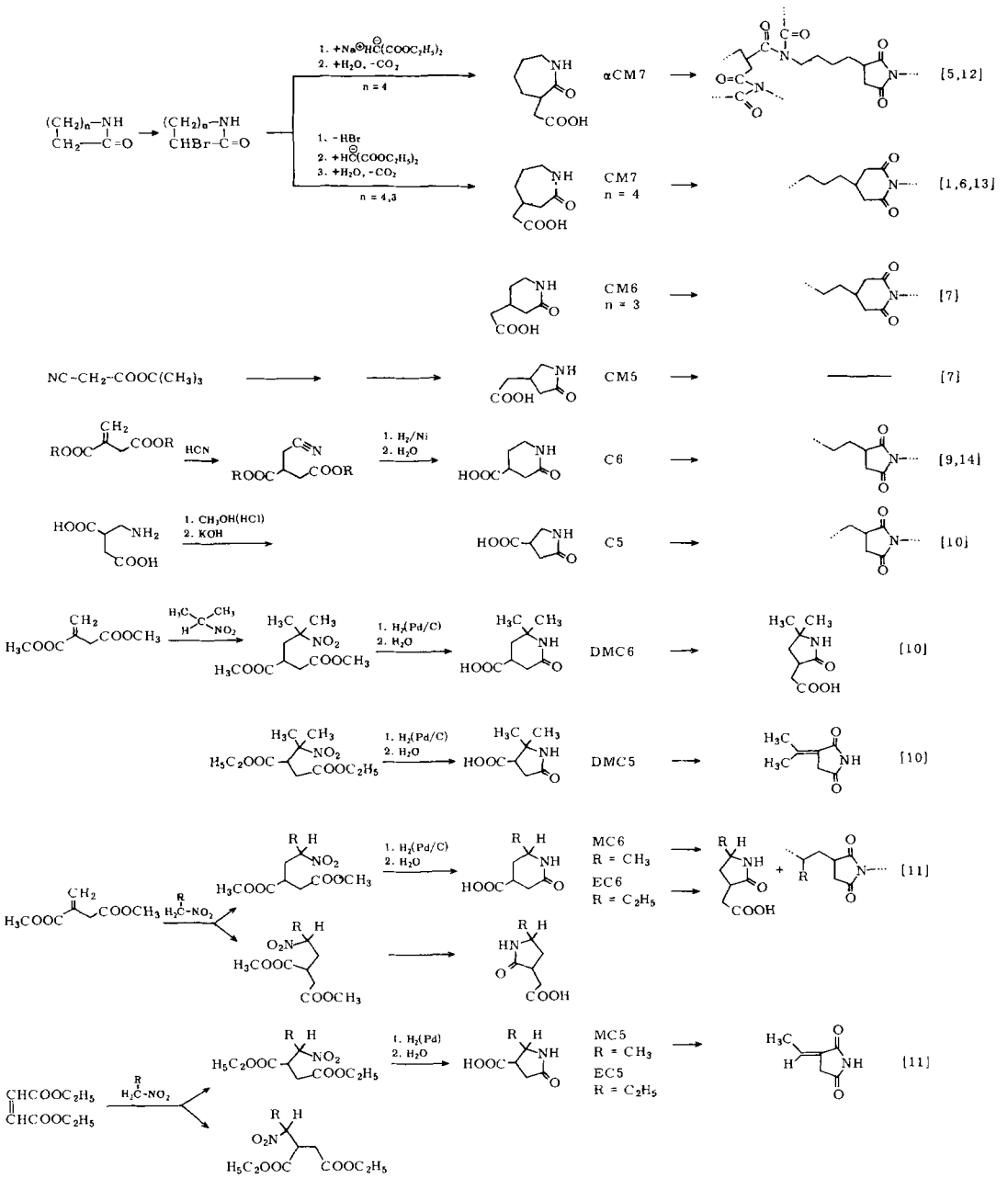
The addition of nitroalkanes to dimethyl itaconate and diethyl maleate (fumarate) yielded in both cases mixtures of diastereoisomers. Thus, in the former case reductive cyclization of the mixtures afforded both MC6 (or EC6) and 5-methyl- (or 5-ethyl)-2-oxopyrrolidine-3-acetic acid, while in the second case MC5 (or EC5) and an appreciable amount of noncrystallizable material were obtained[11]. General reaction schemes are summarized in Table 1.

3. Principal Reactions: Structure and Properties of Reaction Products

Numerous reactions can be envisaged that are peculiar to the functions that characterize the lactams considered. For the present review, however, only those reactions are of interest that are thermally induced by heating a particular lactam in an inert atmosphere to temperatures above its respective melting point. Under these conditions, polymerization and/or rearrangement may occur. Whereas the latter may or may not entail the formation of water, the former always does. CM5 was found to be the only one of four carboxymethyllactams studied that neither polymerized nor rearranged when heated to above its melting point. The others polymerized.

The polymer derived from αCM7 was a colorless transparent material that did not melt or decompose below 300 °C[12]. It was insoluble in all solvents and did not contain soluble

Table 1. Synthesis of carboxy- and carboxymethyl-substituted lactams and structure of their reaction products.



compounds or unreacted monomer. This polymer was obviously highly crosslinked. The polymerization of both CM6 and CM7 resulted in high molecular weight, linear, crystallizable polymers that were soluble in solvents such as formic acid, *m*-cresol, trifluoroethanol, and sulfuric acid, but insoluble in all common organic solvents. The polymer derived from CM6 did not melt below 400 °C but did show signs of decomposition at temperatures above 300 °C. The conversion of monomer into polymer was about 80 to 85 %. Polymerization of CM7 resulted in essentially complete conversion into a polymer that melted at 281 °C and had a glass transition temperature of about 90 °C.

The carboxylactams C6 and C5 polymerized upon heating to temperatures of about 200 °C to form linear amorphous polymers[9, 10] that were soluble in formic acid, *m*-cresol, sulfuric acid, and trifluoroethanol but insoluble in the common organic solvents. Essentially complete conversion of monomer into polymer was also a characteristic of these two cases. The gem-dimethyllactam derivatives did not polymerize but rearranged. Upon heating to temperatures above their respective melting point (232 °C, 206 °C), DMC6 isomerized quantitatively to 5,5-dimethyl-2-oxopyrrolidine-3-acetic acid whereas DMC5 rearranged to isopropylidene succinimide with elimination of water. The occurrence of both polymerization and isomerization upon thermal treatment distinguishes compounds MC6 and EC6. Heating of MC6 or EC6 to 230 °C resulted in both polymerization and the formation of 5-alkyl-2-oxopyrrolidine-3-acetic acid. There was no indication of polymerization when MC5 was heated to temperatures of about 200 °C. The sole reaction product in this case was ethylidenesuccinimide, which was formed with elimination of water.

The structures of both the lactam derivatives and the corresponding reaction products (polymers or/and rearrangement products) are shown in Table 1.

3.1. Spectroscopic Studies

The reaction products were identified by conventional analysis. The chemical structure of the polymers was deduced mainly from the information obtained from infrared and NMR analyses, and solubility characteristics. The infrared spectra of all of the polymers showed strong absorptions related to the imide moiety. Absorptions in the 1675 to 1705 cm^{-1} and 1725 to 1790 cm^{-1} ranges were attributed respectively to asymmetrical and symmetrical carbonyl vibrations, whereas C—N—C antisymmetrical stretching and imide group vibrations accounted for absorptions in the 1350 to 1390 cm^{-1} and 1140 to 1150 cm^{-1} ranges.

A detailed structural analysis has been performed on poly[(2,6-dioxo-1,4-piperidinediyl)trimethylene] (PMC7). This polymer is obtained by thermal polymerization of CM7 (see Table 1)[13]. Depending upon the conditions of polymerization, this polymer could be obtained either as a predominantly crystalline or an essentially amorphous material. Differences observed in the infrared spectra of the crystalline and amorphous polymers have been considered indicative of the existence of two different conformations of the dioxopiperidine ring, which in turn can give rise to two different chain conformations. As indicated in Figure 1a, one is characterized by an equatorial position of the trimethylene moiety with respect to the plane of the imide group, whereas the other (Fig. 1b) pertains to a structural unit in which the trimethylene group is positioned axially to the plane of the ring.

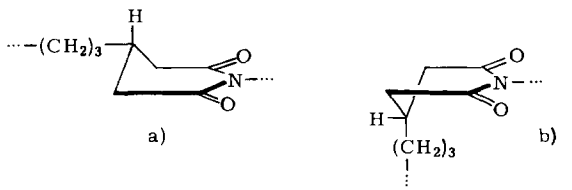


Fig. 1. Conformations of the structural unit in poly[(2,6-dioxo-1,4-piperidinediyl)trimethylene] (PMC7). a) equatorial, b) axial trimethylene group.

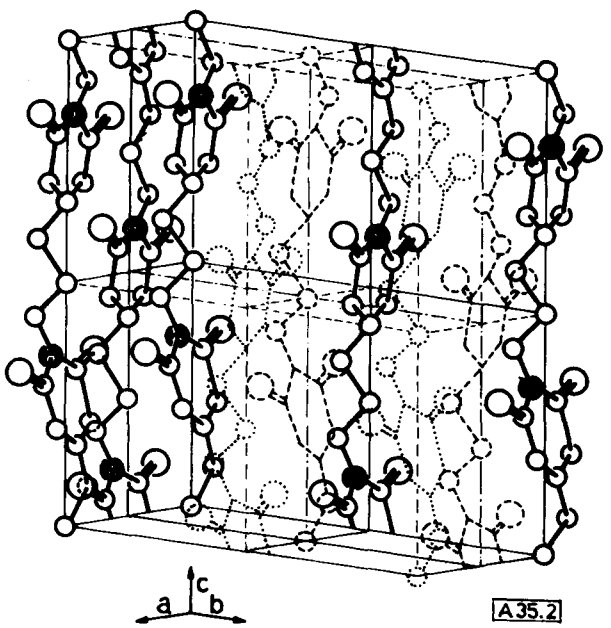


Fig. 2. Configuration of polymer chains in the unit cell of poly[(2,6-dioxo-1,4-piperidinediyl)trimethylene] (PCM7): $a = 9.64$ Å, $b = 11.32$ Å, $c = 15.80$ Å, $\alpha = 98°$, $\beta = 96°$, $\gamma = 114°$.

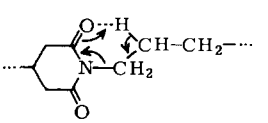
NMR analysis indicated that the axial conformation is the predominant structure of the polymer in formic acid solution. The equatorial conformation has been ascribed to the crystalline modification. This was supported by X-ray analysis, which indicated a triclinic unit cell containing eight structural units (Fig. 2).

The polymer was found to crystallize in positively birefringent spherulites.

The response of the amorphous polymer derived from CM7 to annealing differs from that of polymers such as polyamides and poly(ethylene terephthalate) which readily crystallize when heated above their glass transition temperatures. Even prolonged annealing of the unoriented amorphous polyimide resulted in only insignificant crystallization. Annealing of amorphous polymer which was oriented by cold drawing resulted in rapid and extensive crystallization. However, no crystallization was induced during the orientation process; this is quite different from the behavior of most linear polymers, such as polyamides and polyesters. This phenomenon can be rationalized by assuming that in the glassy state this polyimide contains chain segments of either of the two conformations considered. Crystallization therefore depends, not only upon the mobility of the macromolecules, but also on rate and extent of conformational changes of the dioxopiperidine moiety during the orientation process.

Except for poly[(2,6-dioxo-1,4-piperidinediyl)dimethylene] (PCM6), which is highly crystalline, the other linear polymers of interest (PC6 and PC5) are amorphous. This is readily explained by the presence of an asymmetric center at C^3 of the ring moiety of the repeating unit.

Additional support for the chemical structure of the polymer PCM7 was obtained from mass spectroscopic studies[18]. Subjecting a polymer sample ($\eta_{red} = 2.7$) to 70 eV at 270 °C yielded $[-(CH_2)_3-CH(CH_2CO)_2N-]_2H$, *m/e* 307, as major fragment which corresponds to two repeating units of the polymer. When the monomer was introduced at 270 °C into the preheated source, signals appeared at *m/e* 154, 307, 460, and 613, after unreacted monomer had been flushed off. These values correspond to fragments of the general structure $[-(CH_2)_3-CH(CH_2CO)_2N-]_nH$ where *n* is 1, 2, 3, and 4. A possible mechanism for the formation of these fragments may entail a six-center pyrolysis reaction (see formula) followed by addition of a proton.



3.2 Viscosity-Molecular Weight Relations

The relationship between the viscosities of polymer solutions and polymer molecular weights was studied in detail for poly[(2,6-dioxo-1,4-piperidinediyl)trimethyline] (PCM7) and poly[(2,5-dioxo-1,3-pyrrolidinediyl)dimethylene] (PC6). Intrinsic viscosities were determined in *m*-cresol solutions and evaluated by using the Huggins equation

$$\eta_{sp}/c = [\eta] + k^1[\eta]^2C \qquad (1)$$

The Kuhn-Mark-Houwink-Sakurada equation

$$[\eta] = K_{w(n)} M_{w(n)}^{a} \quad (2)$$

was employed for correlating the viscosities with the molecular weights. The latter were obtained either from light-scattering ($\overline{M}_w$) or osmotic pressure measurements ($\overline{M}_n$). Values for the Huggins constant k^1 and the interaction parameters K and a are listed in Table 2.

Table 2. Values for k^1, $K_{w(n)}$, and a in equations (1) and (2) for PCM7 and PC6.

Polymer	k^1	a	K_w	K_n
PCM7	0.35	0.73	4.5×10^{-4}	7.5×10^{-4}
PC6	0.41	0.65	4.3×10^{-4}	

A Schulz-Flory distribution of molecular weights was indicated by a value of 2 for the ratio $\overline{M}_w/\overline{M}_n$.

The viscosity-molecular weight relations were also derived for these two polymers; the samples exhibited $\overline{M}_w$ values of up to 75000 (PCM7) and 150000 (PC6). However, considerably higher molecular weights are obtainable for these two systems (*e.g.* more than 300000 for PCM7).

3.3. Mechanical Properties

Tensile properties were determined for PCM7 and PC6 according to ASTM D1708 on films obtained by compression molding, and for PCM7 also on monofilaments obtained by melt extrusion and subsequent drawing (draw ratios between 4:1 and 6:1). The values obtained depended upon the molecular weights of the samples and upon the particular conditions of sample preparation. Since no attempts have yet been made to develop optimum processing conditions, the data listed in Table 3 may not be representative of ultimately attainable values. They show, however, that materials of considerable strength are readily obtained.

Table 3. Tensile properties of PCM7 and PC6.

	PCM7 Film	PC6 Film
Tensile strength [kg/mm²]	0.0827—0.124	0.0621—0.110
Elongation [%]	70—90	3—10
Modulus [a] [kg/mm²]	3.103—3.998	2.206—3.585
	PCM7 Monofilament	
Tensile strength [g/denier]	6—8.5	
Elongation [%]	12—16	
Tensile modulus [g/denier]	75—105	

[a] Calculated from the secant at 2% elongation.

The corresponding polymer samples were tested at relative humidities of 0% and 50%. It was found that the moisture content did not significantly affect the tensile properties. This is explained by the rather low equilibrium moisture regain that characterizes these polymers. At relative humidities of 50% and 100%, the moisture content of PCM7 was respectively 0.56 and 1.40%, whereas in case of PC6 it was 3.6 and 11.3%.

3.4. Thermal Characteristics

Differential thermal analysis, loss of stress birefringence, and torsion tests were used to determine the transition temperatures for the linear polyimides. The values are listed in Table 4 together with the main decomposition temperatures as determined by both differential thermal analysis and thermogravimetric analysis at a programmed heating rate of 10°C/min.

Table 4. Thermal analysis data of several polyimides.

	M.p. [°C]	Glass transition [°C]	Main decomposition [°C]
PCM6	>400	168—173	420
PCM7	281	85—91	460
PC6	—	127—135	400
PC5	—	205—210	410

Kinetics and Mechanism

4.1. Kinetic Findings

Information on possible reaction mechanisms was obtained from kinetic studies. The conversions of CM7 into the polyimide PCM7 and of DCM5 into isopropylidene succinimide have been considered as representative examples of the polymerization and rearrangement reactions respectively. In evaluation of experimental polymerization data the extent of reaction

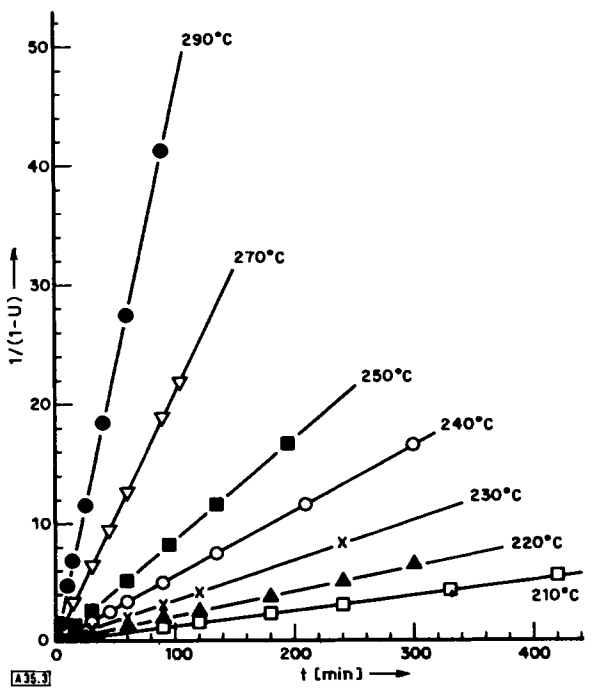


Fig. 3. Second-order rate plot of conversion data for polymerization of CM7 [15].

was assumed to depend upon the momentary concentration of imide groups (I) which is related to the respective concentrations of both unreacted monomer (M) and polymer molecules (c) by the stoichiometric relation:

$$I = M_0 - M - c = U - c \quad (3)$$

Where M_0 is the initial monomer concentration, and U the monomer conversion[15]. From eq. (3) it follows that

$$dI/dt = -dM/dt - dc/dt = dU/dt - dc/dt \quad (4)$$

Experimental data are plotted in Figures 3 and 4. These plots show that both monomer conversion and chain growth

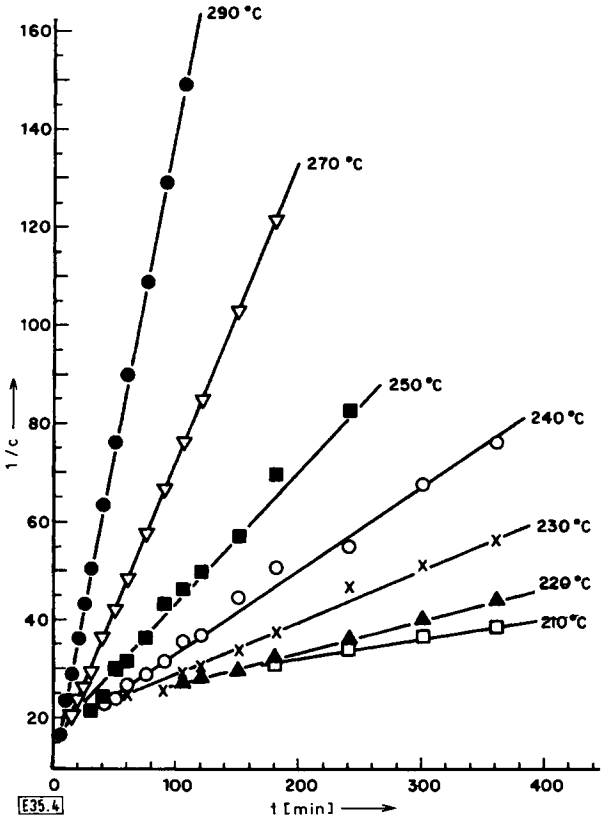


Fig. 4. Second-order rate plot for chain growth on polymerization of CM7 [15].

are second order reactions. For the main phase of the polymerization process considered, the rate of polymerization was found to be adequately represented for the temperature range of 210 to 290 °C by eq. (5):

$$dI/dt = k_p(M^2 + 3.167c^2)$$
$$k_p = 74.9 \times 10^7 \exp(-23800/RT) \quad (5)$$

The conversion of DMC5 into isopropylidene succinimide was studied at the temperatures of 225, 232, and 240 °C[10]. This reaction is also of second order (Fig. 5). The mole fraction x of DMC5 was calculated from the relation $x = a_1/(a_1 + a_2)$ where a_1 and a_2 are the areas of the peaks at $\delta = 1.10$, 1.35 and 1.78, 2.20, respectively, in the corresponding NMR spectrum.

The slopes of the straight lines in Figure 4 represent values for the overall rate constant k_r at the particular temperatures. The temperature dependence of k_r was found to obey the Arrhenius equation, and the activation energy E and the pre-

(the lactam carbonyl function) and a nucleophile (the carboxship

$$\log k_r = \log A - E/(4.574T) \quad (6)$$

to be $A = 25.85 \times 10^{12}$ and $E = 34.346$ kcal/mol.

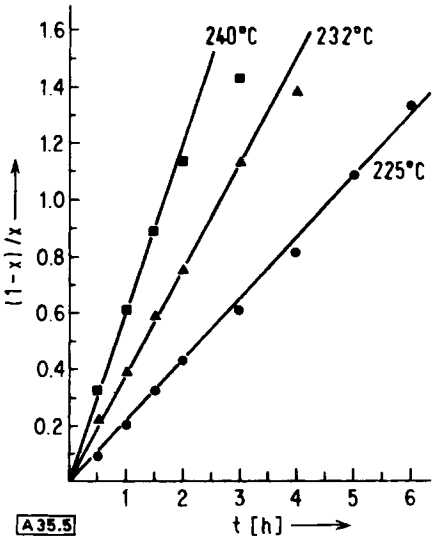
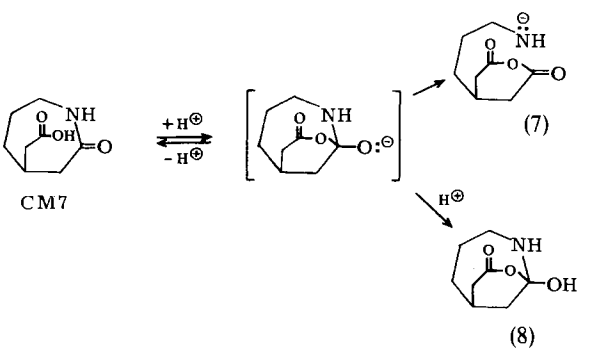


Fig. 5. Conversion of DMC5 into isopropylidene succinimide.

4.2. Mechanism

Comparing the structures of the lactams listed in Table 1 with those of their reaction products indicates that conversion into polymers or transformation into different monomeric ring systems involves isomerization. In the case of CM7, isomerization could be explained in terms of the commonly accepted carbonyl addition-elimination mechanism [eq. (7)][16].

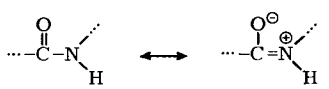


Polymer formation would then consist in polycondensation of the isomerization product *via* an intermolecular reaction between the amino- and anhydride functions of the 3-(3-aminopropyl)glutaric anhydride. Whereas second order kinetics can be readily accommodated for this polycondensation which affects the concentration of the polymer molecules c, a simple isomerization according to eq. (7) should obey first order kinetics. Operation of second order kinetics over fairly large ranges of monomer conversion therefore suggests that the isomerization process may be governed by a more complex mechanism.

On reaction with carboxylic acids, lactams act as nucleophiles of moderate basic power and thus convert acids into their conjugate bases. Since the carboxymethyl- and carboxy lactams under consideration contain both an electrophilic group (the lactam carbonyl function) and a nucleophile (the carboxylate ion) in the same molecule, a bicyclic intermediate of the type shown in eq. (7) will form if the configuration of the particular lactam is conducive to ring formation. The competitive intermolecular reaction is thermodynamically less favored in this case.

It is therefore reasonable to postulate formation of a bicyclic intermediate as the principal initial reaction. Once formed it may undergo any of three fast reactions: (i) elimination of the internal nucleophile from the lactam carbonyl carbon atom; (ii) elimination of the amino moiety; (iii) addition of a proton. The first reaction would be a reversal of the cyclization and thus regenerate the original lactam derivative. The second reaction is the one depicted in eq. (7) for CM7. It is however incompatible with the observed kinetics. Furthermore, this reaction could not participate in the rearrangement of DMC5 to isopropylidenesuccinimide since no opening of the lactam ring was indicated. The third reaction, considered less likely in most of the ordinary addition-elimination reactions involving carboxylic acid derivatives, entails the addition of a proton to the electron pair that stems from the carbon-oxygen double bond of the lactam and has become localized on the oxygen atom.

This addition, as illustrated in eq. (8) for CM7, stabilizes the bicyclic structure by precluding the attainment of coplanarity required for regeneration of the amide moiety.



For the lactam derivatives considered addition of a proton therefore seems to be the most likely reaction. It apparently leads to stable bicyclic structures that have a finite existence and are presumed to be the principal reaction intermediates. The overall kinetics of the conversion of the particular lactam derivatives may thus be determined by reactions involving these species. The second order kinetics observed for the conversion of both the polymerizing lactam derivatives and those that rearrange to monomers may be explained by mechanisms that involve either electrophilic catalysis or interaction between two of the considered protonated species.

Conceivable mechanisms entailing catalysis by ionizable carboxy groups are shown in Figure 6 for the conversion of CM7, rearrangement of DMC5, and isomerization of DMC6.

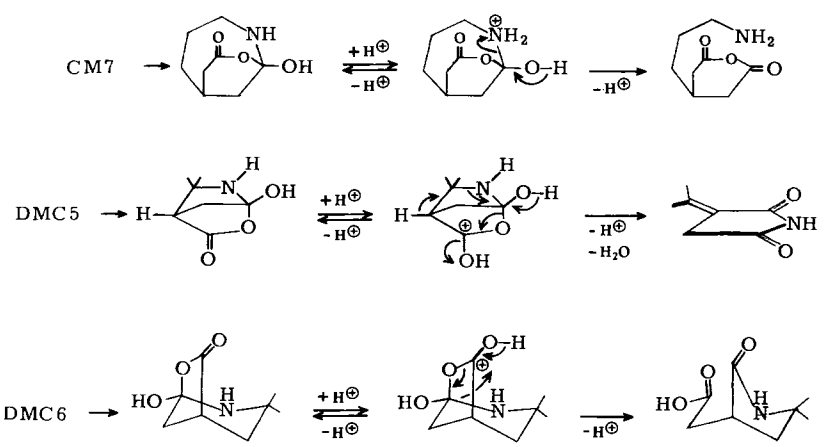


Fig. 6. Electrophilic catalysis in the reaction of carboxy-substituted lactams.

The rate of conversion may be expressed by eq. (9):

$$-dM/dr = k_c[COOH][M] = k_c[M]^2 \qquad (9)$$

according to which the second order kinetic representation can be readily rationalized.

Alternative mechanisms characterized by interactions between intramolecularly protonated species, are illustrated in Figure 7 for the conversion of CM7 and the rearrangement of DMC5. Both involve bimolecular reactions. Whereas the former is an association reaction resulting in the linear dimer of the corresponding polymer, the formulation of the latter corresponds to that of an exchange reaction leading to the succinimide derivative and regeneration of the original pyrrolidone derivative.

Both are multi-center reactions proceeding with elimination of water and rearrangement *via* a six-membered cyclic transition state. In both cases the arrangement yields a coplanar species that has a lower free energy than the strained and highly organized corresponding polycyclic structure. In case of DMC5 the coplanar structure represents the final product, whereas in case of CM7 the coplanar iminolactone rearranges *via* a four-center reaction to the energetically even more favored linear dimer.

Whether it is electrophilic catalysis or a complex bimolecular reaction that constitutes the principal mechanism for the conversion of the particular lactam derivatives cannot be deduced conclusively from presently available information. However, mass spectroscopic examination[18] of low molecular weight polymer which had been obtained from CM7 at temperatures between 200 and 220 °C showed the presence of a *cyclic* dimer. This was not observed in case of high molecular weight samples obtained by polymerization above 280 °C. It could also be shown that this cyclic structure did not result from pyrolysis reactions; it actually disappeared upon prolonged heating at 275 to 300 °C while the linear pyrolysis products $[-(CH_2)_3CH(CH_2CO)_2N-]_nH$ mentioned in Section 3.1 started to appear. This is indicative of the ability of the cyclic dimer to polymerize by ring opening. A possible mechanism for its formation during the initial polymerization reaction is shown in Figure 8.

Molecular models of this cyclic dimer are strain-free.

Detection of the cyclic dimer in the initial reaction products lends some support for the bimolecular reaction mechanism shown in Figure 7. Formation of a bicyclic structure, involving intramolecular nucleophilic addition of the carboxylate ion to the lactam carbonyl group and addition of a proton, appears

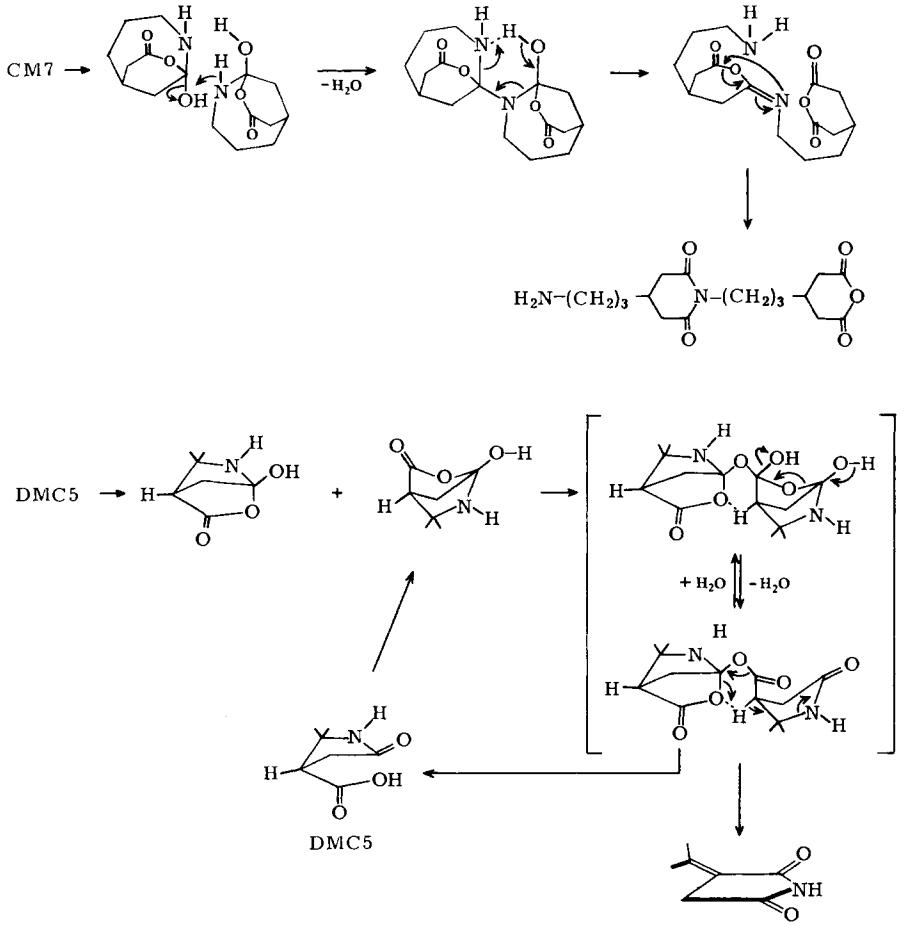


Fig. 7. Bimolecular reactions occurring in the conversions of carboxy-substituted lactams.

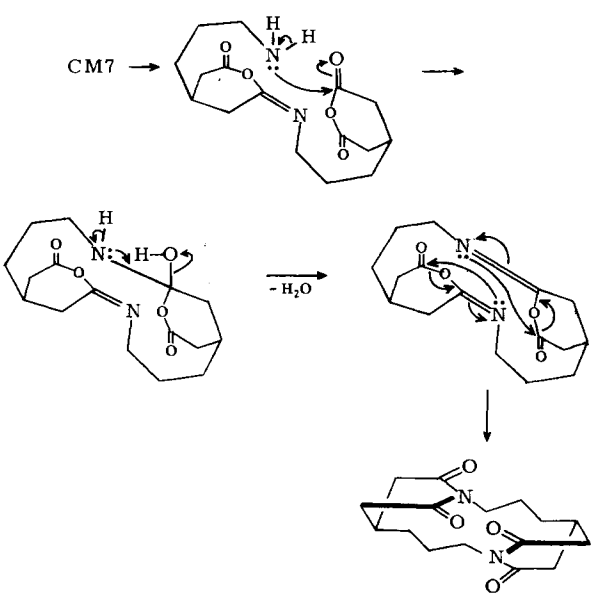


Fig. 8. Formation of cyclic dimer of CM7.

to be the initial reaction in either mechanism. This postulate is further substantiated by the observation that neither polymerization nor rearrangement occurred when the corresponding ester lactams were employed in place of the carboxylactams.

The type of reactions that could be expected in case of the ester lactams was indicated when addition was carried out with 1,5,6,7-tetrahydroazepin-2-one and ethyl phenylacetate. Instead of the expected Michael adduct to the double bond a bicyclic compound was obtained and identified as 6-phenyl-1-azabicyclo[3.2.2]nonane-7,8-dione[17]. As shown in Figure 9, the Michael adduct undergoes cyclization by nucleophilic

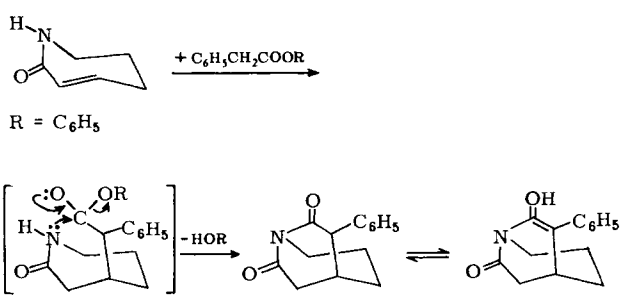
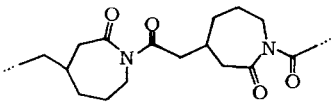


Fig. 9. Formation of 6-phenyl-1-azabicyclo[3.2.2]nonane-7,8-dione.

attack of the amide function on the ester carbonyl with subsequent elimination of ethanol. The formation of this compound demonstrates rather clearly the effect of a substituent on the ease of cyclization. Under comparable conditions this particular reaction did not occur when the phenyl group was replaced by a hydrogen atom, neither was there any indication in this case for the occurrence of the corresponding intermolecular reaction which would have resulted in a polymer having seven-membered rings.



Furthermore, with respect to the ring size, it is well known that among the lactams the six-membered 2-piperidones exhibit the least tendency toward ring-opening polymerization, whereas the five-membered 2-pyrrolidones polymerize rather readily. If one were to assume that the phenomena related to the carboxy group containing lactams were merely the result of some type of activation of the amide bond, then the reactivities of the particular derivatives should in any instance parallel those of the corresponding parent lactams. We have seen that this is not the case: CM6 polymerizes fairly easily upon heating, whereas CM5 did not react at all under corresponding conditions. It has therefore been concluded that a bicyclic intermediate (see, *e.g.*, Fig. 10a) is the reactive species in both polymerization and rearrangement, and that the ability to form such a structure is a necessary condition for the conversion of carboxy- and carboxymethyllactams. The nonreactivity of the CM5 thus appears to be a consequence of this compound's inability to form a corresponding bicyclic structure, as it is indicated in Figure 10b and easily demonstrated with molecular models.

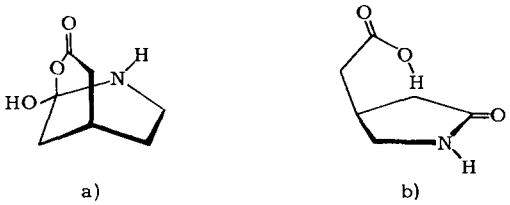


Fig. 10. a) Bicyclic intermediate derived from 2-oxopiperidine-4-acetic acid (CM6); b) structure of 5-oxopyrrolidine-3-acetic acid (CM5).

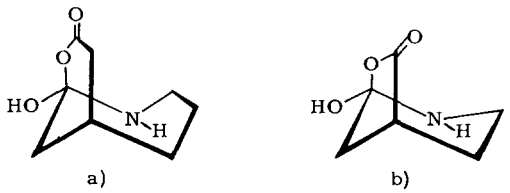


Fig. 11. Bicyclic intermediates derived from a) 2-oxoperhydroazepine-4-acetic acid (CM7) and b) 2-oxopiperidine-4-carboxylic acid (C6).

There appears to be a reciprocal relation between the extent of reaction and the degree of bond angle distortion in the corresponding bicyclic intermediate. Bicyclic structures characterized by essential absence of bond angle bending pertain, as shown in Figure 11, to CM7 and C6. For both compounds the extent of reaction was particularly high with respect to both the monomer conversion and the degree of polymerization. In case of the 6,6-dimethylpiperidone derivative, isomerization to the 5,5-dimethyl-2-oxopyrrolidine-3-acetic acid was essentially quantitative. This is another instance where elimination of nonbonded interactions by introduction of substituents results in a ring formation rather than polymerization.

In contrast, both the conversion in rearrangement reactions and the molecular weights in case of polymerization were low when the attainment of the postulated bicyclic intermediate was accompanied by appreciable bond angle distortion, as indicated for the pyrrolidone derivatives. Whereas CM7, as shown in Figure 11a, can form the bicyclic intermediate with essentially no distortion of bond angles, stereo models indicate that a corresponding structure derived from αCM7 is not favored, though not impossible, since it would be highly strained. It is conceivable that this strain contributes to the observed intermolecular crosslinking occurring upon polymerization, which in this case should result in a polymer structure containing succinic imide units.

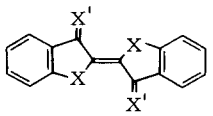
Received: May 7, 1974 [A 35 IE]
German version: Angew. Chem. *87*, 43 (1975)

[1] See *H. K. Reimschuessel*, J. Polym. Sci. Polym. Lett. *B 4*, 953 (1966).
[2] *F. S. Dainton* and *K. J. Ivin*, Quart. Rev. Chem. Soc. *12*, 61 (1958).
[3] *R. Cubbon*, Makromol. Chem. *80*, 44 (1964).
[4] *A. Schaffler* and *W. Ziegenbein*, Chem. Ber. *88*, 1374, 1906 (1955).
[5] *H. K. Reimschuessel*, J. Heterocycl. Chem. *1*, 193 (1964).
[6] *H. K. Reimschuessel*, *J. P. Sibilia*, and *J. V. Pascale*, J. Org. Chem. *34*, 959 (1969).
[7] *H. K. Reimschuessel*, Trans. N. Y. Acad. Sci. Ser. II, *33*, 219 (1971).
[8] *H. Henecka*, *U. Hörlein*, and *K. H. Risse*, Angew. Chem. *72*, 960 (1960).
[9] *H. K. Reimschuessel*, *K. P. Klein*, and *G. J. Schmitt*, Macromolecules *2*, 567 (1969).
[10] *K. P. Klein* and *H. K. Reimschuessel*, J. Polym. Sci. *A-1*, *9*, 2717 (1971).
[11] *K. P. Klein* and *H. K. Reimschuessel*, J. Polym. Sci. *A-1*, *10*, 1987 (1972).
[12] *H. K. Reimschuessel*, US-Pat. 3384625, Brit. Pat. 1042640 (1965), Allied Chemical.
[13] *H. K. Reimschüssel*, *L. G. Roldan*, and *J. P. Sibilia*, J. Polym. Sci. *A-2*, *6*, 559 (1968).
[14] *H. K. Reimschuessel* and *K. P. Klein*, J. Polym. Sci. *A-1*, *9*, 3071 (1971).
[15] *H. K. Reimschuessel*, Advan. Chem. Ser. *91*, 717 (1969).
[16] *M. L. Bender*, Chem. Rev. *60*, 53 (1960).
[17] *H. K. Reimschuessel* and *J. V. Pascale*, unpublished work.
[18] *E. R. McCarthy*, *J. S. Smith*, and *H. K. Reimschuessel*, unpublished work.

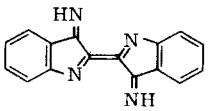
"Indigo Diimine"—A Tautomer with Unsymmetrical Structure[1]

By *Hartmut Sieghold* and *Wolfgang Lüttke*[*]

We have investigated the ways in which the light absorption of the indigo dyes *(1)* is influenced by variation of the electron-acceptor groups X'.

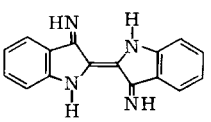


(1a), X = NH, X' = O
(1b), X = X' = NH[≡*(2a)*]
(1c), X = S, X' = NH
(1d), X = S, X' = O

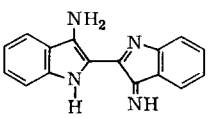


(3)

On spectroscopic characterization of "indigo diimine" *(1b)*[2] we were surprised to find that the substance does not exist in the symmetrical form *(2a)* but in the tautomeric form as 3-amino-2-(3-imino-2-indolyl)-1*H*-indole *(2b)*, both in solution and in the solid state.



(2a) [≡*(1b)*]



(2b)

This structural assignment is based on the following arguments analysis of the IR spectrum (Table 1):

1) The fact that the spectrum is more complex than that of the symmetrical indigo *(1a)* indicates the absence of a center of symmetry.

2) *Four* NH stretching vibrations appear in the IR spectrum of "indigo diimine" both in the solid state and in C_2Cl_4 solution.

3) Partial deuteration[3] proved that the bands at 3441 and 3388 cm^{-1} belong to a primary amino group (appearance of a new NH absorption of the NHD group at 3420 cm^{-1}).

4) The absorption at 3227 cm^{-1} must be assigned to the NH stretching vibration of the ketimino group of *(2b)*[4]. For comparison we synthesized dehydroindigo diimine *(3)* (3219 cm^{-1}) and thioindigo diimine *(1c)*[5] (3234 cm^{-1}).

5) We assign the remaining band at 3286 cm^{-1} to the NH stretching vibration in the indole ring of *(2b)*. [Cf. ν_{NH} of indigo *(1a)*: 3268 cm^{-1}.]

6) ^{15}N labeling of the exocyclic nitrogen atoms shifts the bands at 3441, 3388, and 3227 cm^{-1} strongly, whereas the band at 3286 cm^{-1} exhibits only a small isotope effect. This supports the assignment given in 3–5 above and proves the presence of *(2b)*. The small isotope effect of the band at 3286 cm^{-1} is explained by strong coupling of this stretching vibration with ^{15}N—H vibrations favored by intra- and inter-molecular hydrogen bonding.

7) Four new bands, not present in the indigo spectrum, appear between 1650 and 1500 cm^{-1}; they belong to the complex vibrations of the vinylogous amidine system NH_2—C=C—C=N—.

In addition there are arguments from the ^1H-NMR spectrum in favor of the unsymmetrical structure *(2b)*.

Theory[6] (HMO and PPP calculations) predicts a *hypsochromic shift* of the long-wavelength absorption maximum of the *symmetrical* indigo dye *(1)* when the carbonyl groups (X' = O) are replaced by ketimino groups (X' = NH). We were able to confirm this in the cases of thioindigo *(1d)* which cannot undergo tautomerism and its diimine *(1c)*: their long-wavelength bands (in $CHCl_3$) are at 547 and 518 nm, respectively[6].

Theory also requires that an *unsymmetrical* form such as *(2b)* always absorb at *longer wavelength* than the *symmetrical* one. Experimentally, the absorption maximum of *(2b)* (in $CHCl_3$ solution) is observed at 617 nm, which compares with 604 nm for indigo *(1a)*.

All physical data show, in agreement with theoretical studies, that the unsymmetrical tautomer *(2b)* is the stable form in the solid state and in solution.

Table 1. NH stretching vibration frequencies ν of 3-amino-2-(3-imino-2-indolyl)-1*H*-indole *(2b)* in the associated and monomeric state, together with isotopic shifts Δν on partial deuteration and ^{15}N labeling.

In KBr ν [cm^{-1}]	In C_2Cl_4 soln. ν [cm^{-1}]	D-Labeling [a] in KBr ν [cm^{-1}]	D-Labeling [a] Δν [cm^{-1}]	^{15}N Labeling [b] in KBr ν [cm^{-1}]	^{15}N Labeling [b] Δν [cm^{-1}]	Assignment
3227	3258	2385	−842	3221	−6	$\nu_{=NH}$
3286	3305	2414	−872	3283	−3	$\nu_{>NH}$
3388	3395	2522 (3420)	−866	3382	−6	ν_s (NH_2) (ν_{NHD})
3441	3480	2573	−868	3432	−9	ν_{as} (NH_2)

[a] Partial deuteration of the amino group.
[b] Labeling of the exocyclic nitrogen atoms.

The question of the parent chromophore of this unsymmetrical dye remains a subject for further study.

Received: May 29, 1974 [Z 58 IE]
German version: Angew. Chem. *87*, 63 (1975)
Publication delayed at authors' request

CAS Registry numbers:
(2a), 52147-65-6; *(2b)*, 52147-66-7

[*] Dr. H. Sieghold and Prof. Dr. W. Lüttke
Organisch-Chemisches Institut der Universität
34 Göttingen, Windausweg 2 (Germany)

[1] Theoretical and Spectroscopic Investigations of Indigo Dyes, Part 17.—Part 16: *E. Wille* and *W. Lüttke*, Chem. Ber. *106*, 3240 (1973).

[2] *W. Madelung*, Ber. Deut. Chem. Ges. *46*, 2259 (1913); *W. Madelung*, Liebigs Ann. Chem. *405*, 58 (1914).

[3] *A. G. Moritz*, Spectrochim. Acta *18*, 671 (1962); *A. J. Boulton* and *A. R. Katritzky*, Tetrahedron *12*, 51 (1961); *N. Bacon*, *A. J. Boulton*, *R. T. C. Brownlee*, *A. R. Katritzky*, and *R. D. Topsom*, J. Chem. Soc. *1965*, 5230.

[4] *R. Mathis-Noel*, *Ph. Puig*, and *P. Bourbon*, C. R. Acad. Sci. *C 264*, 1252 (1967); *G. Geiseler* and *A. Jánossy*, J. Mol. Struct. *11*, 393 (1972); *W. Kalus*, Diplomarbeit, Universität Göttingen 1963.

[5] *K. Fries* and *E. Hemmecke*, Liebigs Ann. Chem. *470*, 1 (1929).

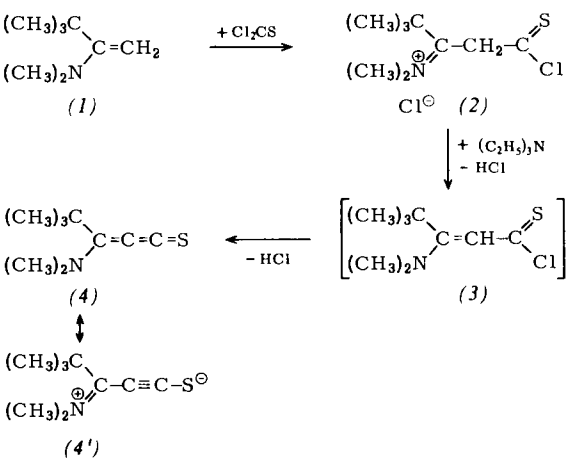
[6] *H. Sieghold*, Dissertation, Universität Göttingen 1973.

Synthesis of a Stable Substituted Thiacumulene: The Concept of Cumulogy

By *Michel Parmantier, Jean Galloy, Maurice Van Meerssche,* and *Heinz Günter Viehe*[*]

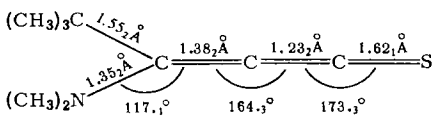
Hetero-trienes and -tetraenes having cumulated double bonds are rare, and expectedly very reactive compounds. We have now synthesized 3-dimethylamino-4,4-dimethyl-1,2-pentadiene-1-thione *(4)*.

Addition of thiophosgene to a solution of 2-dimethylamino-3,3-dimethyl-1-butene *(1)* in ether forms the salt *(2)* which loses HCl on treatment with triethylamine at $-20°C$ to produce *(4)*. The vinylogous thiocarbamoyl chloride *(3)* assumed as intermediate was not isolated.

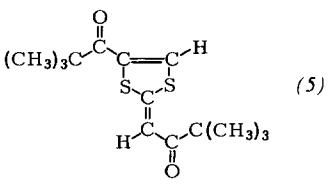


Compound *(4)* melts at 114°C. Further physical data: IR ($CHCl_3$): 2980, 2035, 1530, 1405, 1370 cm^{-1}; UV ($CHCl_3$): $\lambda_{max} = 380$ nm; ^{1}H-NMR ($CDCl_3$): $\delta = 3.4$ (6H, s); 1.4 ppm (9H, s); mass spectrum: $m/e = 169$ (M^+), 154 ($M - CH_3$), 125 [$M - N(CH_3)_2$], 112 [$M - C(CH_3)_3$]; 68 ($S{=}C{=}C{=}C^+$); relative molecular mass (osmometry in $CHCl_3$): 171.

While the expected resonance form *(4')* does not show up in the IR spectrum, its participation is apparent from the ^{13}C-NMR spectrum [two *N*-methyl signals at 41.1 and 47.6 ppm in C_6D_6; only one *N*-methyl signal at 45.8 ppm for *(1)*] and likewise from the X-ray analysis [mean values of two crystallographically independent molecules are shown in *(4a)*].



(4a)

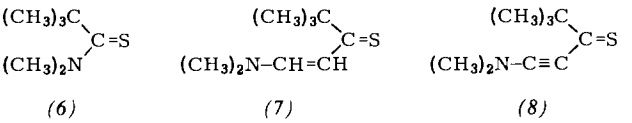


(5)

[*] Prof. Dr. H. G. Viehe and M. Parmantier
Laboratoire de Chimie Organique de l'Université de Louvain
Lavoisier C3, Place L. Pasteur 1
B-1348 Louvain-la-Neuve (Belgium)
Prof. Dr. M. Van Meerssche and J. Galloy
Laboratoire de Chimie Physique et Cristallographie de l'Université de Louvain

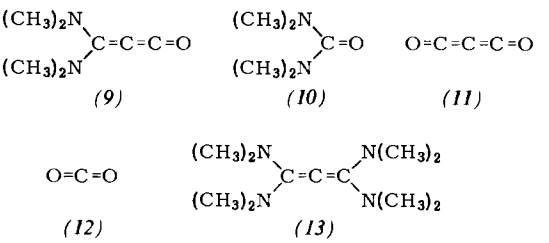
On attempted recrystallization from hexane, *(4)* hydrolyzed and dimerized to *(5)* whose structure was established by X-ray analysis.

We regard compound *(4)* as the "cumulog" of *(6)*, in the same way as *(7)* and *(8)* can be viewed as vinylog and ethynylog of *(6)*, respectively.



(6) *(7)* *(8)*

This cumulogy concept appears heuristically useful in the synthesis of new classes of compounds and in predicting their reactivity. Thus, one might regard the still hypothetical compound *(9)* as the cumulog of tetramethylurea *(10)*, the relatively stable carbon suboxide *(11)* as the cumulog of carbon dioxide *(12)*, and our recently reported[1] allenetetramine *(13)* is the cumulog of methanetetramine. Cumulogous phosphorus ylides are also known[2].



(9) *(10)* *(11)* *(12)* *(13)*

Synthesis of (4):

To a stirred solution of *(1)* (2.5 g, 0.02 mol) and triethylamine (5.6 ml, 0.04 mol) in ether (50 ml) at $-20°C$ is added (during 10 min under nitrogen) thiophosgene (2.3 g, 0.02 mol) dissolved in diethyl ether (20 ml). Stirring is continued until room temperature is attained (*ca.* 30 min). After filtration of the reaction mixture the filtrate is concentrated in vacuum until crystallization occurs. Recrystallization from ether or hexane with traces of dichloromethane affords 0.51 g (15%) of *(4)*.

Received: July 1, 1974 [Z 103 IE]
German version: Angew. Chem. *87*, 33 (1975)
CAS Registry numbers:
(1), 7694-51-1; *(2)*, 53352-49-1; *(4)*, 53352-50-4; thiophosgene, 463-71-8

[1] *H. G. Viehe, Z. Janousek, R. Gompper,* and *D. Lach,* Angew. Chem. *85*, 581 (1973); Angew. Chem. internat. Edit. *12*, 566 (1973); *H. G. Viehe* and *Z. Janousek, ibid. 85*, 837 (1973) and *12*, 806 (1973), respectively.

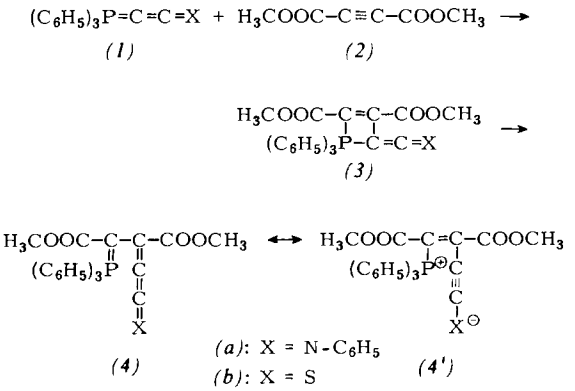
[2] *C. N. Matthews* and *G. H. Birum,* Tetrahedron Lett. *1966*, 5707; J. Amer. Chem. Soc. *90*, 3842 (1968); *H. J. Bestmann* and *G. Schmid,* Angew. Chem. *86*, 274 (1974); Angew. Chem. internat. Edit. *13*, 273 (1974).

Synthesis of a Stable Alkylideneketenimine and an Alkylidenethioketene

By *Hans Jürgen Bestmann, Günter Schmid,* and *Dieter Sandmeier*[*]

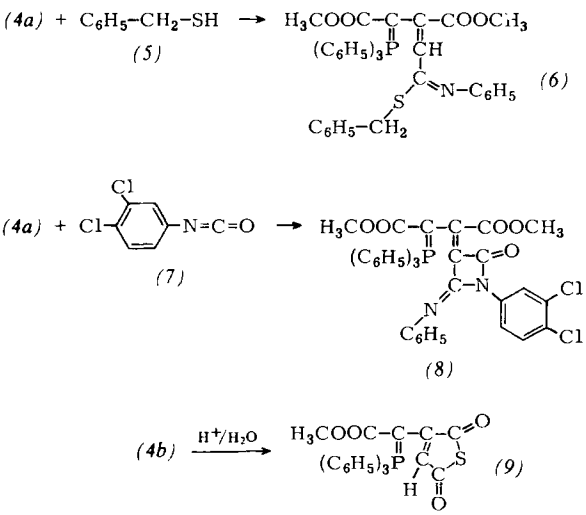
Alkylideneketenimines have previously been known only as unisolable, very reactive intermediates[1], and alkylidenethioketenes have not so far been found at all. We have now synthesized the first stable members of both classes of compounds, by reaction of *N*-phenylketeniminylidenetriphenylphosphorane *(1a)*[2] or thioketenylidenetriphenylphosphorane *(1b)*[2] with dimethyl acetylenedicarboxylate *(2)*.

[*] Prof. Dr. H. J. Bestmann, Dr. G. Schmid, and Dipl.-Chem. D. Sandmeier
Institut für Organische Chemie der Universität Erlangen-Nürnberg
852 Erlangen, Henkestrasse 42 (Germany)



We assume that compounds *(1)* and *(2)* first yield 1-λ^5-phospha-2-cyclobutenes *(3)*, which transform into the red *N*-phenylalkylideneketenimine *(4a)* or the ocher-colored alkylidenethioketene *(4b)* by valence isomerization[3].

(4a): Yield 70%; m.p. 179—180°C; IR: 2080 ($\nu_{C=C=C=N}$), 1724, 1667 cm^{-1} (ν_{CO}); ^{1}H-NMR: τ=6.20, 6.76 ($2OCH_3$); ^{31}P-NMR: δ = −16.88 ppm[4]; MS: M^+ 519.—*(4b)*: Yield 74%; m.p. 170—171°C; IR: 2000 ($\nu_{C=C=C=S}$), 1720, 1690 cm^{-1} (ν_{CO}); ^{1}H-NMR: τ=6.21, 6.68 ($2OCH_3$); ^{31}P-NMR: δ = −15.94 ppm[4]; MS: M^+ 460.



The stability of compounds *(4)* can be explained by the possibility of resonance *(4)* ↔ *(4')*. *(4a)* is more reactive than *(4b)*. We attribute this to the preponderance of the resonance structure *(4b')* that results from the low tendency of sulfur to undergo double-bonding. With phenylmethanethiol, *(4a)* reacts to give the phosphorane *(6)* (m.p. 118°C, dec.) and with 3,4-dichlorophenyl isocyanate *(7)* by cycloaddition to give *(8)* (m.p. 215°C, dec.). If aqueous hydrochloric acid is allowed to act on *(4b)* the thioanhydride *(9)* (m.p. 218°C) is formed. All the new compounds give the expected molecular spectroscopic results and correct elemental analyses.

Received: July 8, 1974 [Z 104 IE]
German version: Angew. Chem. *87*, 34 (1975)

CAS Registry numbers:
(1a), 21385-80-8; *(1b)*, 17507-47-0; *(2)*, 762-42-5; *(3a)*, 53352-21-5; *(3b)*, 53352-52-6; *(4a)*, 53352-53-7; *(4a')*, 53352-54-8; *(4b)*, 53352-55-9; *(4b')*, 53352-56-0; *(5)*, 100-53-8; *(6)*, 53352-57-1; *(7)*, 102-36-3; *(8)*, 53352-58-2; *(9)*, 53466-50-5

[1] *H. J. Bestmann* and *G. Schmid*, Angew. Chem. *86*, 479 (1974); Angew. Chem. internat. Edit. *13*, 473 (1974).

[2] *H. J. Bestmann* and *G. Schmid*, Angew. Chem. *86*, 274 (1974); Angew. Chem. internat. Edit. *13*, 273 (1974).

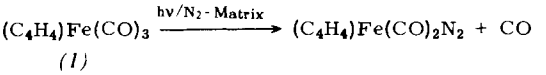
[3] *H. J. Bestmann* and *O. Rothe*, Angew. Chem. *76*, 569 (1964); Angew. Chem. internat. Edit. *3*, 512 (1964).

[4] Pulse Fourier transform spectra, recorded with a PFT 100 instrument manufactured by Jeol (Tokyo), with H_3PO_4 as internal standard.

μ-Carbonylbis(cyclobutadienecarbonyliron), a Complex Containing an Iron-Iron Triple Bond—A Model for the Unusual Behavior of $Fe(CO)_4$ in Solution?[**]

By *Ingrid Fischler*, *Knut Hildenbrand*, and *Ernst Koerner von Gustorf*[*]

In continuation of our photochemical studies on dinitrogen complexes of transition metals[1] we have examined whether the photochemical substitution of CO by N_2 in arenetricarbonylchromium complexes discovered by *Sellmann et al.*[2] can also be applied to dienecarbonyliron complexes. Preliminary experiments with cyclohexadienetricarbonyliron and bis(cyclohexadiene)monocarbonyliron[3a] proved unsuccessful. However, parallel studies by *Rest*[3b] showed that in an N_2 matrix at 20°K CO can be replaced photochemically by N_2 in cyclobutadienetricarbonyliron *(1)* and in trimethylenemethanetricarbonyliron.



Irradiation ($\lambda \geq 280$ nm) of *(1)* in tetrahydrofuran (THF) at −40°C with passage of N_2 gave rise to a color change from yellow to orange-red. On removal of the solvent (−20°C, exclusion of light) the reaction mixture turned dark red, and an extremely sensitive dark red product *(2)* containing no nitrogen was isolated from the residue. According to elemental analysis and its mass spectrum, which contained the fragment ions $[M-2CO]$, $[M-3CO]$, and $[M-3CO-C_4H_4]$ in addition to the molecular ion ($M=300$), the composition $(C_4H_4)_2Fe_2(CO)_3$ is indicated for compound *(2)*. Cryoscopy in benzene yielded a molecular weight of 339. According to its IR spectrum (in pentane, −20°C) compound *(2)* contains two terminal CO groups bonded to iron [ν_{CO}: 2051 (s) and 1980 (vs) cm^{-1}] and a bridging CO group [ν_{CO}: 1861 (vs) cm^{-1}].

In the ^{1}H-NMR spectrum (in $C_6D_5CD_3$, −30°C) a sharp singlet is observed at τ = 5.78 ppm (paramagnetic shift of 1.02 ppm relative to *(1)*). The ^{13}C-NMR data of *(1)* and *(2)* are listed in Table 1. The magnetic equivalence of the carbonyl

Table 1. ^{13}C-NMR data of $(C_4H_4)_2Fe_2(CO)_3$ *(2)* and $(C_4H_4)Fe(CO)_3$ *(1)*.

	(2)	*(1)*
$\delta_{C_4H_4}$ [ppm from TMS]	77.8	64.5
δ_{CO}	238.8	214.9
J_{CH^α} [Hz]	186	187
J_{CH^β}	[a]	4.2
J_{CH^γ}	[a]	12.8

[a] Coupling constant could not be determined owing to insufficient resolution; however, the signal groups of *(1)* and *(2)* have comparable half-widths.

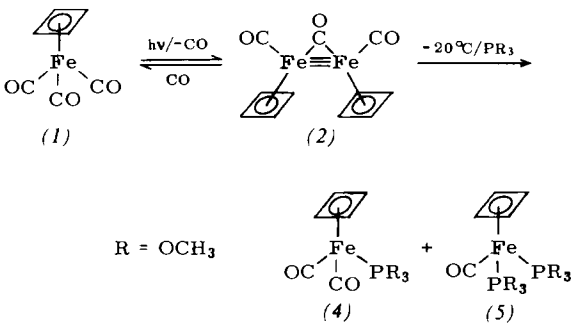
[*] Dr. I. Fischler, Dr. K. Hildenbrand, and Dr. E. Koerner von Gustorf
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
433 Mülheim-Ruhr, Stiftstrasse 34—36 (Germany)

[**] A preliminary report of our findings was presented at the VI. Int. Conf. Organometal. Chem., Amherst, August 1973: *E. Koerner von Gustorf, I. Fischler, F.-W. Grevels, D. Schulz*, and *R. Wagner*, Abstr. p. 46.

C atoms can be attributed to the known fast exchange of such groups[4]; the equivalence of the C atoms linked to protons and the agreement of the ^1H-^{13}C coupling constants of *(1)* and *(2)* suggest that two intact and similar cyclobutadiene units are present in *(2)*[5].

At −20°C, *(2)* reacts quantitatively with CO to give *(1)*. Treatment of *(2)* with an excess of trimethyl phosphite furnishes a 1:1 mixture of the cyclobutadienecarbonyliron complexes *(4)* and *(5)*. For purposes of comparison, compounds *(4)* and *(5)* were prepared by photolysis of *(1)* in the presence of $P(OCH_3)_3$[3a] [*(4)*: ν_{CO}: 1988, 1932 cm^{-1}; $\varepsilon = 2840$, 3930 l mol^{-1} cm^{-1}; *(5)*: ν_{CO}: 1915 cm^{-1}; $\varepsilon = 2030$ l mol^{-1} cm^{-1}].

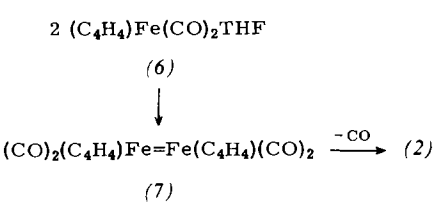
The reactions of *(2)* with CO and $P(OCH_3)_3$ provide additional evidence for intact cyclobutadiene ligands in *(2)*.



All known iron(0) compounds conform to the 18-electron rule[6]. Since *(2)* is diamagnetic we propose that this new complex has a structure containing an Fe—Fe triple bond[15]. The intensity of the CO stretching vibrations indicate the terminal CO groups[7]—and hence also the cyclobutadiene units—to have a *cis* configuration.

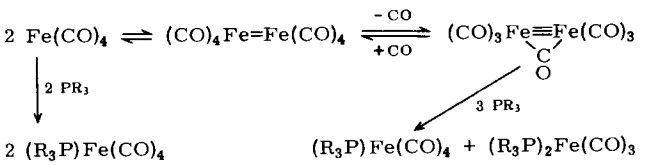
The postulated triple bond between two transition metal atoms is not without its parallels, even though *(2)* apparently represents the first example in the case of iron[8]. We hope that X-ray structure analysis will provide information about the participation of σ-, π-, and δ bonding components. (The necessary low temperature technique is currently being developed by *C. Krüger*.) The coordination in *(2)* corresponds to that in $Fe_2(CO)_9$[9] if it is imagined that two bridging CO groups are replaced by two Fe—Fe bonds.

IR spectroscopy reveals that only one CO is initially lost on photolysis of *(1)* at −40°C in THF; bands at 1975 and 1900 cm^{-1} are to be assigned to the complex $(C_4H_4)Fe(CO)_2THF$ *(6)*. (Confirmatory evidence for the presence of *(6)* comes from reaction with $P(OCH_3)_3$: addition at −40°C affords exclusively compound *(4)*.) The CO stretching vibrations of *(2)* appear on removal of the solvent at −20°C (2051, 1980, 1861 cm^{-1}).



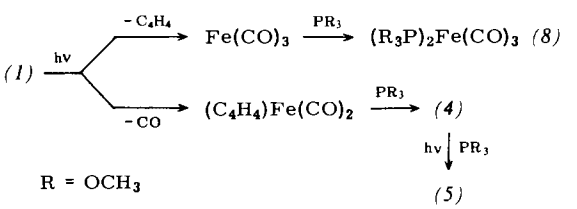
The formation of *(7)* from *(6)* corresponds to that of $Fe_2(CO)_8$ from $Fe(CO)_4$[10]. Transformation of *(7)* into *(2)* with loss of CO apparently proceeds extremely readily since *(7)* could not be observed under our experimental conditions.

The formation of *(2)* from *(6)* *via* *(7)* and the smooth reaction of *(2)* with $P(OCH_3)_3$ may contribute to our understanding of a surprising observation: $Fe(CO)_4$, prepared, for example, by irradiation of $Fe(CO)_5$[10d], from $Fe_2(CO)_9$[11], or from olefintetracarbonyliron[10c, 12], reacts with phosphanes and phosphites to give a mixture of $Fe(CO)_4(PR_3)$ and $Fe(CO)_3(PR_3)_2$ under conditions in which $Fe(CO)_4PR_3$ is not attacked by PR_3. In our opinion this finding can be explained as follows:



Conversion of *(6)*, which can be regarded as substituted $Fe(CO)_4$, into *(2)* provides a model supporting this proposal.

Opposing views have been expressed[13] concerning the primary step of the photolysis of $(C_4H_4)Fe(CO)_3$: whereas *Gunning et al.* favor elimination of cyclobutadiene with formation of $Fe(CO)_3$, *Chapman et al.* were only able to observe the elimination of CO in a matrix. We have therefore examined the photoreaction of *(1)* with trimethyl phosphite (in pentane) which can be expected to afford the following products:



After 40% conversion of *(1)*, only *(4)* could be observed by IR spectroscopy; comparative measurements showed that we would have been able to detect 10% of *(8)* in admixture with *(4)*. Hence it follows that the quantum yield for elimination of CO is at least 10 times higher than that for the loss of cyclobutadiene[14].

Procedure:

Compound *(1)* (8 mmol) was dissolved in dry THF (120 ml) and irradiated at −40°C for 6 h with simultaneous passage of nitrogen in an immersion apparatus with a Philips HPK 125 W high pressure mercury lamp. After removal of solvent at −20°C unreacted *(1)* was also removed by molecular distillation *in vacuo*. Extraction of the black residue with pentane (10 ml) at −20°C and cooling of the solution to −70°C afforded compound *(2)* in approximately 8% yield.

Received: July 25, 1974;
revised: August 5, 1974 [Z 106 IE]
German version: Angew. Chem. *87*, 35 (1975)

CAS Registry numbers:
(1), 12078-17-0; *(2)*, 53778-34-0; $(C_4H_4)Fe(CO)_2N_2$, 53778-35-1; *(4)*, 53778-36-2; *(5)*, 53778-37-3; *(6)*, 53778-38-4; *(7)*, 53778-39-5; *(8)*, 19457-84-2; *(3)*, 50277-83-3

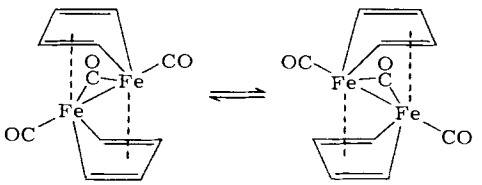
[1] *E. Koerner von Gustorf, I. Fischler, J. Leitich*, and *H. Dreeskamp*, Angew. Chem. *84*, 1143 (1972); Angew. Chem. internat. Edit. *11*, 1088 (1972); *I. Fischler* and *E. Koerner von Gustorf*, Naturwissenschaften *62* (1975), in press.

[2] *D. Sellmann* and *G. Maisel*, Z. Naturforsch. *27b*, 465, 718 (1972).

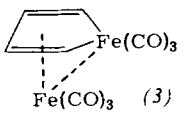
[3] a) *I. Fischler*, Dissertation, Universität Bochum 1974; b) *A. Rest*, personal communication.

[4] *B. E. Mann*, Advan. Organometal. Chem. *12*, 148 (1974).

[5] A conceivable rapid exchange of two ferracyclopentadiene systems



could be ruled out by comparison of the ^{1}H- and ^{13}C-NMR spectra of *(2)* and *(3)* [*W. Hübel* and *E. Weiss*, Chem. Ind. (London) *1959*, 703; *H. D. Kaesz, R. B. King, T. A. Manuel, L. D. Nichols*, and *F. G. A. Stone*, J. Amer. Chem. Soc. *82*, 4749 (1960)].



(3): ^{1}H-NMR (C_6D_6): $\tau = 3.73$, 4.82 ppm. ^{13}C-NMR (C_7D_8): (C_4H_4)-unit $\delta = 111.4$, 156.5 ppm (from TMS); $J_{CH} = 170$, 155 Hz.

[6] *C. A. Tolman*, Chem. Soc. Rev. *1*, 337 (1972).

[7] The coupling of the terminal CO in *(2)*, which is strong in comparison with other dinuclear iron complexes (*P. A. McArdle* and *R. A. Manning*, J. Chem. Soc. *A 1969*, 1498; splitting in $[(\pi\text{-dienyl})Fe(CO)_2]_2$: 40—50 cm^{-1}), manifests itself in a splitting of 71 cm^{-1}, indicating an especially high electron density between the coupling groups in *(2)*.

[8] *M. Chisholm, F. A. Cotton, B. A. Frenz*, and *L. Shive*, J. C. S. Chem. Comm. *1974*, 480; and further literature cited therein.—Examples of FeFe double bonds *J. L. Calderón, S. Fontana, E. Frauendorfer, V. W. Day*, and *S. D. A. Iske*, J. Organometal. Chem. *64*, C 16 (1974); references cited therein; *K. Nicholas, L. S. Bray, R. E. Davis*, and *R. Pettit*, Chem. Commun. *1971*, 608; *H.-J. Schmitt* and *M. L. Ziegler*, Z. Naturforsch., in press.

[9] *F. A. Cotton* and *J. M. Troup*, J. C. S. Dalton *1974*, 800.

[10] a) *M. Poliakoff* and *J. J. Turner*, J. C. S. Dalton *1974*, 2276; b) *N. Harrit, J. M. Kelly, H. Hermann*, and *E. A. Koerner von Gustorf*, unpublished; c) *N. Harrit, F.-W. Grevels, R. Wagner*, and *E. A. Koerner von Gustorf*, unpublished; d) *E. A. Koerner von Gustorf* and *R. Wagner*, unpublished.

[11] *P. S. Braterman* and *W. J. Wallace*, J. Organometal. Chem. *30*, C 17 (1971).

[12] *G. Cardaci*, Inorg. Chem. *13*, 368 (1974); *F.-W. Grevels* and *E. Koerner von Gustorf*, Liebigs Ann. Chem. *1973*, 1821.

[13] *W. J. R. Tyerman, M. Kato, P. Kebarle, S. Masamune, O. P. Strausz*, and *H. E. Gunning*, Chem. Commun. *1967*, 497; *O. L. Chapman, J. Pacansky*, and *P. W. Wojtkowski*, J. C. S. Chem. Commun. *1973*, 681.

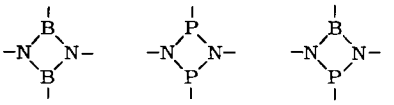
[14] *J. D. Black, J. Boylan, P. S. Braterman*, and *W. J. Wallace*, J. Organometal. Chem. *63*, C 21 (1973). These authors replied to the arguments of *Chapman et al.* by suggesting that loss of the relatively voluminous cyclobutadiene in a matrix defied detection because of rapid reverse reaction in the cage. Our observations indicate that this objection has little, if any, significance.

[15] *Note added in proof*: In the meantime a complex similar to *(2)* has been obtained on photolysis of 1,2-diphenyl-3,4-di-*tert*-butylcyclobutadienetricarbonyliron; however, all CO are bridging in this compound. The Fe-Fe distance of 2.177 Å agrees with a triple bond [*S. Murahashi, T. Mizoguchi, T. Hosokawa, I. Moritani, Y. Kai, M. Kohara, N. Yasuoka*, and *N. Kasai*, J. C. S. Chem. Comm. *1974*, 563].

1,3,2,4-Diazaphosphaboretidines: A Four-Membered Boron-Nitrogen-Phosphorus Heterocycle[**]

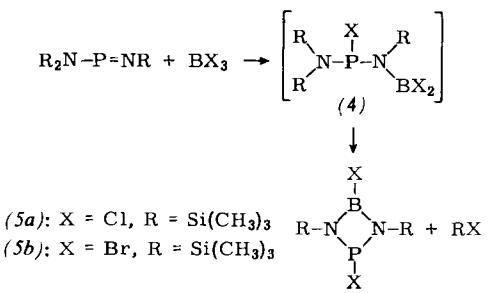
By *Edgar Niecke* and *Wolfhelm Bitter*[*]

Heterocycles of types *(1)* and *(2)* have been known for a long time[1].



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

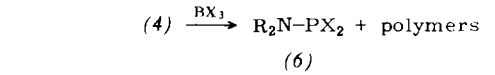
In the context of our studies on "phosphazenes" having phosphorus in an unusual coordination state[2] we have now succeeded in synthesizing cyclic compounds of novel type *(3)* by reaction of bis(trimethylsilyl)aminotrimethylsilyliminophosphane[3] with boron halides.



(4)

(5a): X = Cl, R = $Si(CH_3)_3$
(5b): X = Br, R = $Si(CH_3)_3$

Evidence for the transient formation of an iminophosphane-boron trihalide adduct *(4)* is provided by the appearance of bis(trimethylsilyl)aminodihalophosphanes *(6)*[4] as by-products: they are either formed directly from *(4)* or by the action of boron halide.



(6)

1,3,2,4-Diazaphosphaboretidines *(5)* are stable in the absence of moisture; the corresponding dihalophosphanes *(6)* undergo significant loss of trimethylsilyl halide to form vitreous decomposition products, even at room temperature. The composition and structure of the compounds were established by elemental analysis and mass, vibrational, and NMR (^{1}H, ^{11}B, ^{31}P) spectra.

The mass spectrum [*m/e* (rel. int.)][5] contains the molecular ions M 286 (25%) *(5a)*, M 374 (14%) *(5b)*, and M 261 (20%) *(6a)*, as well as the following characteristic fragments: $M-CH_3$ 271 (100%), M−Cl 251 (12%), $ClPNSi(CH_3)_2$ 138 (49%), $ClBNSi(CH_3)_2$ 118 (35%), $PNSi(CH_3)_3$ 118 (65%), $BNSi(CH_3)_3$ 98 (48%); $M-CH_3$ 359 (15%), M−Br 295 (81%), $BrPNSi(CH_3)_2$ 182 (21%), $BrBNSi(CH_3)_2$ 162 (22%), $PNSi(CH_3)_3$ 118 (100%), $BNSi(CH_3)_3$ 98 (54%); and $M-CH_3$ 246 (20%), M−Cl 226 (25%), $ClPNSi(CH_3)_2$ 138 (100%), $PNSi(CH_3)_3$ 118 (57%).

The stretching vibrations of the skeleton for the heterocycles *(5a)* and *(5b)* (partially with isotopic splittings) are observed at[6]: *(5a)*: 1280 s (1281 m, p), 1224 vs (1223 s, dp), 1064 vs (1065 ss) cm^{-1}; *(5b)* 1279 s (1269 m, p), 1217 vs (1218 s, dp), 1038 vs (1040 ss) cm^{-1}.

The ^{11}B- and ^{31}P-NMR data (50% solution in C_6H_{12}, $F_3B{\cdot}O(C_2H_5)_2$ and 85% H_3PO_4, respectively, as external standard) confirm the coordination number 3 for boron and phosphorus in accord with the structures shown: $\delta_{^{11}B} = -30$ *(5a)*, −27 ppm *(5b)*; $\delta_{^{31}P} = -171.7$ *(5a)*, −191.0 *(5b)*; and −186.1 ppm *(6a)*.

In the ^{1}H-NMR spectrum (30% solution in CH_2Cl_2, TMS internal standard) the trimethylsilyl protons are expectedly observed as a doublet: $\delta_{^1H} = -0.26$ *(5a)*, −0.28 *(5b)*, −0.42 ppm *(6a)*; $^4J_{HP} = 0.68$ *(5a)*, 0.66 *(5b)*, and 2.58 Hz *(6a)*.

[*] Dr. E. Niecke and Dipl.-Chem. W. Bitter
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstrasse 4 (Germany)

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

Experimental:

(5a) and *(6a):* BCl_3 (15 g, 0.13 mol) is condensed into a solution of $(R_3Si)_2NPNSiR_3$ (28 g, 0.1 mol) in light petroleum (100 ml) contained in a 250-ml two-neck flask fitted with two reflux condensers (−70 °C), moisture being rigorously excluded. The reaction mixture is then stirred for 1 h with cooling (< −10 °C). After removal of the solvent and R_3SiCl in a water-jet vacuum at room temperature, the volatile fraction (up to 90 °C/0.1 torr)[7] is separated from the polymeric component of the reaction mixture. Lower boiling fractions (up to 40 °C/0.1 torr)[7] are collected separately and fractionated over a "slit-tube" column[8] at 1.0 torr. *(5a)*[9] (7 g, 25 %) is obtained at 41–42 °C, and *(6a)*[9] (3 g, 12 %) at 46–47 °C.

(5b): BBr_3 (15 g, 0.06 mol) is added dropwise with stirring to $(R_3Si)_2NPNSiR_3$ (14 g, 0.05 mol) under an inert gas at 0 °C. After 1 h at room temperature most of the R_3SiBr is drawn off and the residue is fractionated in an oil-pump vacuum. Redistillation (Vigreux column) of the fraction obtained at 50–65 °C/0.1 torr affords *(5b)*[9] (13 g, 70 %), b.p. 60–61 °C/0.1 torr.

Received: July 25, 1974 [Z 109 IE]
German version: Angew. Chem. *87*, 34 (1975)

[1] *I. Haiduc*: The Chemistry of Inorganic Ring Systems. Wiley-Interscience, London 1970, pp. 124, 805.

[2] *E. Niecke* and *W. Flick*, Angew. Chem. *86*, 128 (1974); Angew. Chem. internat. Edit. *13*, 134 (1974).

[3] *E. Niecke* and *W. Flick*, Angew. Chem. *85*, 586 (1973); Angew. Chem. internat. Edit. *12*, 585 (1973); *O. J. Scherer* and *N. Kuhn*, Chem. Ber. *107*, 2133 (1974).

[4] The formation of bis(trimethylsilyl)aminodibromophosphane *(6b)* could be detected only by NMR spectroscopy: $\delta_{^1H} = -0.44$ ppm, $^4J_{HP} = 2.5$ Hz; $\delta_{^{31}P} = -213$ ppm.

[5] Based on the isotopes ^{11}B, ^{35}Cl, and ^{79}Br.

[6] The missing ring vibration occurs in the range 720–790 cm^{-1}.

[7] The higher boiling component contains a solid, presumably bis(trimethylsilyldichloroborylamino)chlorophosphane, which has not yet been isolated pure.

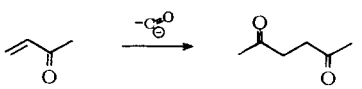
[8] "Spaltrohr" column, Fischer, Labor- und Verfahrenstechnik, Bonn-Bad Godesberg.

[9] *Ca.* 95 % pure. The amount of trimethylsilyl halide present owing to decomposition on distillation is 3–5 %.

Michael Additions of Metalated Thioacetals to Cyclic Enones[**]

By *Dieter Seebach* and *Rainer Bürstinghaus*[*]

The Michael addition of nucleophilic acyl equivalents to α,β-unsaturated carbonyl compounds [eq. (1)] is a reaction of particular synthetic utility[1].



(1)

So far this transformation has succeeded in the case of thioacetals as masked acyl anions only on use of lithium cuprates[1b, 2].

To our surprise, we have now found that the readily accessible[3a] lithiated bis(methylthio)(silyl)- and bis(methylthio)-(stannyl)methanes *(1)* undergo 1,4 addition to cyclic enones *(2)* in good yields—in contrast to the corresponding 1,3-dithiane derivatives which only undergo 1,2 addition[4]. The resulting enolates *(3)* afford the Michael adducts *(4)*, E = H, on aqueous work-up. However, the enolates can be alkylated directly by treatment of the reaction mixture with alkyl iodides to form the α,β-disubstituted ketones *(4)*, E ≠ H, which are isolated predominantly as *trans* isomers. (For examples, see Table 1.)

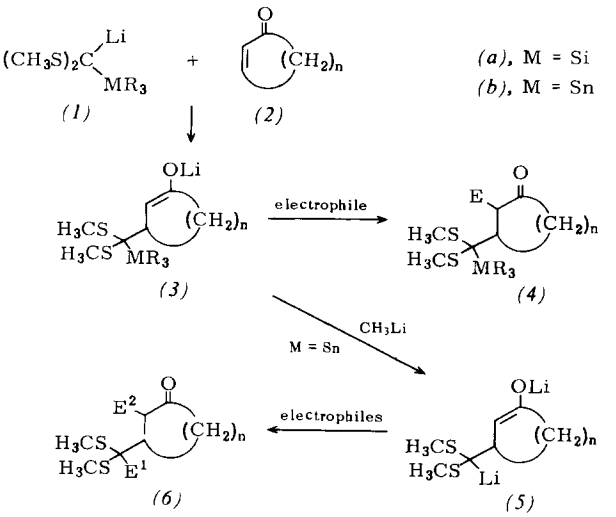
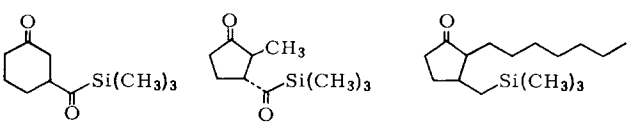


Table 1. Yields of ketones *(4)* prepared from thioacetals *(1)* and enones *(2)*.

M	*n*	R	E	Yield [%] [a]
Si	2	CH_3	H	73
Sn	2	CH_3	H	70
Si	2	CH_3	CH_3	71
Si	2	CH_3	n-C_7H_{15}	65
Sn	2	CH_3	n-C_5H_{11}	65
Si	3	CH_3	H	78 [b]
Sn	3	CH_3	H	75
Sn	3	n-C_4H_9	H	65
Si	3	CH_3	CH_3	75
Sn	3	C_6H_5	H	60
Si	4	CH_3	H	60

[a] Products isolated by molecular distillation *in vacuo*.
[b] M.p. 56 °C.

Finally, in the case of the adducts *(3b)* it is possible to produce the novel dilithium derivatives *(5)* by transmetalation[3b], as we were able to show, *e.g.*, by hydrolysis to the tin-free product *(6)*, $n = 3$, $E^1 = E^2 = H$ [NMR in CCl_4: *one* SCH_3 singlet at δ = 2.1 ppm, 5-Hz doublet of the $(RS)_2CH$ proton at δ = 3.5 ppm]. Apparently, the carbanionoid center adjacent to the S atoms in *(5)* is more nucleophilic than the enolate system, for after addition of *one* equivalent of methyl iodide and subsequent hydrolysis we isolated *(6)*, $n = 3$, $E^1 = CH_3$, $E^2 = H$ [NMR in CCl_4: two SCH_3 singlets separated by 2 Hz (diastereotopic) at δ = 2.0 ppm, $(RS)_2C{-}CH_3$ as singlet at δ = 1.4 ppm].



To our knowledge, the compounds *(1b)* described above and the corresponding 1,3-dithiane derivatives[4b] are the first

[*] Prof. Dr. D. Seebach and Dipl.-Chem. R. Bürstinghaus
Institut für Organische Chemie des Fachbereichs 14 der Universität
63 Giessen, Ludwigstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft (Projects Se-158-6 and Se-158-10) and the Fonds der Chemischen Industrie.

α-stannyl-organolithium compounds to have been prepared by direct metalation (H/Li exchange)[5].

The sulfur-free carbonyl compounds *(7)*, *(8)*, and *(9)* have been prepared by thioacetal hydrolysis or Raney nickel desulfurization of the adducts *(4a)*. Yields: 71, 66, and 60%, respectively; ^{1}H-NMR (CCl_4): $Si(CH_3)_3$ singlets at $\delta = 0.2$, 0.23, and 0.25, respectively; CH_3 in *(8)*: 0.95 (d, 7 Hz); IR: 1710, 1640; 1745, 1635; and 1735, respectively.

Received: August 8, 1974 [Z 112 IE]
German version: Angew. Chem. *87*, 37 (1975)

CAS Registry numbers:
(1a), R = CH_3, 53369-90-7; *(1b)*, R = CH_3, 53369-91-8; *(1b)*, R = n-C_4H_9, 53369-99-6; *(1b)*, R = C_6H_5, 53370-00-6; *(2)*, n = 2, 930-30-3; *(2)*, n = 3, 930-68-7; *(2)*, n = 4, 1121-66-0; *(5)*, n = 3, 53369-93-0; *(6)*, n = 3, $E^1 = E^2 = H$, 53369-94-1; *(6)*, n = 3, $E^1 = CH_3$, $E^2 = H$, 53369-95-2; *(7)*, 53369-96-3; *(8)*, 53369-97-4; *(9)* 53369-98-5; *(4)*, M = Si, n = 2, R = CH_3, E = H, 53370-01-7; *(4)*, M = Sn, n = 2, R = CH_3, E = H, 53370-02-8; *(4)*, M = Si, n = 2, R = E = CH_3, 53370-07-3; *(4)*, M = Si, n = 2, R = CH_3, E = n-C_7H_{15}, 53418-35-2; *(4)*, M = Sn, n = 2, R = CH_3, E = n-C_5H_{11}, 53370-10-8; *(4)*, M = Si, n = 3, R = CH_3, E = H, 53370-03-9; *(4)*, M = Sn, n = 3, R = CH_3, E = H, 53370-04-0; *(4)*, M = Sn, n = 3, R = n-C_4H_9, E = H, 53370-05-1; *(4)*, M = Si, n = 3, R = E = CH_3, 53370-08-4; *(4)*, M = Sn, n = 3, R = C_6H_5, E = H, 53370-06-2; *(4)*, M = Si, n = 4, R = CH_3, E = H, 53370-09-5

[1] a) Cyanohydrin derivatives: *H. Stetter* and *M. Schreckenberg*, Angew. Chem. *85*, 89 (1973); Angew. Chem. internat. Edit. *12*, 81 (1973); Tetrahedron Lett. *1973*, 1461; Chem. Ber. *107*, 210 (1974); *E. Leete*, *M. R. Chedekel*, and *G. B. Bodem*, J. Org. Chem. *37*, 4465 (1972). b) Cuprates of thioacetals: *T. Mukaiyama*, *K. Narasaka*, and *M. Furusato*, J. Amer. Chem. Soc. *94*, 8641 (1972). c) Anions of thioacetal monosulfoxides: *R. H. Schlessinger et al.*, Tetrahedron Lett. *1973*, 2595, 2599, 2603, 3267, 3271, 3275. d) Nitroalkane anions: *J. E. McMurry et al.*, J. Amer. Chem. Soc. *93*, 5309 (1971); J. Org. Chem. *38*, 4367 (1973); *39*, 258, 259 (1974). e) Carbonylnickel derivatives: *E. J. Corey* and *L. S. Hegedus*, J. Amer. Chem. Soc. *91*, 4926 (1969). f) Anions of oxazolones: *W. Steglich et al.*, Angew. Chem. *83*, 725, 727 (1971); Angew. Chem. internat. Edit. *10*, 653, 655 (1971).

[2] In the Michael additions described in ref. [1c], further stabilized anions derived from thioacetals are employed.

[3] a) For production of *(1a)*, see ref. [4a]. For preparation of *(1b)*, $(CH_3S)_2CHLi$ [4] is reacted with chlorostannanes and the resulting $(CH_3S)_2CHSnR_3$ is metalated with lithium diisopropylamide in THF/HMPA at −78 to −30°C. b) Prior to transmetalation of *(3)* to *(5)* (CH_3Li at −100°C) the diisopropylamine is distilled off with the major portion of the THF (replaced later) at 0°C bath temperature and 0.001 torr pressure.

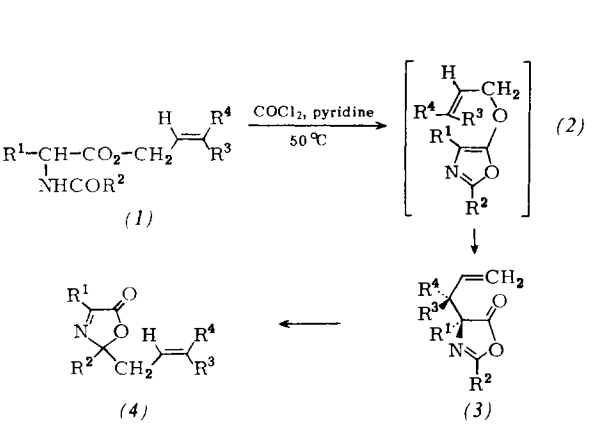
[4] a) Lithiated silylthioacetals: *D. Seebach*, *M. Kolb*, and *B.-Th. Gröbel*, Chem. Ber. *106*, 2277 (1973). b) Lithiated stannyldithianes: *I. Willert* and *B.-Th. Gröbel*, Universität Giessen, 1973 (hitherto unpublished).

[5] For $(R_3Sn)_2CCl_2 + RLi \rightarrow (R_3Sn)CCl_2Li$, see: *D. Seyferth*, *F. M. Armbrecht jr.*, and *E. M. Hanson*, J. Organometal. Chem. *10*, P-25 (1967); $(R_3Sn)CBr_3 + RLi \rightarrow (R_3Sn)CBr_2Li$: *D. Seyferth et al.*, *ibid.* *44*, 299 (1973).

Hetero Cope Rearrangements in the Cyclization of Allyl and Propargyl Esters of *N*-Acyl Amino Acids to Oxazolin-5-ones[**]

By *Börries Kübel*, *Gerhard Höfle*, and *Wolfgang Steglich*[*]

Alkyl esters of *N*-acyl amino acids are converted on treatment with dehydrating agent into 5-alkoxyoxazoles[1, 2]. We have found that 5-allyloxyoxazoles *(2)*, formed from the *N*-acylamino acid allyl esters *(1)*[3], rearrange directly under the reaction conditions to 4-allyloxazolin-5-ones *(3)*. Cyclization is accomplished by dropwise addition of a solution of phosgene (1.5 mol) in toluene to a solution of the ester *(1)* and pyridine (3—6 mol) in chloroform and warming the mixture after 30



(1) *(2)* *(3)* *(4)*

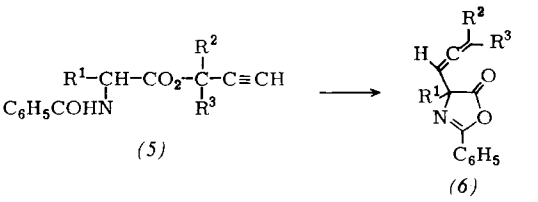
minutes' stirring at 20°C to 50—70°C for 1—3 h[2]. P_2O_5 in chloroform proved to be less satisfactory as reagent since acid-sensitive allyl residues are liberated (see Table 1).

From the ^{1}H-NMR spectra of *(3e)* and *(3f)* it is evident that only one diastereoisomer is formed in each of these cases; this is in agreement with the stereospecific course of the Claisen rearrangement[5].

On prolonged heating, the 2-oxazolin-5-ones *(3)*, R^3, $R^4 \neq H$, obtained from 3,3-disubstituted allyl esters are converted by further hetero Cope rearrangement into 2-allyl-3-oxazolin-5-ones *(4)*. For the preparative synthesis of *(4)* it is recommended that esters *(1)* be used as starting material, without isolating *(3)* (Table 1).

The ease of the secondary reaction *(3)* → *(4)* depends on the spatial requirements of the groups R^1, R^3, R^4. Thus *(3f)* rearranges completely into *(4f)* on boiling in chloroform for 3 h, while 12 hours' boiling in benzene is necessary for the rearrangement *(3e)* → *(4e)*. Under the conditions used for cyclization ($COCl_2$/pyridine, 1.5 h, 50°C), *N*-isobutyryl-2-phenylglycine geranyl ester affords *(4h)* directly—as a result of additional stabilization of the 3-oxazolinone form by conjugation of the C=N double bond with a phenyl residue.

4-Allenyl-2-oxazolin-5-ones *(6)* are accessible in the same way as *(3)* if the propargyl esters of *N*-acyl amino acids *(5)* are cyclized instead of *(1)* (Table 2).



(5) *(6)*

If cyclization of the esters *(1c)* and *(5i)* is carried out with P_4S_{10} in 1,2-dichloroethane (24 h, reflux)[6], the 2-thiazolin-5-ones (m.p. 53 and 59°C resp.)[4] corresponding to *(3c)* and *(6i)* are formed in 40% yield.

4-Isopropyl-4-linalyl-2-phenyl-2-oxazolin-5-one (3f) and 2-geranyl-4-isopropyl-2-phenyl-3-oxazolin-5-one (4f)

Butyllithium (2.5 mmol) followed by 4-isopropyl-2-phenyl-2-oxazolin-5-one (4.0 g, 20 mmol) are added with stirring to a solution of geraniol (3.1 g, 20 mmol) in benzene (30 ml). The mixture is stirred for one day, washed with 0.5 N HCl, dried over $MgSO_4$, and finally concentrated by evaporation under vacuum [yield 6.1 g (86%) *(1f)*, pale yellow oil].—A solution of $COCl_2$ (10.3 mmol) in toluene (3 ml) is now added slowly with stirring to a solution of the ester *(1f)* (2.5 g,

[*] Dr. B. Kübel, Dr. G. Höfle, and Prof. Dr. W. Steglich
Organisch-Chemisches Institut der Technischen Universität
1 Berlin 12, Strasse des 17. Juni 135 (Germany)

[**] The work was supported by the ERP Special Fund. We thank BASF Ludwigshafen for supplying the starting materials.

Table 1. 4-Allyl-2-oxazolin-5-ones *(3)* [4] and 2-allyl-3-oxazolin-5-ones *(4)* [4].

	R^1	R^2	R^3	R^4	Cyclization conditions	*(3)* Yield [%] Work up	B.p. [°C/torr] (M.p. [°C])	Reaction conditions	*(4)* Yield [%]
(a)	CH_3	C_6H_5	H	H	2.5 h [a] 55 °C	82 [c]	99—100/0.03		
(b)	$CH(CH_3)_2$	C_6H_5	H	H	3 h [a] 70 °C	70 [c]	99/0.2		
					[b]	32 [c]			
(c)	C_6H_5	C_6H_5	H	H	[b]	40	oil [f]		
(d)	$CH(CH_3)_2$	C_6H_5	CH_3	CH_3	2 h [a] 55 °C	52 [d]	oil [f]	[g]	41 [d] oil
(e)	CH_3	C_6H_5	CH_3	$(CH_2)_2CH=C(CH_3)_2$	1.5 h [a] 55 °C	55 [d]	oil [f]	12 h [h]	100 [j] oil
(f)	$CH(CH_3)_2$	C_6H_5	CH_3	$(CH_2)_2CH=C(CH_3)_2$	1.5 h [a] 50 °C	27 [d]	(65—67)	3 h [h] 2.5 h [i]	100 oil 41 [d] oil
(g)	$CH(CH_3)_2$	C_6H_5	H	C_6H_5	1.5 h [a] 50 °C	26 [d, e]	(67)	1.5 h [i] 50 °C	12 [d, e] oil
(h)	C_6H_5	$CH(CH_3)_2$	CH_3	$(CH_2)_2CH=C(CH_3)_2$				1.5 h [i] 50 °C	67 [d] oil

[a] $COCl_2$-pyridine method. [b] P_2O_5 method. [c] Distillation. [d] Chromatography on silical gel, eluent CCl_4. [e] Crude yield 63%; according to NMR a mixture of 60% *(3g)* and 40% *(4g)*. [f] Decomposition on distillation. [g] From *(1a)*, $COCl_2$ and pyridine (2.5 h, 55 °C), then 16 hours' heating in benzene. [h] From *(3)* by heating in benzene. [i] From *(1)*, $COCl_2$, and pyridine. [j] Crude product, not analyzed.

Table 2. 4-Allenyl-2-oxazolin-5-ones *(6)* [4].

	R^1	R^2	R^3	Cyclization conditions	Yield [%]	B.p. [°C/torr] (M.p. [°C])
(6i)	$CH(CH_3)_2$	H	H	6 h [a]	43	88 – 89/0.03
				[b]	68	
(6j)	C_6H_5	H	H	15 h [a]	30	(56)
(6k)	$CH(CH_3)_2$	H	CH_3	[c]	78	103 – 106/0.04
(6l)	$CH(CH_3)_2$	CH_3	CH_3	[c]	65	123/0.1

[a] P_2O_5-method (chloroform, reflux). [b] P_2O_5 in DMF, 4 h, 125 °C. [c] $COCl_2$-pyridine method, 3 h, 65 °C.

7 mmol) and pyridine (4 ml, 40 mmol) in $CHCl_3$ (30 ml). The mixture is stirred for 30 min at 20 °C, for a further 1.5 h at 50 °C, and finally washed with 0.5 N HCl, dried, and evaporated down under vacuum at 35 °C. Filtration of the residue through a short column of silica gel with CCl_4 as eluent and recrystallization from petroleum ether affords 0.65 g (27 %) *(3f)*, m. p. 65—67 °C, IR (CCl_4): 1815, 1660 cm^{-1}.—A solution of *(3f)* (0.5 g) in benzene (5 ml) is boiled under reflux for 3 h. Evaporation under vacuum affords analytically pure *(4f)* as a light yellow oil, IR (CCl_4): 1780, 1645 cm^{-1}.

Received: August 30, 1974 [Z 113 IE]
German version: Angew. Chem. *87*, 64 (1975)

CAS Registry numbers:
(1a), 53777-87-0; *(1b)*, 53777-88-1; *(1c)*, 53777-89-2; *(1d)*, 53777-90-5; *(1e)*, 53777-91-6; *(1f)*, 53777-92-7; *(1g)*, 53777-93-8; *(3a)*, 53777-94-9; *(3b)*, 53777-95-0; *(3c)*, 53777-96-1; *(3d)*, 53777-97-2; *(3e)*, 53777-98-3; *(3f)*, 53777-99-4; *(3g)*, 53778-00-0; *(4d)*, 53778-01-1; *(4e)*, 53778-02-2; *(4f)*, 53778-03-3; *(4h)*, 53778-04-4; *(5i)*, 53778-05-5; *(5j)*, 53778-06-6; *(5k)*, 53778-07-7; *(5l)*, 53778-08-8; *(6i)*, 53778-09-9; *(6j)*, 53778-10-2; *(6k)*, 53778-11-3; *(6l)*, 53778-12-4; *N*-isobutyryl-2-phenylglycine geranyl ester, 53778-13-5.

[1] *J. W. Cornforth* in *H. T. Clarke, J. R. Johnson*, and *R. Robinson*: The Chemistry of Penicillin, Princeton University Press 1949, p. 695, 708; cf. also *R. A. Firestone, E. E. Harris*, and *W. Reuter*, Tetrahedron *23*, 943 (1967).

[2] *J. Maeda, M. Takehara, K. Togo, S. Asai*, and *R. Yoshida*, Bull. Chem. Soc. Jap. *42*, 1435 (1969).

[3] The esters are formed in high yield by reaction of the oxazolin-5-ones with alcohols in benzene and addition of 0.1 mol butyllithium [in the case of *(1d)*, *(1f)*, *(1g)* *(5l)*], acid catalyzed esterification of the *N*-acyl amino acids [in the case of *(1a)*, *(1b)*, *(1c)*, *(5i)*, *(5j)*, *(5k)*], or alkylation of the *N*-acyl amino acid sodium salt in HMPT with allyl halides [in the case of *(1e)*, *(1h)*].

[4] All compounds gave correct elemental analyses. The ^{1}H-NMR and IR spectra are consistent with the given structures.

[5] The stereochemistry of formula *(3)* follows from assumption of a chair form in the transition state, as has been quoted for other examples: *P. Vittorelli, T. Winkler, H.-J. Hansen*, and *H. Schmid*, Helv. Chim. Acta *51*, 1457 (1968).

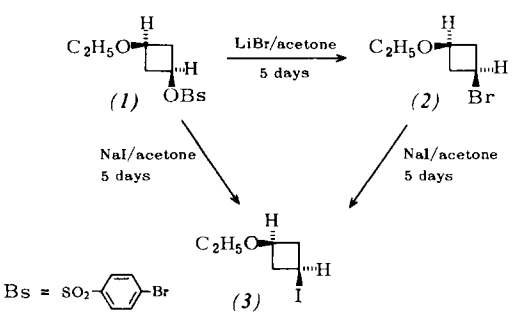
[6] *L. Wilschowitz*, Dissertation, Technische Universität München 1973.

Experimental Evidence for a Novel Limiting Mechanism of Aliphatic Nucleophilic Substitutions[**]

By *Tarek ElGomati, Dieter Lenoir*, and *Ivar Ugi*[*]

Reaction of *cis*-3-ethoxycyclobutyl brosylate *(1)*[1] (7.00 g, 21 mmol) with sodium iodide (11.20 g, 75 mmol) in refluxing acetone (70 ml), *i.e.* under typical S_N2 conditions[2], leads to the formation of a stereochemically uniform iodide *(3)*; according to a ^{1}H-NMR comparison with *(1)*, *(3)* is the *cis*-isomer.

Exchange of the brosylate by iodide *via* a two-step sequence of reactions, including isolation of the bromide *(2)*, affords a product which according to its IR and NMR spectra and refractive index, is identical with the directly formed iodide *(3)*. The yields of the products *(2)* and *(3)* (Scheme 1) were 60—80 % after destillation.



Scheme 1

[*] T. ElGomati, Dr. D. Lenoir, and Prof. Dr. I. Ugi
Institut für Organische Chemie der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[**] We thank Dr. *Herbert Eck* of Wacker-Chemie, Burghausen, for 3-ethoxycyclobutanone.—Support is acknowledged from the National Science Foundation, Grant G.P. 28927 X, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie.

This result lends itself to the following alternative interpretations:

a) The substitution *(1)*→*(3)* proceeds with retention[3], whereas the others occur with inversion[3,4].

b) Compound *(3)* and its *trans*-isomer equilibrate, with the equilibrium lying predominantly on the side of *(3)*.

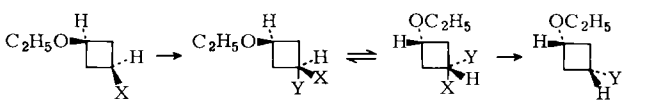
c) All substitutions, *(1)*→*(2)*, *(1)*→*(3)* and *(2)*→*(3)*, are retentive.

Since all reactions have been carried out under the same conditions and belong to the same substitution type[4], interpretation (a) is improbable[5]. Interpretation (b) can be ruled out because *(3)* is obtained in high purity, while, as a rule, in the thermodynamic equilibrium of the *cis*- and *trans*-isomers of 1,3-disubstituted cyclobutane derivatives, the *cis*-isomer predominates to the extent of 70–80 %[6].

Hence the conclusion is that all three substitutions proceed according to (c) with retention.

Considering the reaction conditions, and the fact that the S_N reaction of the brosylate *(1)* in aqueous acetone leads to 98 % inversion, the above reaction cannot involve a mechanism entailing ionic intermediates[7].

The most reasonable explanation is offered by a recently postulated type of bimolecular substitution[7], proceeding *via* the penta-coordinated intermediates *(4)* and *(5)*, which are interconverted by a turnstile rotation (TR)[8], or a resultwise equivalent Berry pseudorotation (BPR)[8]; however, the latter is less likely here because of the presence of the 4-membered ring (Scheme 2). The second order S_N2 limiting mechanism otherwise observed in aliphatic nucleophilic substitutions, with pentacoordinated transition state *(6)* (or pentacoordinated intermediate in the limiting case) having apical leaving and entering groups, and a diequatorial 4-membered ring is at an energetic disadvantage in contrast with *(4)* and *(5)*, because of strain. An S_N1 nucleophilic substitution with "edge attack" can be ruled out; all available experimental and theoretical evidence indicates that in aliphatic second order nucleophilic substitution the formation and decomposition of pentacoordinate transition states, or of intermediates takes place through apical entry of the entering group and apical departure of the leaving group[9].



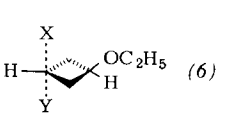
(1), X = OBs
(2), X = Br

(4)
(a), X = OBs, Y = Br
(b), X = OBs, Y = I
(c), X = Br, Y = I

(5)

(2), Y = Br
(3), Y = I

Scheme 2

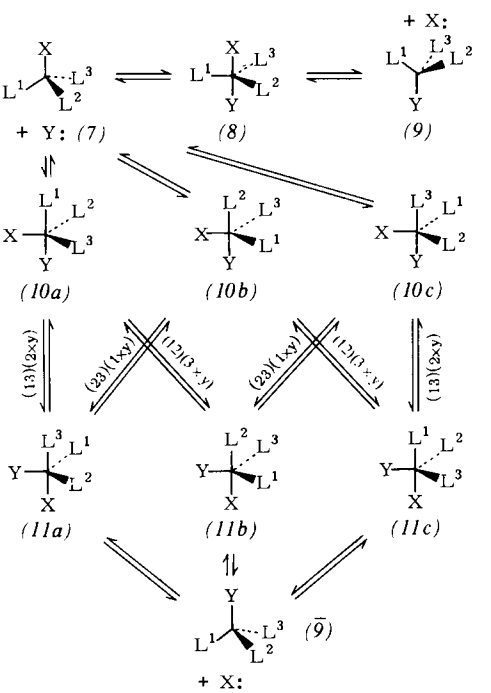


(6)

Thus the reactions of Scheme 1 indicate that there exist S_N with pentacoordinate intermediates, whose lifetime is long enough for permutational isomerization. This is in contrast to the presently accepted belief of the transition state nature of the pentacoordinate species *via* which S_N processes proceed.

From the perspective of apical entry and departure of ligands during the interconversion of tetra- and pentacoordinated configurations, and with due consideration of the present results, one is led to the following view of second order nucleophilic substitutions (Scheme 3): A nucleophile, Y, enters a "tetrahedral free face" of *(7)*, a compound with a tetracoordinate central atom and four ligands L^1, L^2, L^3, X one of which, X, is a leaving group. The entering group Y becomes thus an apical ligand of a pentacoordinate configuration *(8)* or *(10)*.

If the nucleophile enters opposite to X, *(8)* results, with the leaving group X in an apical position, from which it can depart directly giving rise to a "normal" S_N2. Otherwise pentacoordinate species *(10a)*, *(10b)*, or *(10c)*, result, with the leaving group X in an equatorial position. In this case X can only leave from an apical position after rearrangement (by TR, or BPR) into *(11a)*, *(11b)*, or *(11c)*, respectively. The product is $(\bar{9})$, the enantiomer of *(9)*. When there are no constraints that affect the skeletal placement of the ligand set $\{L^1, L^2, L^3, X, Y\}$, a "normal" S_N2 according to *(7)*→*(8)*→*(9)* is observed—with *(8)* as transition state, or intermediate—since *(8)* [or *(10)*] loose X much faster than they undergo the isomerization *(10)*→*(11)* which would be required for a retentive S_N. If, however, the attack on *(7)* by Y to form *(8)* is substantially retarded relative to the formation of *(10)* by constraints originating with the ligand set, then *(7)*→*(10)*→*(11)*→$(\bar{9})$ prevails. Here *(10)* and *(11)* cannot be transition states, but must be intermediates, because of the lifetime requirement for the permutation isomerization *(10)*→*(11)*. Let L^1 and L^2, for example, belong to a 3- or 4-membered ring, or maybe also a 5-membered ring, then the species *(8)*, *(10c)* and *(11a)* with a diequatorial ring are too strained to be S_N intermediates, and *(7)*→*(10a)*→*(11b)*→$(\bar{9})$ and *(7)*→*(10b)*→*(11c)*→$(\bar{9})$ are the fastest S_N reactions.



Scheme 3

A mechanism analogous to that in Scheme 2 may also be responsible for the observed preferential retention encountered in the reduction of gem. dihalocyclopropanes with $LiAlH_4$ and $LiAlD_4$[10] and analogous reactions[11].

According to quantum mechanical calculations[12] cyclopropane derivatives, with pentacoordinate carbon in a geometrical arrangement resembling a TR barrier situation, are energetically more favorable than arrangements corresponding to *(6)*.

The steric course of nucleophilic substitution at a tetracoordinate phosphorus center[13] incorporated in a 4-membered

ring proceeds analogously to the scheme *(1)*→*(3)*→*(2)*. Recently, however, a nucleophilic substitution at phosphorus in a 4-membered ring was observed to involve inversion[14]. Perhaps in this case the permutational isomerization of the pentacoordinate intermediate not only follows the TR mechanism, but also an interconversion by TR2[8]. The retentive nucleophilic substitutions at silicon[15] could also proceed *via* interconverting pentacoordinate intermediates.

Received: August 12, 1974 [Z 114 IE]
German version: Angew. Chem. *87*, 66 (1975)

CAS Registry numbers:
(1), 27829-84-1; *(2)*, 53778-40-8; *(3)*, 53778-41-9; LiBr, 7550-35-8; NaI, 7681-82-5

[1] *I. Lillien* and *L. Handloser*, Tetrahedron Lett. *1970*, 1213.

[2] *A. Streitwieser:* Solvolytic Displacement Reactions. McGraw-Hill, New York, 1962, pp. 1–34, and literature cited therein.

[3] For the definition of 'retention' and 'inversion' see: a) *J. Gasteiger, P. Gillespie, D. Marquarding*, and *I. Ugi*, Top. Curr. Chem. *48*, 1 (1974); b) *J. Blair, J. Gasteiger, C. Gillespie, P. D. Gillespie*, and *I. Ugi*, Tetrahedron *30*, 1845 (1974).

[4] *L. Fowden, E. D. Hughes*, and *C. K. Ingold*, J. Chem. Soc. *1955*, 3187, and literature cited therein.

[5] See Ref. [2], pp. 11 and 12.

[6] *G. M. Lampman, G. D. Hager*, and *G. L. Couchan*, J. Org. Chem. *35*, 2398 (1970).

[7] *P. D. Gillespie* and *I. Ugi*, Angew. Chem. *83*, 493 (1971); Angew. Chem. internat. Edit. *10*, 503 (1971), and literature cited therein.

[8] *I. Ugi, D. Marquarding, H. Klusacek*, and *P. Gillespie*, Accounts Chem. Res. *4*, 288 (1971); *P. Gillespie, P. Hoffmann, H. Klusacek, D. Marquarding, S. Pfohl, F. Ramirez, E. A. Tsolis*, and *I. Ugi*, Angew. Chem. *83*, 691 (1971); Angew. Chem. internat. Edit. *10*, 687 (1971).

[9] a) *D. Marquarding, F. Ramirez, I. Ugi*, and *P. D. Gillespie*, Angew. Chem. *85*, 99 (1973); Angew. Chem. internat. Edit. *12*, 91 (1973); b) *L. Tenud, S. Farooq, J. Seibl*, and *A. Eschenmoser*, Helv. Chim. Acta *53*, 2059 (1970).

[10] *H. Yamanaka, T. Yagi, K. Teramura*, and *T. Ando*, Chem. Commun. *1971*, 380; *C. W. Jefford, U. Burger, M. H. Laffer*, and *T. Kabengele*, Tetrahedron Lett. *1973*, 2483.

[11] *J. T. Groves* and *K. W. Ma*, Tetrahedron Lett. *1974*, 909.

[12] a) Pentacoordinate C-anions: *A. M. Wooley* and *M. S. Child*, Mol. Phys. *19*, 625 (1970); *A. Dedien* and *A. Veillard*, J. Amer. Chem. Soc. *94*, 6730 (1972); *R. F. Bader, A. J. Duke*, and *R. R. Messer*, *ibid. 95*, 7715 (1973); b) Pentacoordinate cyclopropane derivatives: *W. D. Stohrer*, Chem. Ber. *107*, 1795 (1974); CNDO/2 and *ab initio* calculations concerning the $H^{\ominus}$-adduct of 1,1-difluorocyclopropane were carried out at our institute by *J. Gasteiger, W. Schubert*, and *R. Kopp*.

[13] See Ref. [9a]: references [34], [49], [51–54], [57]; *C. R. Hall* and *D. J. H. Smith*, Tetrahedron Lett. *1974*, 1696.

[14] *J. Emsley, T. B. Middleton*, and *J. K. Williams*, J. C. S. Dalton *1974*, 633.

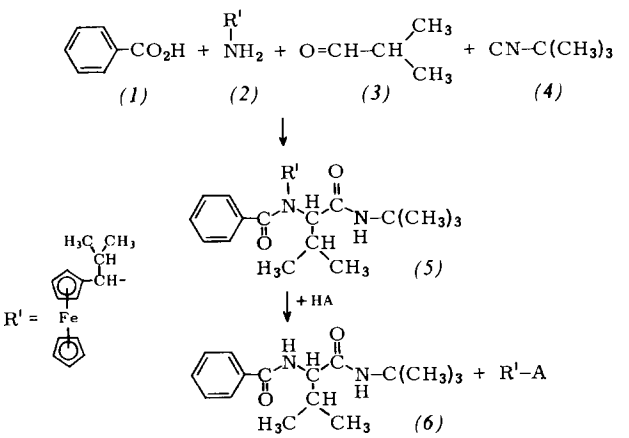
[15] *L. H. Sommer:* Stereochemistry, Mechanism and Silicon, McGraw-Hill, New York 1965; *B. G. McKinnie, N. S. Bhacca, F. K. Cartledge*, and *J. Faysonx*, J. Amer. Chem. Soc. *96*, 2537 (1974).

Asymmetrically Induced Four Component Condensation with Extremely High Stereoselectivity and Multiplication of Stereoselectivity[**]

By *Reinhard Urban* and *Ivar Ugi*[*]

In the synthesis of peptide fragments by four component condensations[1] it is essential to form the new α-amino acid unit in the desired configuration with maximum stereoselectivity.

The stereoselectivity of the asymmetrically induced model four component condensation *(1)*+*(2)*+*(3)*+*(4)*→*(5)* reaches $c_{(R,S)\text{-}(5)}$: $c_{(R,R)\text{-}(5)}$ 99.5 : 0.5 under suitably chosen reaction conditions.



No.	Amine *(2)*	T [°C]	C_0 [mol/l] [b]	Q_{pn} $c_{(R,R)\text{-}(5)}$: $c_{(R,S)\text{-}(5)}$	*(5)*, Yield [%]
1	rac.	−30	0.02	26.4 : 73.6	32
2	rac.	0	0.02	38.7 : 61.3	40
3	rac.	20	0.02	51.5 : 48.5	45
4	rac.	−78	0.02	0.5 : 99.5	26
5	*R*(−) [a]	−78	0.05	0.94 : 99.06 [c]	97 [b]
6	*R*(−) [a]	0	0.05	40.9 : 59.1 [c]	77
7 [d]	*S*(+) [a]	−78	0.05	20.0 : 80.0	61

[a] $[\alpha]_D^0 = \pm 79.8°$ ($c = 1$, benzene). Preparation and configurational assignment of *(2)*: *H. Klusacek, D. Marquarding, I. Ugi*, and *R. Urban*, unpublished.
[b] Concentration of all starting materials, except in experiment 5 where a 10% excess of *(1)*, *(2)* and *(3)* was used.
[c] Gravimetric determination.
[d] Addition of 0.02 mol/l triethylammonium benzoate.

The unusually high degree of stereoselectivity is due to the fact that under the conditions of reaction 4 (Table 1)[2a] the rather bulky optically active amine component *(2)* leads to an almost uniform reaction mechanism, a pair of corresponding reactions involving solvent separated immonium ions and nitrilium ions[1–3]; the decrease in stereoselectivity on the addition of triethylammonium benzoate is evidence for this[2b]. The latter pair of corresponding reactions has high intrinsic stereoselectivity[1c], because the bulky groups reduce the number of participating conformations in the selectivity determining pair of transition states, and effect thus the high degree of selectivity which is characteristic for rigid systems[3].

The ratio of the isomers formed, $Q_{pn} = c_{(R,R)\text{-}(5)} : c_{(R,S)\text{-}(5)}$, was determined by high pressure liquid chromatography (Hupe

[*] Dipl.-Chem. R. Urban and Prof. Dr. I. Ugi
Organisch-Chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

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

& Busch, Karlsruhe, UFC 1000) on a Perisorb column (Merck) in cyclohexane/ethyl acetate 100:3.3. The evaluation was based on reference mixtures of the pure isomers.

The products were identified as the (*R,R*) or (*S,S*), and (*R,S*) or (*S,R*) isomers by NMR comparison with the known products of α-phenylethylamine and α-ferrocenylethylamine[4]. The absolute configuration of the condensation product *(5)* was assigned by removal of the α-ferrocenylalkyl group R^1. After the cleavage reaction *(5)* → *(6)* of the predominating product of reaction 5 the optical rotation of the resulting valine derivative was found to correspond to that of *N*-benzoyl-(*S*)-valine *tert*-butylamide[4, 5]. Accordingly, the configuration of the above product *(5)* is: *N*-benzoyl-*N*-[(*R*)-α-ferrocenylisobutyl]-(*S*)-valine *tert*-butylamide.

In this context it is interesting to note that the cleavage by 0.1 M trichloroacetic acid in methanol of (*R,R*)-*(5)* is about 50 times faster than that of (*R,S*)-*(5)*. An accurate determination of the rate ratios has not been carried out yet. This enables a multiplication of stereoselectivities with regard to *(6)*.

Let the cleavage of (*R,R*)-*(5)* be 50 times faster than that of (*R,S*)-*(5)*, and a 1:200 mixture of (*R,R*)-*(5)* and (*R,S*)-*(5)* be subjected to the cleavage reaction for five halflives—which correspond to 1/10 of the halflife time of (*R,S*)-*(5)*—then a 0.03:187 mixture of (*R,R*)-*(5)* and (*R,S*)-*(5)* results. The subsequent complete cleavage of this mixture would yield (*R*)-*(6)* and (*S*)-*(6)* in a ratio 0.016:99.984. In the products of the first cleavage step which were obtained according to such a procedure the presence of (*R,R*)-*(5)* could not be detected by the usual methods (NMR, TLC).

This model experiment with its high primary and subsequent multiplication of selectivity opens the way to highly selective peptide syntheses by four component condensations[1c].

N-Benzoyl-N-[(R)-α-ferrocenyl-isobutyl]-(S)- and -(R)-valine tert-butylamide, (R,S)-(5) and (R,R)-(5)

10 mmol of the aldimine formed from *R*(−)-*(2)* and *(3)* is dissolved in 2/3 of the total amount of methanol and thermostated (see Table 1, reaction 5 and 6).

Solutions of *(4)* (10 mmol) and *(1)* (10 mmol) in the rest of the methanol are added dropwise with stirring and in this sequence to the first mentioned solution during 30 min. After 2—4 days the reaction mixture is poured into water, extracted with ether, and washed with 3% aqueous tartaric acid, 1 N aqueous sodium hydroxide, and finally with water.

The crude product is purified by chromatography on silica gel 60[70—230 mesh ASTM (Merck)]. (*R,S*)-*(5)*: m.p. 155—156 °C, $[\alpha]_D^{20} = -123.5°$, $[\alpha]_{546}^{20} = -242.5°$ (*c* = 1, benzene); (*R,R*)-*(5)*: m.p. 178—180 °C, $[\alpha]_D^{20} = -431.7°$, $[\alpha]_{546}^{20} = -657.0°$ (*c* = 1, benzene).

Received: September 4, 1974 [Z 115 IE]
German version: Angew. Chem. *87*, 67 (1975)

[1] a) *I. Ugi*, Angew. Chem. *74*, 9 (1962); Angew. Chem. internat. Edit. *1*, 8 (1962); b) Rec. Chem. Progr. *30*, 289 (1969); c) Intra-Sci. Chem. Rep. *5*, 229 (1971); d) Isonitrile Chemistry. Academic Press, New York 1971, Chap. 8 and 9; e) Proceedings of the 13th European Peptide Symposium, Jerusalem 1974.

[2] a) *I. Ugi, K. Offermann, H. Herlinger*, and *D. Marquarding*, Liebigs Ann. Chem. *709*, 1 (1967); b) *I. Ugi* and *G. Kaufhold*, *ibid.* *709*, 11 (1967).

[3] a) *D. Marquarding* and *I. Ugi* in *F. Korte:* Methodicum Chimicum. Vol. II. Thieme, Stuttgart, in press; b) *J. Gasteiger, D. Marquarding*, and *I. Ugi* in *H. Kagan:* Handbook of Stereochemistry. Thieme, Stuttgart, in press.

[4] *D. Marquarding, P. Hoffmann, H. Heitzer*, and *I. Ugi*, J. Amer. Chem. Soc. *92*, 1969 (1970).

[5] *I. Ugi* and *K. Offermann*, Chem. Ber. *97*, 2996 (1964).

σ-Complex Intermediates in Acylation and Sulfonylation of 1,3,5-Tripyrrolidinobenzene—Preparation, Reactions, and Structure[1]

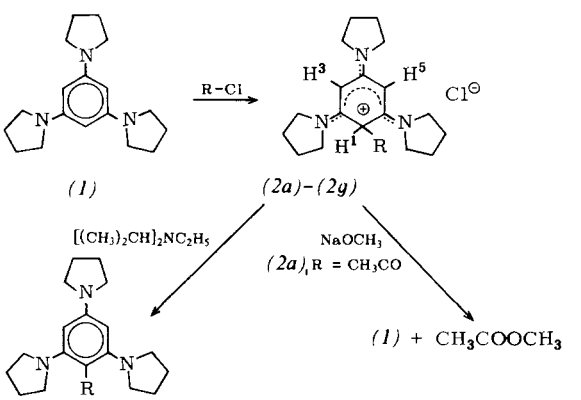
By *Peter Menzel* and *Franz Effenberger*[*]

In the acylation of arenes, σ-complex (Wheland) intermediates have been cited[2] for the formyl fluoride/boron trifluoride reaction of alkylbenzenes; they have received no mention, however, in more recent spectroscopic work[3]. σ-Complex intermediates have been established unequivocally by NMR spectroscopy for the sulfonylation of persubstituted benzenes[4]. With the extremely electron-rich 1,3,5-triaminobenzenes, such complexes have even been isolated in the case of protonation[5], alkylation[6], and halogenation[7]; we now report analogous results for the acylation and sulfonylation of triaminobenzenes.

If 1,3,5-tripyrrolidinobenzene *(1)* is treated with acetyl or benzoyl chloride in anhydrous dichloromethane at 0 °C, the orange-yellow σ-complexes *(2a)* and *(2b)*, respectively, can be precipitated with ether from the brownish yellow reaction solutions. Sulfonylation of *(1)* with tosyl chloride under similar conditions yields *(2d)*, while *(2c)* [formed upon reaction with mesyl chloride in $CDCl_3$] can be identified only by NMR spectroscopy. Compounds *(2e)*, *(2f)*, and *(2g)* which have proved essential for assessing the conformation of Wheland intermediates[8], are prepared analogously (Table 1).

Except for *(2c)*, the σ-complexes *(2)* are stable at room temperature for a reasonable time. The chloride ion may be exchanged with either $AgClO_4$ or $AgBF_4$.

Deprotonation of *(2)* to *(3)* is effected with *N,N*-diisopropylethylamine; no deprotonation but rather cleavage of the acetyl group is observed with sodium methoxide.



Nonplanarity of the cyclohexadienylium ring has been established by X-ray crystallography for σ-complexes of type *(2)* with R = CH_3 and R = Br[10]. If *(2a)*—*(2g)* are also nonplanar only two extreme conformations (*syn* or *anti*) are possible for steric reasons. In case of restricted rotation about the C^1—C^7 or C^1—S bonds these two conformations could be differentiated by NMR spectroscopy. There is no significant change, however, in the NMR signals over a wide temperature range, thus ruling out rotation or an alteration of rotational behavior.

For the acyl σ-complexes *(2a)* and *(2b)*, the olefinic protons $H^{3,5}$ exhibit nearly identical shifts, while H^1 is less shielded by 1.63 ppm in *(2b)* as compared with *(2a)* (Table 1). The acyl complexes must therefore be assigned the *syn* conformation (A *syn*) where H^1 is strongly deshielded if R′ = phenyl.

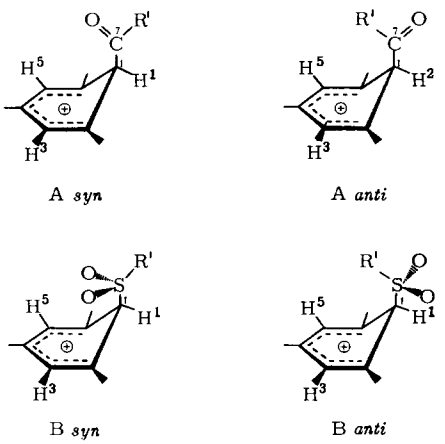
[*] Dr. P. Menzel and Prof. Dr. F. Effenberger
Institut für Organische Chemie der Universität
7 Stuttgart 80, Pfaffenwaldring 55 (Germany)

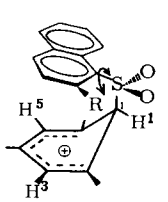
Table 1. σ-Complexes *(2)* prepared.

	R	^{1}H-NMR, δ [ppm] [a] H^1	$H^{3,5}$	IR [cm^{-1}] [b] C=N and C=C
(2a)	CH_3CO	4.86	5.07	1610; 1520; 1435
(2b)	C_6H_5CO	6.49	4.92	1615; 1523; 1430
(2c)	CH_3SO_2	5.66	5.00	
(2d)	p-CH_3—$C_6H_4SO_2$	5.55	4.63	1620; 1540; 1430
(2e)	9-Anthryl-SO_2	5.75	3.84	1620; 1540; 1430
(2f)	1-Naphthyl-SO_2	5.66	4.21	1620; 1545; 1427
(2g)	2-Methyl-1-naphthyl-SO_2	5.58	4.59 3.93	1620; 1545; 1425

[a] 0.1 M in $CDCl_3$, 30°C, internal reference TMS.
[b] KBr pellet. The three intense bands listed are characteristic of 1,3,5-triaminobenzene σ-complexes [9].

In contrast, the analogous sulfonyl complexes *(2c)* and *(2d)* exhibit different shifts for $H^{3,5}$ and almost identical shifts for H^1, and must therefore exist in the *anti* conformation (B *anti*). In this arrangement, the olefinic protons of *(2d)* come to lie within the diamagnetic shielding cone of the tolyl ring, and thus experience an upfield shift as compared with *(2c)*. If this rationalization is correct, the effect should be much more pronounced for an anthracenesulfonyl complex: indeed, $H^{3,5}$ of *(2e)* appear better shielded by another 0.8 ppm while the H^1 signal is shifted slightly downfield. For the naphthalenesulfonyl compound *(2f)* where only one proton experiences additional shielding by the annelated benzene ring, separate resonances are expected for H^3 and H^5. Due to rapid oscillation of the naphthyl moiety about the S-aryl bond, however, the spectrum shows only one singlet of intermediate shift.





(2f), R = H
(2g), R = CH_3

Upon introduction of a methyl group in the β position of *(2)*, this oscillation is no longer possible for steric reasons; accordingly, the $H^{3,5}$ signal of *(2g)* is split into two resonances. Concomitant with the increasing shielding by larger and larger π-systems, the ^{1}H signal shows a systematic downfield shift in the series *(2d)*→*(2f)*→*(2e)*, thus providing further confirmation that the aryl rings are fixed above the cyclohexadienylium system. Differing conformations of acyl and sulfonyl σ-complexes would be impossible in a planar structure; furthermore, the marked influence of the aryl substituents upon the $H^{3,5}$ signal of *(2d)*—*(2g)* would be hard to explain. The σ-complexes, at least of triaminobenzenes, must therefore exist in a nonplanar conformation with the substituent at C^1 in axial position, both in solution and in the solid state.

Received: September 16, 1974 [Z 116 IE]
German version: Angew. Chem. *87*, 71 (1975)

CAS Registry numbers:
(1), 16857-93-5; *(2a)*, 53973-55-0; *(2b)*, 53973-56-1; *(2c)*, 53973-57-2; *(2d)*, 53973-58-3; *(2e)*, 53973-59-4; *(2f)*, 53973-60-7; *(2g)*, 53973-61-8; acetyl chloride, 75-36-5; benzyl chloride, 98-88-4; mesyl chloride, 124-63-0; tosyl chloride, 98-59-9; 9-anthrylsulfonyl chloride, 53973-96-9; 1-naphthylsulfonyl chloride, 85-46-1; 2-methyl-1-naphthylsulfonyl chloride, 53973-97-0

[1] Electrophilic Substitution of Aromatic Compounds, Part 10.—Part 9: *F. Effenberger* and *K. Huthmacher*, Angew. Chem. *86*, 409 (1974); Angew. Chem. internat. Edit. *13*, 409 (1974). This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[2] *G. A. Olah* and *J. S. Kuhn*, J. Amer. Chem. Soc. *80*, 6541 (1958).

[3] *G. A. Olah*, *H. C. Lin*, and *Y. K. Mo*, J. Amer. Chem. Soc. *94*, 3667 (1972).

[4] *A. N. Detsina* and *V. A. Koptyug*, Zh. Org. Khim. *8*, 2158 (1972); Chem. Abstr. *78*, 57931 u (1973).

[5] *F. Effenberger* and *R. Niess*, Angew. Chem. *79*, 1100 (1967); Angew. Chem. internat. Edit. *6*, 1067 (1967).

[6] *R. Niess*, *K. Nagel*, and *F. Effenberger*, Tetrahedron Lett. *1968*, 4265.

[7] *P. Menzel* and *F. Effenberger*, Angew. Chem. *84*, 954 (1972); Angew. Chem. internat. Edit. *11*, 922 (1972).

[8] *P. Rys*, *P. Skrabal*, and *H. Zollinger*, Angew. Chem. *84*, 921 (1972); Angew. Chem. internat. Edit. *11*, 874 (1972).

[9] *P. Fischer*, Dissertation, Universität Stuttgart 1970.

[10] Dihedral angle between the planar cyclopentadienylium part and the tetrahedral C^1 *ca.* 15°; *J. J. Stezowski*, personal communication.

Stable Solutions of 1-Aza-2-cyclopentadienone Salts in Thionyl Chloride/Antimony Pentachloride[**]

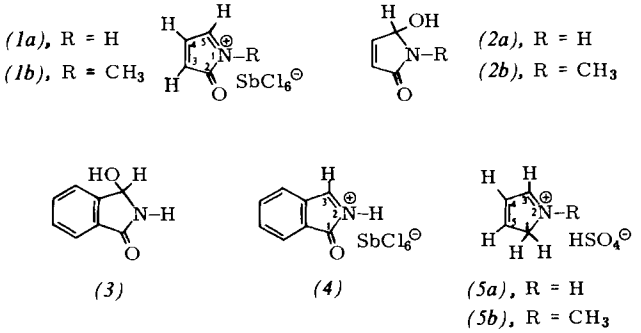
By *Wilhelm Flitsch* and *Klaus Gurke*[*]

The stability of cyclopentadienones is not essentially enhanced by the presence of nitrogen atoms in the ring: unsubstituted azacyclopentadienones are unknown[11]; diazacyclopentadienones are unstable compounds which have only rarely been isolated and readily dimerize[12].

In the salts of azacyclopentadienones dimerization is opposed by intermolecular repulsion between the ions. We have been able to prepare stable solutions of the salts of 1-aza-2-cyclopentadienones (2-oxopyrrolium salts) *(1)* from the hydroxylactams *(2)*[13] with thionyl chloride and antimony pentachloride by mixing the reactants at −80°C and then slowly warming the reaction mixture to room temperature. The known benzoannelated analog *(4)* is formed similarly from the hydroxylactam *(3)*[14].

[*] Prof. Dr. W. Flitsch and Dipl.-Chem. K. Gurke
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)

[**] This work was supported by the Landesamt für Forschung des Landes Nordrhein-Westfalen and by the Fonds der Chemischen Industrie.



(1a), R = H
(1b), R = CH_3

(2a), R = H
(2b), R = CH_3

(3)

(4)

(5a), R = H
(5b), R = CH_3

^{1}H-NMR data of the salts are listed in Table 1. The correlation of the signals was confirmed by double resonance experiments. The chemical shifts and coupling constants were assigned by computer simulation. Comparison with the ^{1}H-NMR spectra of protonated 2*H*-pyrroles, *e.g.* 2*H*-pyrrolium hydrogen sulfate shows that the ring proton signals of the salts *(1)* and *(4)* lie at surprisingly high field. Similar observations were made with substituted cyclopentadienones.

Table 1. ^{1}H-NMR data of the salts *(1)* and *(4)* (δ values in ppm, CH_2Cl_2 as internal standard, δ = 5.28; solvent $SOCl_2/SbCl_5/CH_2Cl_2$). Corresponding signals are placed under one another.

Cpd.	H-1	H-3	H-4	H-5
(1a)	9.32	6.91	7.82	6.57
	(J_{13} = 1.80, J_{14} = 1.99, J_{15} = 1.43, J_{34} = 5.76, J_{35} = 0.66, J_{45} = 1.37 Hz)			
(1b)	(3.51)	7.00	7.75	6.32
	J_{34} = 6.05, J_{35} = 0.61, J_{45} = 1.21 Hz)			
	H-2	aromatic H		H-3
(4) [a]	9.45	7.7	−8.3	6.97

[a] No NMR spectrum has previously been reported for *(4)*.

Received: July 11, 1974;
supplemented: September 16, 1974 [Z 117 IE]
German version: Angew. Chem. *87*, 39 (1975)

CAS Registry numbers:
(1a), 54036-78-1; *(1b)*, 54036-80-5; *(4)*, 30678-33-2

[1] In the oxodipyrromethenes, the 1-aza-2-cyclopentadienone (2-oxopyrrole) forms part of a more extensive resonance system: *H. v. Dobeneck* and *E. Brunner*, Hoppe-Seylers Z. Physiol. Chem. *341*, 157 (1965); 3-acetyl-5-benzyl-4-phenyl-1-aza-2-cyclopentadienone: *T. Kato*, *Y. Yamamoto*, and *M. Sato*, Yakugaku Zasshi *91*, 384 (1971); Chem. Abstr. 75, 20058 (1971).

[2] *P. J. Fagan* and *M. J. Nye*, Chem. Commun. *1971*, 537; *B. M. Trost* and *P. J. Whitman*, J. Amer. Chem. Soc. *94*, 8634 (1972); *B. T. Gillis* and *R. Weinkam*, J. Org. Chem. *32*, 3321 (1967); *B. T. Gillis* and *J. C. Valentour*, J. Heterocycl. Chem. *7*, 1131 (1970).

[3] *B. de Mayo* and *R. S. Reid*, Chem. Ind. (London) *1962*, 1576.

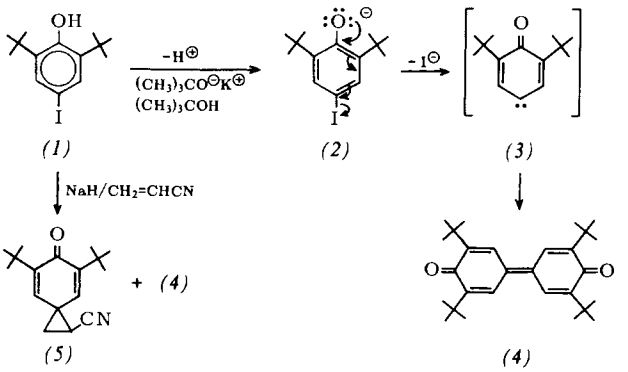
[4] *R. R. Schmid* and *E. Schlimpf*, Chem. Ber. *103*, 3783 (1970).

3,5-Di-*tert*-butyl-4-oxo-2,5-cyclohexadien-1-ylidene by 1,5-Elimination[**]

By *Peter Bartholmei* and *Peter Boldt*[*]

On thermolysis or photolysis 4-diazo-2,6-di-*tert*-butyl-2,5-cyclohexadien-1-one decomposes into 3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadien-1-ylidene *(3)* which dimerizes to the diphenoquinone *(4)*[1] and can be trapped with alkenes to form spirodienones of type *(5)*[2].

We attempted to prepare the keto carbene *(3)* by elimination of hydrogen halide from *p*-halophenols: reaction of 2,6-di-*tert*-butyl-4-iodophenol *(1)* with strong bases such as potassium *tert*-butoxide or sodium hydride afforded the diphenoquinone *(4)* in 95% yield. Use of acrylonitrile as solvent and sodium hydride as base furnished 80% of *(4)* and 18% of *(5)*. Hence it may be deduced that the carbene *(3)* or a corresponding carbenoid had been generated from the initially formed phenoxide *(2)* by extrusion of an iodide ion.



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

3,3',5,5'-Tetra-tert-butyl-4,4'-diphenoquinone (4)

Potassium *tert*-butoxide (2 g, 18 mmol) in *tert*-butyl alcohol (60 ml) was mixed with compound *(1)* (3.3 g, 10 mmol) in *tert*-butyl alcohol (60 ml). After 14 hours' stirring under nitrogen, the reaction mixture was treated with water (200 ml) and extracted with light petroleum. The evaporation residue *(in vacuo)* of the dried organic phase yielded 1.9 g (95%) of compound *(4)* after recrystallization (methanol/water).

5,7-Di-tert-butyl-6-oxospiro[2.5]octa-4,7-diene-1-carbonitrile (5)

A solution of *(1)* (3.3 g, 10 mmol) in acrylonitrile (100 ml) was added dropwise with stirring to NaH (1 g, 40 mmol) at 0 °C. After 5 hours' stirring under nitrogen the solution was poured into light petroleum (500 ml), any excess NaH destroyed with ethanol, and the mixture washed with water, dried, and evaporated *in vacuo*. The evaporation residue was chromatographed from light petroleum/acetone (9 : 1) on silica gel. The eluates of the first and second zones contained *(4)* (1.6 g, 80%) and *(1)* (0.06 g, 2%), respectively, and that of the third zone *(5)* (0.46 g, 18%) which, after recrystallization from cyclohexane, exhibited m.p. 120 °C (literature value[2]: 118.5—119.5 °C). The NMR, IR, and mass spectra were in accord with formula *(5)*.

Received: September 18, 1974 [Z 118 IE]
German version: Angew. Chem. *87*, 39 (1975)

CAS Registry numbers:
(1), 40084-31-9; *(3)*, 21205-90-3; *(4)*, 2455-14-3; *(5)*, 19510-09-9

[1] *G. A. Nikiforov* and *V. V. Ershov*, Izv. Akad. Nauk SSSR, Ser. Khim. *1967*, 2341.

[2] *G. A. Nikiforov*, *B. D. Sviridov*, and *V. V. Ershov*, Izv. Akad. Nauk SSSR, Ser. Khim. *1968*, 558.

Hydrazinoribose—An Intermediate for the Specific Formation of Natural Nucleosides and Their Derivatives[**]

By *Richard R. Schmidt*, *Jochen Karg*, and *Wolfgang Guilliard*[*]

The final step of nucleoside syntheses usually consists in coupling of the glycosidic C—N bond by kinetically controlled

[*] Dipl.-Chem. P. Bartholmei and Prof. Dr. P. Boldt
Lehrstuhl B für Organische Chemie der Technischen Universität
33 Braunschweig, Postfach 3329 (Germany)

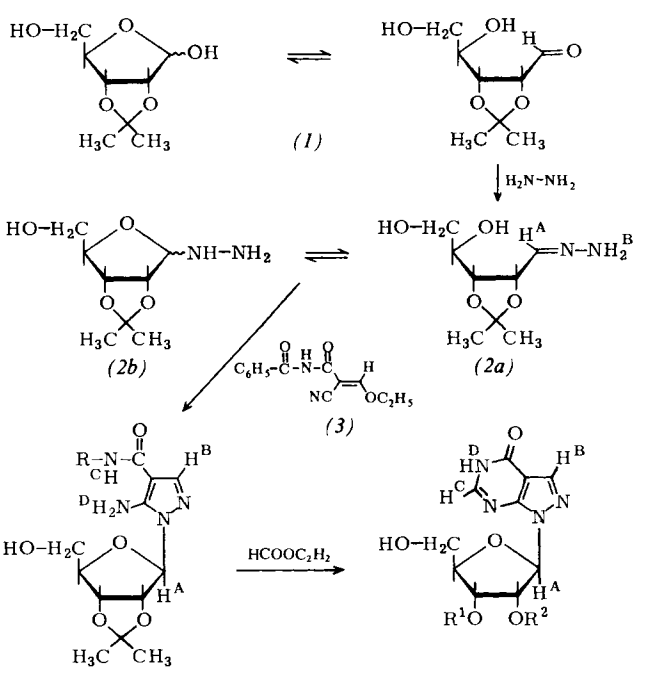
[**] This work was supported by the Fonds der Chemischen Industrie.

[*] Doz. Dr. R. R. Schmidt, Dr. J. Karg, and Dipl.-Chem. W. Guilliard
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
7 Stuttgart 80, Pfaffenwaldring 55 (Germany)

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

reaction of a protected D-ribofuranose with a heterocyclic compound, its heavy metal salt, or its trimethylsilyl derivative[1]. We now describe a method for the preparation of pyrazole nucleosides and their derivatives which avoids the difficulties of the above methods by stepwise formation of the product starting from the D-ribose, as in the biosynthetic pathway[2]. This technique provides a convenient route to, *e.g.*, the biologically important allopurinol riboside *(5b)*[3].

Protected D-ribose derivatives such as 2,3-*O*-isopropylidene-D-ribose *(1)* can be transformed quantitatively into the hydrazine derivative *(2)* by treatment with hydrazine[4]. NMR observations in D_6-DMSO show that *(2)* comprises an equilibrium mixture of the hydrazone form *(2a)* and the hydrazinofuranose form *(2b)*, in which *(2a)* predominates (≈90%). The configuration of *(2b)* at the anomeric center could not be deduced from the NMR spectrum; it can however be assumed on the basis of consecutive reactions and other findings[4] that the hydrazino group is at least partly β configurated.



(4a), R = C_6H_5-CO

(4b), R = H

(5a), R^1–R^2 = $>C(CH_3)_2$

(5b), R^1 = R^2 = H

Thermodynamically controlled reaction of *(2)* with polyfunctional cyclization reagents such as the ethoxymethyleneacrylamide derivative *(3)*[5], which form the pyrazole system, results in double ring closure and specific β-glycosidic linkage of the furanose and pyrazole ring in a single step to give the pyrazole nucleoside derivative *(4a)* (m.p. 160—161 °C, yield 58%). On reaction of *(3)* with *(2)* the equilibrium *(2a)*⇌*(2b)* apparently shifts towards the furanose form, in which the hydrazino group adopts the β configuration under the influence of three chiral centers.

The action of sodium methoxide on *(4a)* afforded the amide *(4b)* (m.p. 181 °C, yield 72%), which furnished the isopropylidene-protected allopurinol riboside *(5a)* (yield 85%) on treatment with ethyl formate. Compound *(5a)* was converted into the allopurinol riboside *(5b)* (m.p. 204 °C[6], yield 80%) by an acidic ion exchanger (Amberlite IR 120 in the H^+ form).

NMR data of compounds *(2a)*, *(4a)*, *(4b)*, *(5a)*, and *(5b)* are listed in Table 1.

Table 1. NMR data of the ribose derivatives prepared (in δ relative to tetramethylsilane as internal standard).

Cpd.	Solvent	H^A	H^B	H^C	H^D
(2a)	D_6-DMSO	7.03 (d, 1H)	6.25 (s, 2H)		
(4a)	D_6-DMSO	6.10 (s, 1H)	7.97 (s, 1H)	10.23 (s, 1H)	6.93 (s, 2H)
(4b)	D_6-DMSO	6.00 (s, 1H)	7.73 (s, 1H)	6.6—7.2 (4H)	
(5a)	CD_3CN	6.40 (d, 1H)	8.01 and 8.10 (2s, 2H)		7.39 (s, 1H)
(5b)	D_2O	6.32 (s, 1H)	8.23 (s, 1H)	8.23 (s, 1H)	

Received: September 30, 1974 [Z 119 IE]
German version: Angew. Chem. *87*, 69 (1975)

CAS Registry numbers:
(1), 13199-25-2; *(2a)*, 53762-10-0; *(2b)*, 53762-11-1; *(3)*, 53762-12-2; *(4a)*, 53762-13-3; *(4b)*, 53762-14-4; *(5a)*, 53762-15-5; *(5b)*, 16220-07-8; hydrazine, 302-01-2; ethyl o-formate, 122-51-0

[1] *W. Zorbach* and *R. S. Tipson*: Synthetic Procedures in Nucleic Acid Chemistry. Vol. 1. Wiley, New York 1968, see, *e.g.*, pp. 137 and 313.

[2] Nucleoside syntheses starting from aminoribose: *N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg*, and *G. Shaw*, J. C. S. Perkin I *1973*, 1720.

[3] a) *T. A. Krenitsky, G. B. Elion, R. A. Strelitz*, and *G. H. Hitchings*, J. Biol. Chem. *212*, 2675 (1967); b) *R. A. Earl, R. P. Panizica*, and *L. B. Townsend*, J. C. S. Perkin I *1972*, 2672; *H. Steinmaus*, DOS 2226673, Henning Berlin GmbH; Chem. Abstr. *80*, 60154q (1974).

[4] Other hydrazinoribose derivatives were obtained in similar manner and converted, like *(2)*, into numerous types of nucleosides; see *R. R. Schmidt et al.*, to be published.

[5] *G. Shaw*, J. Chem. Soc. *1955*, 1834.

[6] M.p. 201—202 °C [3c]; *(5b)* is found by chromatography and NMR and IR spectroscopy to be identical with a sample prepared according to [3a].

Synthesis of Novel Anti-inflammatory Steroids

By *Henry Laurent, Erich Gerhards*, and *Rudolf Wiechert*[*]

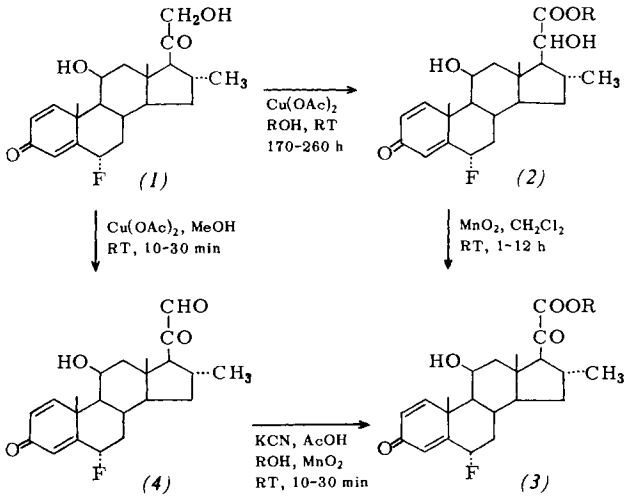
Fluocortolone *(1)*, developed by *Raspé et al.*[1, 2], was shown to be a strong anti-inflammatory corticoid suitable for local or systemic application. After oral administration of *(1)* there could be isolated a number of metabolites from human urine[3]. One of these was identified as the water-soluble, α-keto acid *(3a)*. We have synthesized this metabolite *(3a)* and a number of ester derivatives in order to investigate the anti-inflammatory activity of these substances.

Reaction[4] of *(1)* with alcohols in the presence of copper(II) acetate and oxygen leads initially to the aldehyde *(4)* which rearranges to a mixture of the epimeric 20-hydroxy esters *(2)* upon prolonged reaction.

Selective oxidation of the 20-hydroxy compounds *(2)* to the α-keto esters *(3b)*—*(3e)* can be accomplished with activated

[*] Dr. H. Laurent, Prof. Dr. Dr. E. Gerhards, and Prof. Dr. R. Wiechert
Forschungslaboratorien der Schering AG, Berlin/Bergkamen
1 Berlin 65, Müllerstrasse 170—178 (Germany)

MnO_2. Hydrolysis of *(3b)* with methanolic sodium hydroxide and subsequent treatment with hydrochloric acid affords the free acid *(3a)*.



ester *(3b)*. Replacement of methanol by butanol or isopropyl alcohol yields the corresponding esters *(3c)* and *(3h)*.

In the vasoconstriction test on human skin, these ester derivatives *(3)* were found to possess a local anti-inflammatory activity. However, upon subcutaneous and oral administration to animals in the adjuvant paw edema assay, spleen and thymus assay test and in the eosinophile test, these esters are practically inactive. They are also found to have no effect upon gluconeogenesis or electrolyte excretion in the rat. As a result of these and other findings, the butyl ester *(3c)* is currently undergoing clinical trials for use as a topically-active corticoid without the usual systemic activity.

Other corticosterone derivatives *(5)*, some of which exhibit pronounced corticoid effects, have been transformed into the 21-esters *(6)* by means of the methods developed for fluocortolone *(1)*.

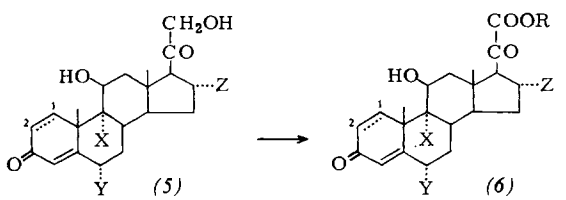
Procedure A:

a) 6α-Fluoro-11β,21-dihydroxy-16α-methyl-1,4-pregnadiene-3,20-dione *(1)* (300 g) in *n*-butanol (4.5 l) is stirred vigorously

	R	Procedure	Yield [%]	M.p. [°C] [a]	$[\alpha]_D^{25}$ [°] [c]	UV Maximum [nm] ε [e]
(3a)	H			237.7 [b]	+200 [d]	242 (16600)
(3b)	CH_3	A; C	46; 48	196.9	+144	242 (16900)
(3c)	*n*-C_4H_9	A; C	33; 61	195.1	+136	242 (16800)
(3d)	$(CH_2)_2CH(CH_3)_2$	A	51	192.1	+135	242 (16900)
(3e)	$C(CH_3)_3$	A	6	176.5	+127	241 (17000)
(3f)	C_2H_5	B	47	183.1	+143	242 (17000)
(3g)	C_3H_7	B	43	180.4	+140	242 (17000)
(3h)	$CH(CH_3)_2$	B; C	28; 48	225.1	+134	242 (16800)

[a] Mettler FP 11, 2°C/min.
[b] With decomposition.
[c] $c = 0.5$ in chloroform.
[d] $c = 0.5$ in pyridine.
[e] In methanol.

The esters *(3f)*—*(3h)* were synthesized by transesterification of the α-keto esters *(3b)* and *(3c)* in the presence of basic catalysts. Using the method described by *Corey et al.*[5] for oxidative esterification of α,β-unsaturated aldehydes with manganese(IV) oxide and methanol in the presence of cyanide ions, the 21-aldehyde *(4)* could be converted into the methyl



with copper(II) acetate (150 g) for 260 h. The solution is evaporated *in vacuo*, the residue dissolved in dichloromethane; the resulting solution is washed several times with 12% ammonium hydroxide solution, then with sodium chloride solution, and finally dried and evaporated to dryness. The residue is chromatographed over silica gel. Elution with 20 to 50% acetone/hexane affords 289.5 g of a mixture of butyl 6α-fluoro-11β,20α- and 6α-fluoro-11β,20β-dihydroxy-16α-methyl-3-oxo-1,4-pregnadien-21-oate *(2c)*. b) The ester *(2c)* (275 g) is stirred vigorously for 3 h with manganese(IV) oxide (3.0 kg) in dichloromethane (2 l). The filtrate obtained from the reaction mixture is evaporated down and the residue chromatographed with hexane/acetone/dichloromethane over silica gel. Recrystallization twice from acetone/hexane gives

		X	Y	Z	R	Δ^1	Procedure	Yield [%]	M.p. [°C] [a]	$[\alpha]_D^{25}$ [°] [b]	UV Maximum [nm] ε [c]
Corticosterone	*(6a)*	H	H	H	C_4H_9	–	A	26	139.4	+218	240 (17000)
16α-Methylcorticosterone	*(6b)*	H	H	CH_3	C_4H_9	–	A	45	162.2	+198	241 (16900)
6α-Fluoro-16α-methylcorticosterone	*(6c)*	H	F	CH_3	C_4H_9	–	A	48	188.0	+176	236 (16100)
1,2-Didehydrocorticosterone	*(6d)*	H	H	H	C_2H_5	+	C	61	191.4	+173	243 (15700)
16α-Methyl-1,2-didehydrocorticosterone	*(6e)*	H	H	CH_3	C_4H_9	+	A	48	154.5	+149	243 (15600)
Deoxymetasone	*(6f)*	F	H	CH_3	CH_3	+	A	42	220.9	+144	239 (16300)
Diflucortolone	*(6g)*	F	F	CH_3	C_4H_9	+	A; C	34; 64	193.6	+122	237 (17400)
Clocortolone	*(6h)*	Cl	F	CH_3	C_4H_9	+	A; B	16; 61	180.8	+150	238 (16900)

[a] Mettler FP 11, 2°C/min.
[b] $c = 0.5$ in chloroform.
[c] In methanol.

112.0 g of butyl 6α-fluoro-11β-hydroxy-16α-methyl-3,20-dioxo-1,4-pregnadien-21-oate *(3c)*.

Procedure B:

A solution of *(3c)* (5.0 g) in *n*-propanol (300 ml) is refluxed with potassium *tert*-butoxide (250 mg) under argon for 1 h. The product is precipitated with 1% acetic acid, filtered off, dried, and recrystallized from acetone/hexane. One obtains 2.07 g of propyl 6α-fluoro-11β-hydroxy-16α-methyl-3,20-dioxo-1,4-pregnadien-21-oate *(3g)*.

Procedure C:

a) To a solution of *(1)* (1.0 g) in methanol (125 ml) is added a solution of cooper(II) acetate (250 mg) in methanol (125 ml). The mixture is stirred for 15 min at room temperature with passage of air. After dilution with dichloromethane, it is washed with 5% ammonium chloride solution and water, dried over sodium sulfate, and the solvent evaporated off *in vacuo*. Yield: 1.05 g of 6α-fluoro-11β-hydroxy-16α-methyl-3,20-dioxo-1,4-pregnadien-21-al *(4)*. b) The aldehyde *(4)* is stirred in methanol (20 ml) with potassium cyanide (1 g), conc. acetic acid (1 ml), and manganese(IV) oxide (10 g) for 10 min at room temperature. The filtrate obtained from the reaction mixture is diluted with dichloromethane, washed with water, dried with sodium sulfate, and evaporated to dryness *in vacuo*. The residue is chromatographed over silica gel. Elution with 18 to 22% acetone/hexane affords 525 mg of methyl 6α-fluoro-11β-hydroxy-16α-methyl-3,20-dioxo-1,4-pregnadien-21-oate *(3b)* after recrystallization from acetone/hexane.

Received: October 7, 1974 [Z 120 IE]
German version: Angew. Chem. *87*, 70 (1975)

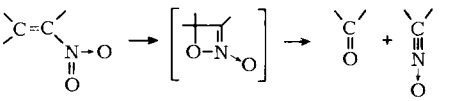
CAS Registry numbers:
(1), 152-97-6; (20α-OH)-*(2c)*, 41767-27-5; (20β-OH)-*(2c)*, 41767-28-6; *(3a)*, 33124-50-4; *(3b)*, 41767-25-3; *(3c)*, 41767-29-7; *(3d)*, 50681-46-4; *(3e)*, 50681-47-5; *(3f)*, 50681-53-3; *(3g)*, 52092-84-9; *(3h)*, 50681-45-3; *(4)*, 53733-52-1; *(5a)*, 50-22-6; *(5b)*, 857-19-2; *(5c)*, 387-73-5; *(5d)*, 13479-38-4; *(5e)*, 57-86-3; *(5f)*, 382-67-2; *(5g)*, 2607-06-9; *(5h)*, 4828-27-7; *(6a)*, 53746-43-3; *(6b)*, 53746-44-4; *(6c)*, 53733-47-4; *(6d)*, 53733-50-9; *(6e)*, 53733-51-0; *(6f)*, 53733-49-6; *(6g)*, 50681-70-4; *(6h)*, 50681-50-0

[1] *G. Raspé, K. Kieslich*, and *U. Kerb*, Arzneim.-Forsch. *14*, 450 (1964).
[2] *A. Domènico, H. Gibian, U. Kerb, K. Kieslich, M. Kramer, F. Neumann*, and *G. Raspé*, Arzneim.-Forsch. *15*, 46 (1965).
[3] *E. Gerhards, B. Nieuweboer, G. Schulz*, and *H. Gibian*, Acta Endocrinol. *68*, 98 (1971).
[4] *M. L. Lewbart* and *V. R. Mattox*, J. Org. Chem. *28*, 1779 (1963).
[5] *E. J. Corey, N. W. Gilman*, and *B. E. Ganem*, J. Amer. Chem. Soc. *90*, 5616 (1968).

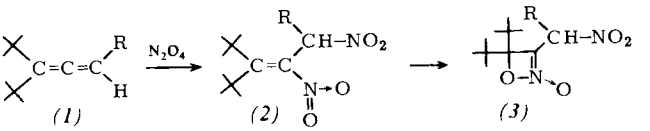
4*H*-1,2-Oxazete *N*-Oxides from 1,1-Di-*tert*-butylallenes [1]

By *Karlheinz Wieser* and *Armin Berndt* [*]

Apart from the sterically stabilized 4*H*-1,2-oxazete *N*-oxide *(6)* [2], derivatives of this heterocycle have hitherto only been reported as reactive intermediates in thermal [3] and photochemical [4] cleavages of α,β-unsaturated nitro compounds to form carbonyl compounds and nitrile oxides. Preparation of other isolable derivatives was precluded by the poor accessibility of sterically hindered nitroalkenes.

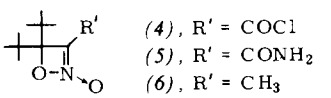


We have now found that the readily accessible 1,1-di-*tert*-butylallenes *(1)* [5] are ideal starting materials for the synthesis of 3-substituted 4,4-di-*tert*-butyl-4*H*-1,2-oxazete *N*-oxides. Addition of N_2O_4 to *(1)* leads directly to the readily crystallizing oxazete *N*-oxides *(3)* after work-up at room temperature. On careful work-up at *ca.* 0 °C the dinitroalkenes *(2)* can be isolated, which undergo smooth first-order reaction to give *(3)* on heating.



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

(a), R = H; *(b)*, R = Br; *(c)*, R = Cl



(4), R′ = COCl
(5), R′ = $CONH_2$
(6), R′ = CH_3

On standing *(3c)* undergoes partial transformation to the acyl chloride *(4)*, from which other derivatives, *e.g. (5)*, can be prepared. All new compounds have been unequivocally characterized by their spectroscopic data (see Table 1), and the oxazete *N*-oxides also by elemental analysis and their mass spectra.

While *(4)* and *(5)* can be stored at room temperature, the derivatives *(3a)*—*(3c)* decompose even at 0 °C to oily mixtures of products from which di-*tert*-butyl ketone could be isolated by gas chromatography.

Table 1. Compounds of types *(2)*—*(5)* prepared.

Cpd.	Yield [%]	M.p. [°C]	IR [cm^{-1}] (CCl_4) C=N	C=O	=C—NO_2	—C—NO_2	^{1}H-NMR [ppm] (CCl_4) [a] $C(CH_3)_3$	$C(CH_3)_3$	C—H	N—H
(2a)	52	47 [b]	—		1535	1570	1.35	1.40	5.43	
(2b)	27	35 [b]	—		1535	1590	1.38	1.50	6.95	
(2c)	78	45 [b]	—		1585	1590	1.40	1.55	6.90	
(3a)	77	80–81	1690		—	1570	1.20		5.02	
(3b)	35	98	1675		—	1572	1.20 [c]	1.20 [c]	6.20	
							0.91 [d]	0.89 [d]	5.90 [d]	
(3c)	78	95–96	1685		—	1580	1.21	1.26	6.40	
(4)	17	54	1660	1730	—	—	1.26		—	
(5)	61	146	1660	1680	—	—	1.27		—	6.73, 7.03

[a] δ scale, all signals are singlets. [b] Conversion temperature. [c] Diastereotopic, accidently isochronic. [d] In C_6D_6.

Procedure:

Compound *(1)* (0.65 mol) is added dropwise to a stirred solution of N_2O_4 (11 g, 0.13 mol) in dry ether (40 ml) cooled to −10 °C. After 1 hour's stirring at −5 °C, excess N_2O_4 and ether are removed in a vacuum.—Isolation of *(2)*: The precipitate is rapidly filtered off and washed with a small volume of ice-cold ether.—Preparation of *(3)*: The reaction mixture is stirred for 20 min with water (30 ml), then taken up in benzene, and the benzene phase is washed neutral with water, dried with $MgSO_4$, and evaporated in a Rotavapor. The crystalline residue is filtered, washed with a small amount of ice-cold light petroleum, and recrystallized from the same solvent.

Received: September 20, 1974 [Z 121a IE]
German version: Angew. Chem. *87*, 72 (1975)

CAS Registry numbers:
(1a), 22585-31-5; *(1b)*, 10575-75-4; *(1c)*, 16487-16-4; *(2a)*, 53762-72-4; *(2b)*, 53762-73-5; *(2c)*, 53762-74-6; *(3a)*, 53762-75-7; *(3b)*, 53762-76-8; *(3c)*, 53762-77-9; *(4)*, 53762-78-0; *5)*, 53762-79-1

[*] Prof. Dr. A. Berndt and Dr. K. Wieser [**]
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

[**] Part of Dissertation of *K. Wieser*, Universität Marburg 1974.

[1] Reactions of Sterically Hindered Nitro Compounds, Part 3.—Part 2: *A. Berndt*, Tetrahedron Lett. *1970*, 173. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We also acknowledge support by Deutsche Shell AG and Chemische Werke Hüls.

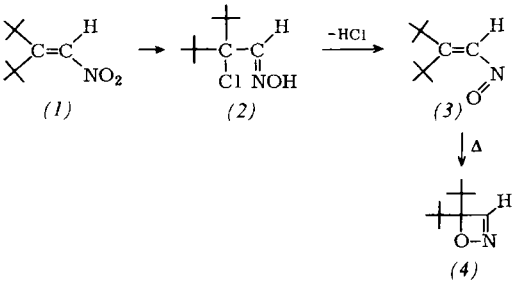
[2] *A. Berndt*, Angew. Chem. *80*, 666 (1968); Angew. Chem. internat. Edit. *7*, 637 (1968).

[3] *T. H. Kinstle* and *J. G. Stam*, J. Org. Chem. *35*, 1771 (1970).

[4] *J. T. Pinhey* and *E. Rizzardo*, Tetrahedron Lett. *1973*, 4057.

[5] *J. K. Crandall, W. W. Conover, J. B. Komin*, and *W. H. Machleder*, J. Org. Chem. *39*, 1723 (1974); *S. R. Landor, A. N. Patel, P. F. Whiter*, and *P. M. Greaves*, J. Chem. Soc. *C 1966*, 1223.

Since reactive molecules can be stabilized by introduction of bulky substituents and nitroalkenes subject to strong steric hindrance cyclize to 4*H*-1,2-oxazete *N*-oxides[4], we have attempted to synthesize stable 4*H*-1,2-oxazetes by thermal cyclization of correspondingly substituted nitrosoalkenes. For this purpose, the α-chloro oxime *(2)* (2-*tert*-butyl-2-chloro-3,3-dimethylbutanal oxime) was prepared from the nitroalkene *(1)*[5, 6]. Compound *(2)* was then converted into 2-*tert*-butyl-3,3-dimethyl-1-nitroso-1-butene *(3)* by elimination of HCl with 1,5-diazabicyclo[4.3.0]non-5-ene[7]. Compound *(3)* is the first nitrosoalkene to be stable at room temperature.



(1) *(2)* *(3)* *(4)*

Brief heating of *(3)* to 220 °C, accomplished by drawing it at 10^{-4} torr through a 90-cm vertical glass tube packed with glass rings at this temperature into a cold trap (−196 °C), furnishes 4,4-di-*tert*-butyl-4*H*-1,2-oxazete *(4)* in 54% crude yield. The by-products of the reaction are di-*tert*-butyl ketone and hydrogen cyanide which are apparently decomposition products of *(4)* since they are formed in low yields at low temperature, in greater yields at higher temperatures, and are the sole products above 240 °C. Below 220 °C the reaction product still contains unreacted *(3)*. Compound *(4)* can be isolated by preparative layer chromatography.

The structure of *(4)* follows from mass-spectrometric elemental analysis, fragmentation to ions of di-*tert*-butyl ketone and hydrogen cyanide[8], and the spectral data listed in Table 1. It is confirmed by degradation of *(4)* to di-*tert*-butyl ketone and sodium cyanide on heating with sodium methoxide in methanol.

Table 1. Compounds *(2)*—*(4)*, *(6)*, and *(7)* prepared.

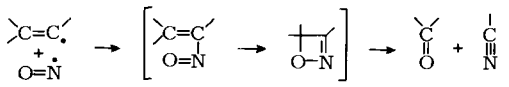
Cpd.	Yield [%]	M.p. [°C]	^{1}H-NMR [ppm] (CCl_4) [a]		IR [cm^{-1}] (CCl_4)
			$C(CH_3)_3$	others	
(2)	53	150—160	1.25	7.50 (CH), 9.55 (OH)	3580, 3300 (OH)
(3)	84	38	1.34, 1.85	6.30 (C)	1485 (N=O)
(4)	54 (crude), 26 (pure)	[b]	1.18	8.0 (CH)	1595 (C=N)
(6)	20	167	1.30	1.90 (CH_3), 7.35 (OH)	3600 (OH), 1540 (NO_2)
(7)	100	27—29	1.15	1.95 (CH_3)	1610 (C=N)

[a] δ scale, all signals are singlets.
[b] B.p. 182—183 °C.

Stable 4*H*-1,2-Oxazetes by Intramolecular Cyclization of α,β-Unsaturated Nitroso Compounds[1]

By *Karlheinz Wieser* and *Armin Berndt*[*]

Derivatives of 4*H*-oxazete have hitherto only[2] been postulated as reactive intermediates in the formation of carbonyl compounds and nitriles from vinyl radicals and NO[3].



To stabilize 4*H*-1,2-oxazetes, we have attempted to synthesize 4*H*-1,2-oxazetes with bulky substituents by intramolecular cyclization of correspondingly substituted nitrosoalkenes. For this purpose, the α-chloro oxime *(2)* (2-*tert*-butyl-2-chloro-3,3-dimethylbutanal oxime) was prepared from the nitroalkene *(1)*[4, 5]. Compound *(2)* was then converted into 2-*tert*-butyl-3,3-dimethyl-1-nitroso-1-butene *(3)* by elimination of HCl with 1,5-diazabicyclo[4.3.0]non-5-ene[6]. Compound *(3)* is the first nitrosoalkene to be stable at room temperature.

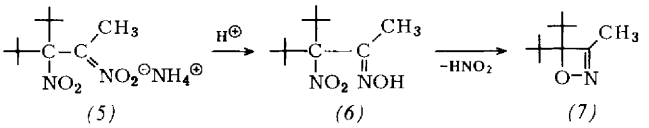
(1) *(2)* *(3)* *(4)*

Brief heating of *(3)* to 220 °C, accomplished by drawing it at 10^{-4} torr through a 90-cm vertical glass tube packed with glass rings at this temperature into a cold trap (−196 °C), furnishes 4,4-di-*tert*-butyl-4*H*-1,2-oxazete *(4)* in 54% crude yield. The by-products of the reaction are di-*tert*-butyl ketone and hydrogen cyanide which are apparently decomposition products of *(4)* since they are formed in low yields at low temperature, in greater yields at higher temperatures, and are the sole products above 240 °C. Below 220 °C the reaction product still contains unreacted *(3)*. Compound *(4)* can be isolated by preparative layer chromatography.

The structure of *(4)* follows from mass-spectrometric elemental analysis, fragmentation to ions of di-*tert*-butyl ketone and hydrogen cyanide[7], and the spectral data listed in Table 1. It is confirmed by degradation of *(4)* to di-*tert*-butyl ketone and sodium cyanide on heating with sodium methoxide in methanol.

The starting material for the preparation of another stable 4*H*-1,2-oxazete was obtained by reaction of ammonium 3-*tert*-butyl-4,4-dimethyl-2,3-dinitro-2-pentanide *(5)*[8] with dilute sulfuric acid. Preparative layer chromatography of the product mixture afforded the nitro oxime *(6)* (3-*tert*-butyl-4,4-dimethyl-3-nitropentanone 2-oxime). On reaction of *(6)* with an equivalent amount of sodium methoxide in methanol sodium nitrite is eliminated to give 4,4-di-*tert*-butyl-3-methyl-4*H*-1,2-oxazete *(7)*, whose structure is established unequivocally by elemental analysis, the spectral data listed in Table 1, and its mass-spectrometric fragmentation to ions of di-*tert*-butyl ketone and acetonitrile.

[*] Prof. Dr. A. Berndt and Dr. K. Wieser
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)



(5) (6) (7)

Since no blue coloration is observed during the transformation *(6)* → *(7)*, we assume that the expected nitrosoalkene cyclizes considerably faster than *(3)*. Attempts to prepare 4*H*-1,2-oxazetes having sterically less demanding substituents were unsuccessful.

Received: October 23, 1974 [Z 121 b IE]
German version: Angew. Chem. *87*, 73 (1975)

[1] Reactions of Sterically Hindered Nitrosoalkenes, Part 1.—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We also acknowledge support by Deutsche Shell AG and Chemische Werke Hüls.

[2] A product described by *M. Jovitschitsch*, Ber. Deut. Chem. Ges. *28*, 2093 (1895) as 4-bromo-3-methyl-4-nitro-4*H*-1,2-oxazete without any experimental proof could not be reproduced in spite of numerous attempts.

[3] *A. G. Sherwood* and *H. E. Gunning*, J. Amer. Chem. Soc. *85*, 3506 (1963); *J. M. Surzur, C. Dupy, M. P. Bertrand*, and *R. Nousier*, J. Org. Chem. *37*, 2782 (1972).

[4] *A. Berndt*, Angew. Chem. *80*, 666 (1968); Angew. Chem. internat. Edit. *7*, 637 (1968); *K. Wieser* and *A. Berndt*, Angew. Chem. *87*, 72 (1975); Angew. Chem. internat. Edit. *14*, 67 (1975).

[5] *A. Berndt*, Tetrahedron *25*, 37 (1969).

[6] *A. Dornow, H. D. Jordan*, and *A. Müller*, Chem. Ber. *94*, 67 (1961).

[7] *H. Oediger, F. Möller*, and *K. Eiter*, Synthesis *1972*, 591.

[8] Fragmentation of oxazetidinones: *T. Sheradsky, U. Reichman*, and *M. Frankel*, J. Org. Chem. *33*, 3619 (1968).

[9] *A. Berndt*, Angew. Chem. *81*, 567 (1969); Angew. Chem. internat. Edit. *8*, 613 (1969).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

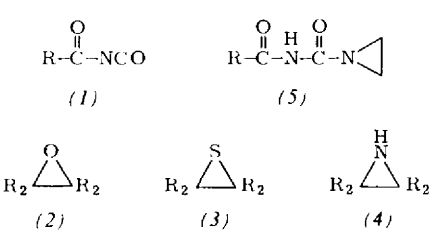
The synthesis of polychloro compounds with chlorinated functional groups such as $-CH_2Cl$, $\geq CCl_2$, $-CCl_3$, *etc.* by direct chlorination of the substrate is unsatisfactory. Addition and telomerization reactions open up new routes for the direct synthesis of a number of types of polychloro compounds. *R. Kh. Freidlina* and *E. C. Chukovskaya* describe such reactions of unsaturated compounds (alkenes, vinyl, alkyl, acryl monomers) with compounds containing a trichloromethyl group, *e.g.* 1,1,1-trichloroethane, 1,1,1,3-tetrachloropropane, 1,1,1,5-tetrachloropentane, pentachloroethane, DDT, 1,1,1-trichloro-2-methyl-2-propanol, trichloroacetates. The reactions are initiated by systems consisting of an iron compound, particularly pentacarbonyliron, in combination with cocatalysts such as acetonitrile, methanol (in large amounts), *N*,*N*-dimethylaniline, DMF, hexamethylphosphoric triamide (in small amounts). The reactions proceed *via* cleavage of the C—Cl bond of the trichloromethyl group and formation of polychloro derivatives having a $R-CCl_2-CH_2-C(Cl)\leq$ group. [Synthesis of Polychloro Derivatives with Various Functional Groups Containing Chlorine. Synthesis *1974*, 477—488; 47 references]

[Rd 736 IE—M]

The synthesis of cyclobutanes from olefins by photochemical cyclodimerization, metal-catalyzed cyclodimerization, and radical-cationically induced dimerization is dealt with in an article by *L. J. Kricka* and *A. Ledwitch*. The photochemical cyclodimerization of simple olefins to cyclobutanes is limited to a few examples, whereas strained cyclic olefins readily cyclodimerize. There are numerous examples for the photochemical cyclization of polycyclic olefins, unconjugated dienes, and vinylarenes. A few examples are known for the metal-catalyzed cyclodimerization of olefins. A number of vinyl-substituted aromatic amines, particularly carbazole derivatives, cyclodimerize in the presence of oxidizing agents such as Fe^{III}, Ce^{IV}, and Cu^{II} and on irradiation with UV and daylight, especially under the action of sensitizers. Linear dimers occur as by-products. The reactions proceed *via* intermediary radical cations. [Cyclobutanes from Photochemical, Metal-Catalyzed, and Cation-Radical Induced Dimerization of Mono-Olefins. Synthesis *1974*, 539—548; 89 references]

[Rd 737 IE—M]

Cycloaddition reactions of aliphatic and aromatic acyl isocyanates *(1)* are summarized in a review by *B. A. Arbuzov* and *N. N. Zobova*. Suitable methods have been found in recent years for the preparation of these compounds (which are more reactive than alkyl and aryl isocyanates) and their thio and seleno analogs. Owing to their double-bond system, acyl isocyanates *(1)* can undergo $[\pi 2+\pi 2]$ and $[\pi 4+\pi 2]$ cycloadditions with numerous unsaturated compounds and thus afford new routes to the synthesis of heterocyclic systems. A description of the physical and chemical properties of *(1)* is followed by an account of their reactions with unsaturated compounds (*e.g.* olefins, enamines, enol ethers, isocyanides, acetylenes, diazo compounds, carbonyl compounds, dialkyl sulfoxides), oxiranes *(2)*, thiiranes *(3)*, and aziridines *(4)*. Reactions of *(1)* with *(2)* or *(3)* usually



(1) (5)

(2) (3) (4)

yields open chain and cyclic derivatives, the latter with ring expansion. Reaction with aziridine leads to the urea derivative *(5)*, whose benzoyl derivative can rearrange to a five-membered ring system, an imidazoline derivative. *N*-Substituted aziridines react in a similar way with benzoyl isocyanate at high temperatures in the presence of LiBr *via* ring expansion to give an imidazolidine derivative. [Cycloaddition Reactions

of Aliphatic and Aromatic Acyl Isocyanates. Synthesis *1974*, 461—476; 70 references]

[Rd 739 IE—M]

Mixed cyanide phosphane complexes of transition metals are reviewed by *P. Rigo* and *A. Turco*. So far complexes of this type are known with metals of the eighth group and the first subgroup of the periodic table. Phosphane ligands stabilize low oxidation numbers of metals and promote the formation of otherwise unstable transition metal compounds as organometallics, hydrides, dinitrogen complexes, *etc.* As cyanide phosphane complexes of a certain metal may occur in different oxidation and coordination numbers, they can play an important role in homogeneous catalysis of organic reactions. This is exemplified in the synthesis of organic nitriles catalyzed by nickel complexes. Bi- and polynuclear cyanide phosphane complexes with cyanide bridges have also been prepared. [Cyanide Phosphine Complexes of Transition Metals. Coord. Chem. Rev. *13*, 133—172 (1974); 151 references]

[Rd 740 IE—H]

The importance of nickel as a trace element in organisms is the subject of a review by *F. H. Nielsen* and *D. A. Ollerich*. The essential function of this element has been long recognized from pharmacological, toxicological, biochemical, and chemical investigations. Recently, it has been possible to induce nickel deficiency in experimental animals. This results in biochemical and morphological changes in the liver. A deficiency of nickel in the organism leads to slower oxidation of α-glycerophosphate and the lipid level increases, while the phospholipid level sinks. Morphological changes can be observed by the increase in volume of cisterna of the rough endoplasmic reticulum and of the mitochondria. [Nickel: A New Essential Trace Element Fed. Proc. *33*, 1767—1772 (1974); 52 references]

[Rd 744 IE—R]

Recent results of hemoglobin research are reported by *E. Antonini*. Since a resolution down to 2.8 Å has been achieved in X-ray structural analyses, it is possible to distinguish quite accurately the individual groups participating in interactions and to recognize changes in conformation. The discovery of further anomalous hemoglobins has led to a better understanding of the relationship between structure and function. The assembly of subunits has been studied in detail since it became possible to isolate α- and β-chains preparatively. The equilibrium and kinetics of the ligand binding have gained new importance, especially as regards the influence of polyanions such as ATP or 2,3-diphosphoglycerate on the addition of oxygen. [Heme Proteins: Hemoglobin FEBS Lett. *40*, S98—S104 (1974); 98 references]

[Rd 746 IE—R]

Lipids and membranes are reviewed in an article by *J. A. Lucy*. Membranes which primarily act as barriers are particularly rich in lipids, whereas in "functional" membranes the protein content predominates. In addition, differences are also found in the cholesterol content, in the degree of unsaturation, and in other chemical criteria. An important function of the lipids is the modification of the activity of membrane-bound enzymes. Membranes have a certain fluidity, the extent of which is determined, *inter alia*, by cholesterol content. At present, particular interest is being shown in the stability of membranes and the role of lipids in membrane fusion. [Lipids and Membranes. FEBS Lett. *40*, S105—S111 (1974); 45 references]

[Rd 747 IE—R]

The specificity of enzymes of D-glucose metabolism toward anomers is discussed in an article by *B. Wurster* and *B. Hess*. The substrates of carbohydrate metabolism generally exist as mixtures of cyclic and open chain substances. In order to make speculations on structure or on metabolic processes it is important to know which form of substrate is the reaction partner of the enzyme. The specificity at high enzyme activity is determined so as to be able to follow the anomerization as the slowest step. There are non-specific (hexokinase), specific (dehydrogenases), and other enzymes with more or less distinct α- or β-specificity (mutases, isomerases). The open-chain form also serves as substrate (aldolase). Some enzymes catalyze the anomerization process. As a rule the enzymes with highest specificity are those which catalyze reactions at, or directly adjacent to, the anomeric carbon atom. [Anomeric Specificity of D-Glucose Metabolism. FEBS Lett. *40*, S112—S118 (1974); 69 references]

[Rd 748 IE—R]

Insect hormones and their bioanalogs as potential insecticides is the subject of a review by *F. Šorm*. This topic has recently commanded a great deal of interest, since it is hoped that methods will be found for the selective control of insects. Distinction is made between activating, molting and juvenile hormones. The latter are potential insecticides since they hinder development to the adult form. Numerous compounds have recently been isolated from plant sources or chemically synthesized, some of which are even species specific. Difficulties are still encountered in the use of these compounds in the open country. [Insect Hormones and Their Bioanalogues as Potential Insecticides. FEBS Lett. *40*, S128—S132 (1974); no references]

[Rd 749 IE—R]

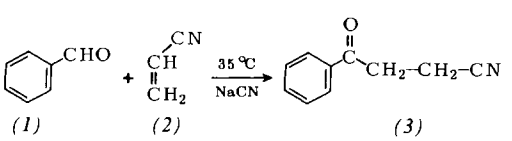
New approaches to immunosuppression is the title of a review authored by *L. R. Lyle* and *C. W. Parker*. Particular emphasis is placed on the potential use of "toxic" antigens. They are synthesized by binding a toxin or a toxin-producing enzyme to an antigen; these conjugates can then destroy antigen-sensitive cells selectively. Another interesting possibility is the use of non-metabolizable antigens. [New Approaches to Immunosuppression. Fed. Proc. *33*, 1889—1893 (1974); 38 references]

[Rd 751 IE—R]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Ketones are prepared by treatment of aromatic or heterocyclic aldehydes with activated unsaturated compounds in the presence of cyanide ions. Thus, β-benzoylpropionitrile *(3)* is formed in 80% yield from benzaldehyde *(1)* and acrylonitrile *(2)*. The following aldehydes are cited among others as exam-

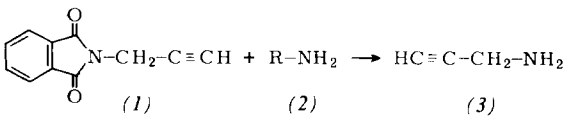


(1) *(2)* *(3)*

ples: *p*-chlorobenzaldehyde, *p*-methoxybenzaldehyde, furfuraldehyde, and 2-pyridinecarbaldehyde. As well as *(2)*, the following unsaturated compounds are suitable components for this reaction: esters of crotonic, maleic, and cinnamic acid, benzylideneacetone, phenyl vinyl ketone, and enamines. [DOS 2262343; Bayer AG, Leverkusen]

[PR 231 IE—G]

Propargylamine *(3)* is obtained in high yield when *N*-propargylphthalimide *(1)* is treated with high-boiling amines *(2)* [b.p. above 130°C, preferably above 170°C; in examples, R = $HO(CH_2)_2$—, benzyl and $(C_2H_5)_2N(CH_2)_3$—] in a solvent



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

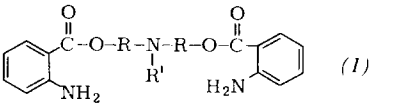
of similar high boiling point [DOS 2405370; Centre d'Études pour l'Industrie Pharmaceutique, Toulouse (France)]

[PR 232 IE—K]

Acetonedicarboxylic acid and its derivatives are formed in high yield when ketene and phosgene react in a suitable organic solvent at −30 to +50°C with molar ratio of total ketene: total phosgene < 2.0 and the product is allowed to react with a compound containing active hydrogen, *e.g.* with an alcohol. The acetonedicarboxylic esters prepared by this process can be converted into citric acid or citrates by a cyanohydrin synthesis and subsequent hydrolysis. [DOS 2409 342; Akzo GmbH, Wuppertal]

[PR 233 IE—D]

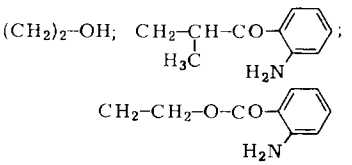
Aromatic polyamines such as *(1)*, **suitable for the production of polyurethane plastics** with improved tensile strength, are obtained by reaction of (i) compounds containing at least one tertiary nitrogen atom and at least two hydroxyl groups and with molecular weights within the range 119 to 1000 with (ii) isotoic anhydride in maximally equivalent amount.



(1)

R = $-(CH_2)_2-$; $-\underset{CH_3}{CH}-CH_2-$; $-(CH_2-CH_2-O)_2-$

R' = CH_3; $n\text{-}C_4H_9$; C_2H_5; $c\text{-}C_6H_{11}$; C_6H_5;



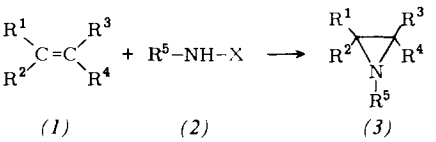
The groups favored for R and R' are given in the formula scheme. [DOS 2160590; Bayer AG, Leverkusen]

[PR 235 IE—W]

Transparent plastics reinforced by glass fibers can be obtained from 5—50 wt.-% of glass fibers or glass beads and 95—50 wt.-% of a mixture of at least two compatible thermoplastic materials whose proportions have been so assigned that the refractive index of the mixed plastics and the glass fibers is less than 0.002. Mixtures with poly(methyl methacrylate) and styrene-maleic anhydride copolymers are described. [DOS 2229129; BASF AG, Ludwigshafen]

[PR 236 IE—W]

Aziridines *(3)* are obtained on reaction of olefins *(1)* with *N*-haloamines *(2)*. R^1 to R^4 represent H, alkyl, cycloalkyl,



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

or aryl; R^5 is H or alkyl; X is Cl or Br. [DOS 2354470; Akademie der Wissenschaften der DDR, Berlin (GDR)]

[PR 237 IE—K]

BOOK REVIEWS

Ullmanns Encyklopädie der technischen Chemie (Ullmann's Encyclopedia of Technical Chemistry). Editional board: *E. Bartholomé, E. Biekert, H. Hellmann*, and *H. Ley*. Acaricide bis Antihistaminica (Acaricides to Antihistamines). Verlag Chemie GmbH, Weinheim 1974. 4th Edit., xvi, 720 pp., 208 figures, 211 tables, subscription price DM 345.—; final price *ca.* DM 385.—.

This is the first of the alphabetically arranged volumes constituting the main part of the new (4th) edition, as in previous editions of "Ullmann"[*]. As in the thematic part, the text in the alphabetical volumes has been completely rewritten. However, the general concept has been retained, *i.e.* the main emphasis is on industrial methods of production and related problems. The presentation has become more terse than previously which was a necessity in order to accommodate the increased amount of material relating to new products and processes within a work of reasonable size. At the same time, the new layout (two columns on each page and more pronounced optical subdivision) has improved the clarity of presentation.

Under the various key words the sub-sections on properties, occurrence and raw materials, preparation, quality, storage and transport, uses, economics, toxicology, are accompanied by a special section on the problems of liquid and gaseous effluents. Each entry is followed by a bibliography for further information, divided into surveys and specialized references.

Pharmaceuticals are particularly well represented in the key words in this volume, together with alkaloids (57 pp.), analgetics (25 pp.), antibiotics (60 pp.), and antihistamines (14 pp.). The raw materials include ammonia (70 pp.), acetylene (29 pp.), and acetaldehyde (13 pp.), and of the metals there is aluminum (including alloys and compounds, 112 pp.). Other large entries are for acetone (18 pp.), aliphatic aldehydes (24 pp.), alcohols (including polyhydric ones, 33 pp.), amines (aliphatic 19 pp., aromatic 10 pp., aniline 11 pp.), and anthraquinone dyes (62 pp.). Recognized industrial experts are responsible for the individual key word entries; the sections

[*] Cf. Angew. Chem. internat. Edit. *13*, 423 (1974).

on toxicology are written by *H. Oettel* (Ludwigshafen), and many of those on economics by *L. Franke* (Frankfurt/Main).

With the appearance of this, the first, new alphabetical volume it can be stated that in its new edition "Ullmann" retains its unbeaten record as a handbook of technical chemistry in respect to both the quality of its contents and to its lay-out. Particular credit should go to the editors, who, in spite of the large number of authors, have preserved the pleasant and homogeneous presentation.

Ulfert Onken [NB 236 IE]

Die Struktur der Atome und Moleküle (The Structure of Atoms and Molecules). By *J. Barrett*. Translated by *M. Ziegler*. Verlag Chemie GmbH, Weinheim 1973. 1st Edit., x, 348 pp., 205 figures, 62 tables, paperback, DM 38.—.

The book leads from the particle-wave dualism of photons and electrons to atomic structure and the periodic system. The major part of the work is concerned with bonding in diatomic molecules and gives a detailed treatment of Walsh diagrams and the electron pair repulsion model. The whole is rounded off by a chapter on π-electrons and bonding in solids and transition metal complexes.

The text is intended for first-year students and for teachers who want an introduction to theoretical chemistry that does not involve complicated derivations. Such readers demand a clear text in which simplicity is not achieved at the expense of correctness, and the important point to note is that since most of today's introductory chemistry books contain increasingly longer and better theoretical chapters, a book devoted solely to theory must offer some advantages over the general chemistry textbooks.

Unfortunately, this is not true of the book in question. The observant reader will find so many mistakes that its usefulness for students must often be questioned. For example, already on page 3 the electrostatic nature of nuclear forces leads to serious fears about the stability of our world, whereas the nucleus and the electrons are held together by "nuclear forces". The translation is not particularly careful; for example, we find "*virtuelles Vakuum*", "*degenerierte d-Orbitale*" and "*nicht müssen*" (for "must not"). This type of mistake, whether trivial or grave, could be easily removed, but the language mastery of either the author or the translator seems inadequate for the conceptual difficulties of modern physics; for instance, on page 48 it is interchangeably asserted that the wave nature of electrons should be understood as statistical and non-statistical.

It is true that such mistakes and inaccuracies occur mainly in the first part, but it seems dangerous to burden beginners or other readers with them, particularly as this book may remain the only one on theoretical chemistry that the reader works through.

It should not be overlooked that the chemical part, in particular the last two chapters, is considerably more successful, but the book cannot really be recommended until it has received more careful—and editorial—revision.

Finally, some suggestions may be permissible. In recent years quantum-chemical calculations have been used increasingly in organic chemistry, so that a new edition should contain chapters on the Woodward-Hoffmann rules and on Hückel theory. Also, photoelectron spectroscopy could be used as convincing support for the shell structure of atoms and as an experimental basis for the introduction of the MO model.

Klaus Wittel [NB 238 IE]

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 4036, 4037, Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

Correspondence concerning advertisements shoulds be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim, Pappelallee 3, P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 4031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE

Volume 14 · Number 2
February 1975
Pages 75–116

International Edition in English

Geochemistry of Stable Isotopes

By Jochen Hoefs[*]

During the past 25 years a new branch of research has developed under the name "stable isotope geochemistry", and its importance within the earth sciences has steadily increased. The present progress report considers the scope, and also the limitations, of this discipline.

1. Introduction

The foundations of isotope geochemistry were laid by *Urey et al.*[1] about 40 years ago with the discovery of the heavy isotope of hydrogen (deuterium). Even the preliminary experimental studies revealed that a partial separation or fractionation of the isotopes is possible by natural processes. The breakthrough to a degree of experimental precision adequate for most of the problems of isotope geochemistry came in the guise of a mass spectrometric technique, known as the "compensation bridge", developed by *Nier et al.*[2] in 1947.

Isotope geochemistry is concerned not so much with absolute isotope ratios but rather with differences in isotopic composition between a sample and a standard, which are expressed as "δ values". The δ value is defined as:

$$\delta[^0/_{00}] = \frac{R_{(sample)} - R_{(standard)}}{R_{(standard)}} \times 1000$$

where R is the isotope ratio of the pertinent element (*e.g.* $^{18}O/^{16}O$). The precision is generally $\pm 0.1\,^0/_{00}$. Positive (negative) δ values signify that the sample contains more heavy (light) isotopes than the standard.

Natural variations in isotopic composition can arise in two fundamentally different ways:

1) By genesis of nuclides on radioactive decay, particularly of the isotopes ^{40}K, ^{87}Rb, ^{232}Th, ^{235}U, and ^{238}U. Decay reactions provide a means of dating minerals and rocks. This discipline is known as geochronology.

2) By processes attributable to differing zero point energies of the isotopes and thus to their differing masses[3–7].

This progress report will be concerned exclusively with processes of the second kind.

2. Isotope Fractionation

The isotopes of an element can be fractionated in the following ways: by isotope exchange reactions in chemical equilibria, by kinetic processes, and by changing the state of aggregation.

Isotope exchange reactions between several phases of a system are generally not accompanied by chemical changes. Such exchange reactions can be described in a similar manner to "true" chemical reactions. Typically:

$$CaC^{16}O_3 + H_2{}^{18}O \rightleftharpoons CaC^{18}O^{16}O_2 + H_2{}^{16}O$$

The equation means that when calcium carbonate and water are present together the heavy isotope ^{18}O becomes enriched in the calcium carbonate. All isotope exchange reactions show temperature-dependent equilibrium constants. The equilibrium constant at 0 °C and 25 °C, respectively, is $K_0 = 1.0326$ and $K_{25} = 1.0286$. In other words: at 0 °C the oxygen in calcium carbonate contains $32.6\,^0/_{00}$ more ^{18}O than the oxygen in the water. With rising temperatures the equilibrium constant tends to unity, *i.e.* the separation effects disappear. This is the principle underlying determinations of "paleotemperatures" for geological objects, which will be considered in greater detail in Section 4.

[*] Doz. Dr. J. Hoefs
Geochemisches Institut der Universität
34 Göttingen, Goldschmidtstrasse 1 (Germany)

Kinetic isotope fractionations are generally due to differing reaction rates of isotopic molecules. These effects can occur in chemical reactions and in physical processes, *e.g.* diffusion of gases. On average the molecules containing the light isotope move faster in the gas phase than those containing the heavy isotope. The relative velocities can be deduced from the square root of the molecular weight ratio. For instance, the following relationship applies to CO_2:

$$\frac{\text{velocity } (^{13}C^{16}O^{16}O)}{\text{velocity } (^{12}C^{16}O^{16}O)} = \sqrt{\frac{45}{44}} = 1.011$$

i.e., the average velocity of $^{12}CO_2$ is $11\,^0/_{00}$ higher than that of $^{13}CO_2$. In Nature, typical examples of kinetic isotope fractionations are found in photosynthesis and bacterial sulfate reduction.

Isotope fractionations also occur during changes of phase, *e.g.* on crystallization and fusion. From the standpoint of isotope geochemistry, the evaporation and condensation of water occupies a position of paramount importance. The molecules H_2O and HDO, and $H_2{}^{16}O$ and $H_2{}^{18}O$, have different vapor pressures; the lighter isotope accumulates in the vapor phase. On evaporation of water, the light hydrogen isotope becomes enriched in the vapor phase more than the light oxygen isotope owing to a greater relative mass difference $\Delta m/m$. However, both undergo proportional fractionation so that in all samples of water that have participated in the atmospheric cycle a correlation exists between δD and $\delta^{18}O$, which is expressed empirically as

$$\delta D = 8\delta^{18}O + 10$$

(see Fig. 1).

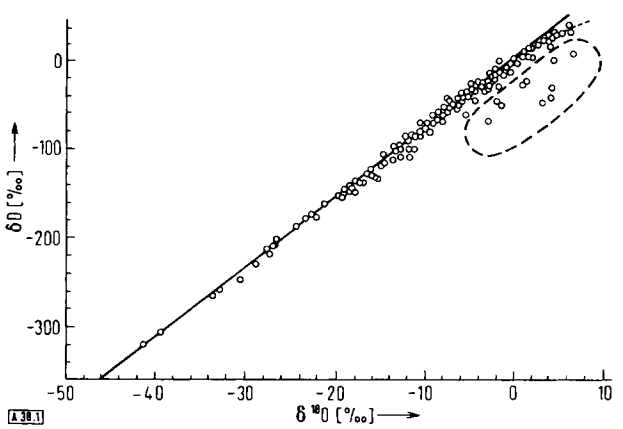


Fig. 1. Isotopic composition of meteoric water samples. The standard employed is SMOW (Standard Mean Ocean Water). The enclosed points apply to samples where evaporation took place under nonequilibrium conditions (after ref. [8]).

The most detailed studies have so far been performed on isotope fractionation for the elements hydrogen, carbon, oxygen, and sulfur; the elements boron, nitrogen, and silicon have been investigated less extensively[9].

The isotopic composition is determined by mass spectrometry, a high precision being attainable only for gaseous samples. Hence it is essential that a suitable gaseous compound of the element to be analyzed should exist, and that the element can be converted into that compound. Furthermore, it is of utmost importance that each step of the chemical preparation procedures should proceed quantitatively. Otherwise the results may be falsified by relatively large fractionation effects.

For elements which do not form suitable gaseous compounds such as potassium, magnesium, and calcium—a mass spectrometric determination of solid substances must be performed, the precision attainable then being about 10 times lower. Since the theoretically predicted fractionation effects for these elements are themselves rather small, the differences measured are of the same order as the experimental error. Precise statements are therefore still impossible for these elements (with the possible exception of potassium for which the differences are somewhat larger).

Prior to a discussion of applications, a number of generally valid rules of isotope geochemistry should be mentioned.

1) Isotopic fractionation is especially pronounced for elements whose isotopic masses differ widely. Hence the greatest isotopic fractionations are encountered with hydrogen. The maximum differences in isotopic composition are of the order of 50% in terrestrial samples and considerably higher in lunar samples owing to the influence of the solar wind (proton current). With carbon-13 and oxygen-18 the natural differences amount to 10—11% in extreme cases, and 15% with sulfur-34. As the atomic number increases, the expected fractionation contributions decrease. Contemporary analytical techniques permit recognition of fractionations up to bromine (atomic number around 35).

2) The elements best suited for geochemical studies are those which form solid, liquid, and gaseous compounds that are stable over a wide temperature range.

3) The heavier isotope is very often incorporated in the more highly oxidized form. Examples: sulfates are "heavier" than sulfides, and carbonates are "heavier" than organic carbon compounds. Exceptions to this rule can provide clues to a special origin.

4) Differences in isotopic composition decrease with rising temperature. Thus isotopic composition is a fundamental indicator of the formation temperature of minerals and rocks.

5) In biochemical reactions, *e.g.* photosynthesis and bacterial sulfate reduction, the light isotope is enriched in the reaction product since kinetic isotope fractionations occur preferentially in biological processes. In other words, biologically formed compounds should tend towards negative δ values.

3. Water

Water plays a crucial role in numerous geological processes. This applies not only to events on the earth's surface, but also to those occurring at greater depths (*e.g.* in the earth's mantle, even though the mantle most probably contains no more than 0.1% of H_2O). In this context, we shall merely consider the question whether the various volcanic phenomena such as hot springs, geysers, *etc.* involve surface water or juvenile water. The relationship shown in Figure 1 provides an unequivocal answer to this question, as is apparent from Figure 2.

The solid circles represent the isotopic composition of rain water in volcanic regions, and the open circles indicate the isotopic composition of the hot water. While the hydrogen

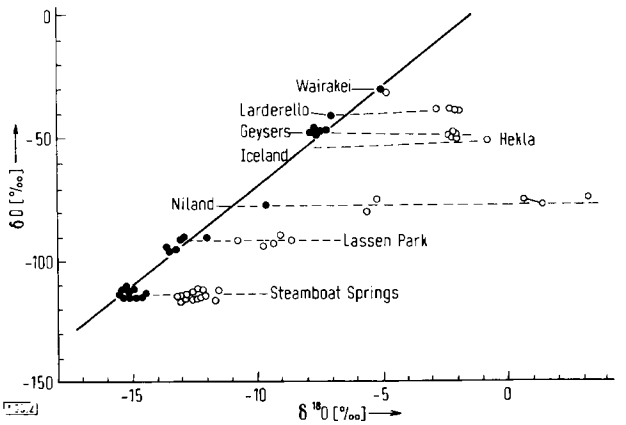


Fig. 2. Isotopic composition of "hot springs". ●, local rainwater; o, "hot springs" (after ref. [10]).

isotope composition of the hot water agrees well with that of the local rainwater, the oxygen isotope composition is always displaced to a greater or lesser extent towards higher values. This shift occurs because at high temperatures the water exchanges its oxygen isotopes with the ^{18}O-enriched silicates and, above all, carbonates in the surrounding rocks to become enriched in ^{18}O itself. Isotope analyses reveal that natural hot spring water are fed to at least 95 % by percolating surface water.

4. Thermometry

The determination of the "temperature of formation" of minerals and rocks can be regarded as one of the central questions in earth sciences. However, most of the "thermometers" so far described suffer from the disadvantage that not only the temperature, but also the pressure, have to be considered in the calculations. This is not the case with thermometers based on the determination of isotopic composition since the volumes of isotopically substituted molecules are independent of pressure. The first and best known thermometer of this kind is connected with the term "paleotemperature". In 1947, *Urey* postulated that the oxygen isotope ratio in calcereous organisms should provide a measure of the water temperature from which the organisms secrete carbonate. Thus the ^{18}O content of fossil chalk shells is measured and the temperature at which the animal lived and built up its shell is derived from the known temperature dependence of the oxygen isotope exchange between water and carbonate. In principle, it should therefore be possible to establish the past temperature of the oceans. Application of this thermometer requires that three prerequisites be fulfilled:

1) The isotopic composition of the seawater in the geological past must be known. Balance calculations strongly suggest that the isotopic composition of the oxygen in the oceans has not changed significantly during the past 400 million years.

2) The secreted carbonate must have been in isotopic equilibrium with the surrounding water. On passage through the calcereous organisms and during the actual secretion metabolic processes occur which can lead to isotopic fractionation. In recent years, evidence has accumulated that very many, if not most, organisms secrete carbonate selectively by metabolic processes[11-14] and therefore no longer reflect the original isotopic composition of the seawater.

3) After secretion of the carbonate, no isotopic exchange should occur between the shell and circulating pore water. However, the question whether recrystallization has occurred in a fossil after its deposition in a sediment cannot always be answered with certainty[15, 16].

Owing to the uncertainties mentioned, the above three prerequisites will certainly not be fulfilled in most cases. It is therefore not surprising that the method of paleotemperatures has recently commanded less interest.

In contrast, the determination of "formation temperatures" from the oxygen isotopic composition in silicates is becoming increasingly important.

Studies on minerals and rocks from widely differing sources have repeatedly shown that silicate, carbonate, and oxide minerals contain varying amounts of ^{18}O[17, 18]. Table 1 lists the most important minerals in the order of their ability to enrich ^{18}O.

Table 1. Important minerals arranged in the order of decreasing ^{18}O content of their oxygen.

Quartz SiO_2
Alkali metal feldspar $KAlSi_3O_8$ or $NaAlSi_3O_8$
Calcite, aragonite $CaCO_3$
Muscovite $KAl_2Si_3AlO_{10}(OH)_2$
Anorthite $CaAl_2Si_2O_8$
Garnet $(Mg,Fe^{II})_3Al_2(SiO_4)_3$
Pyroxenes $(Ca,Mg,Fe)_2Si_2O_6$
Amphiboles $Ca_2(Mg,Fe)_5Si_8O_{22}(OH)_2$
Biotite $K(Mg,Fe)_3Si_3AlO_{10}(OH)_2$
Olivine $(Mg,Fe)_2SiO_4$
Magnetite Fe_3O_4

That this order is nearly always fulfilled in all rocks can be interpreted as a criterion of equilibration. Failure to comply in isolated cases indicates disequilibrium, at least for the mineral occupying the wrong place. Such disequilibrium can be caused by isotopic exchange with an aqueous solution after crystallization of the mineral; feldspars in particular, and also micas, are susceptible to such processes.

The ^{18}O concentration of the minerals listed in Table 1 have been related to crystallochemical properties[18]. Those silicates containing the most Si—O—Si bonds have the greatest tendency to concentrate ^{18}O. It can be deduced from numerous

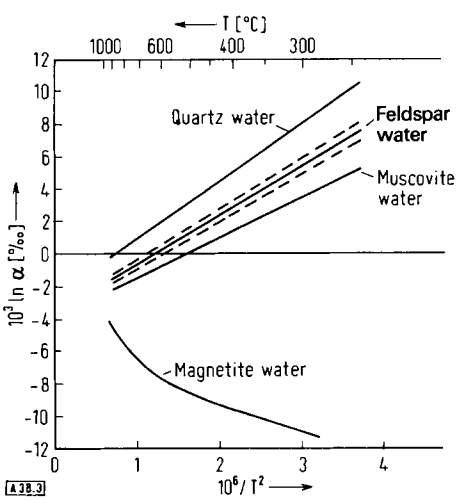


Fig. 3. Experimentally determined ^{18}O fractionation curves for several minerals. Ordinate: Fractionation factor $10^3 \ln\alpha \sim {}^{18}O_{(mineral)} - {}^{18}O_{(water)}$ in ‰ (after ref. [19]).

experimental data that at the temperature of formation of magmatic rocks the Si—O—Al bonds contain about $4\,^0/_{00}$ less ^{18}O then the Si—O—Si bonds, and the Si—O—Mg and Si—O—Fe bonds contain $2\,^0/_{00}$ less again.

Experimentally determined calibration curves (Fig. 3) permit calculation of the "formation temperatures" of rocks. The method requires measurement of the $^{18}O/^{16}O$ ratios of at least two minerals coexisting in the rock sample. The most successful application of this thermometer has been with metamorphic rocks in the temperature range of 250 to 600 °C[17, 20–22]. The value actually determined is the temperature of the last isotope exchange between the minerals and a fluid phase which in many cases can deviate considerably from the true "formation temperature". One may therefore ask what the measured temperatures have to tell us. However, in the most favorable case, particularly against a background of detailed knowledge of geological and petrological data, such a temperature value can certainly be of assistance.

5. Biosphere

The expression biosphere as used here embraces all living organisms—plants, animals, and microorganisms—and their remains in the geological milieu, *e.g.* coal and petroleum. Photosynthesis plays an essential role in fractionations occurring in the biosphere. This applies not only to carbon but also to hydrogen and oxygen. However, we shall restrict our attention to carbon in this article. Photosynthesis entails kinetic fractionation processes which can be divided into two steps[23]:

Step 1: the plant surface preferentially absorbs $^{12}CO_2$;

Step 2: of this CO_2, the $^{12}CO_2$ is preferentially incorporated into the primary photosynthetic product.

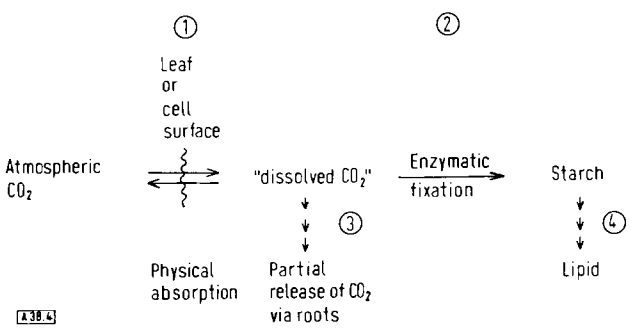


Fig. 4. Model for fractionation of carbon isotopes during photosynthesis. ①—④ are the steps in which fractionation can occur (after ref. [23]).

A fairly detailed model is depicted in Figure 4; four steps are shown in which the isotopes can undergo fractionation. The relative weights and efficiencies of the individual steps differ within species and families so that the isotopic composition can vary widely in plants[24]. Furthermore, numerous studies on plant material have shown that the isotopic composition of the carbon can provide information about the metabolism of organisms. Plants whose photosynthesis involves the enzyme ribulose 1,5-diphosphate carboxylase (RuDPC) can be distinguished from those which require the enzyme phosphoenol pyruvate carboxylase (PEPC) instead[26].

The organic constituents such as proteins, carbohydrates, *etc.* extracted from organisms are characterized by various $^{13}C/^{12}C$ ratios (Table 2). This gives us an opportunity to trace the history of these constituents during and after deposition in sediments. For instance, a decarboxylation is generally associated with a lowering of the ^{13}C content of the residual organic material since the carboxyl group is enriched in ^{13}C[27]. Fossil sediments are enriched in ^{12}C relative to recent sediments because "isotopically heavy" proteins and, to a lesser extent, carbohydrates (see Table 2)—as the most unstable organic compounds in the geological milieu—undergo very fast degradation[28]. Moreover, it can be shown that petroleums arise from the lipid fractions of plants and animal primary products[29].

Table 2. Isotopic composition of organic compounds in marine plankton (after ref. [25]).

	$-\delta^{13}C\ [^0/_{00}]$
Pectin	16—17
Proteins	17—19
Hemicellulose	17—20
Total carbohydrates	18—20
Total organic matter	19—20
Cellulose	20—24
Lignin	21—25
$CHCl_3$-extractable lipids	24—33

6. Sulfide Ore Deposits

The sulfide ore minerals such as FeS_2, $CuFeS_2$, PbS, ZnS, *etc.* belong to the least soluble compounds of the respective elements. How can these relatively insoluble metal sulfides be enriched and transported without enormous volumes of water?

With the advent of "isotope geochemistry" attempts were made—almost inevitably—to find fresh answers to such old questions. Numerous studies have been undertaken (*e.g.*[30–34]) to establish the origin of the sulfur by means of the $^{34}S/^{32}S$ ratio in sulfide mineral ores. In these investigations it was assumed that the sulfides from magmatic-hydrothermal ores, whose sulfur should come from greater depths, exhibit a fairly constant isotopic composition comparable with that of sulfides in meteorites. In contrast, ore deposits whose sulfur has come from surface-near sediments and can often be derived from the action of sulfate reducing bacteria have a highly variable isotopic composition with a predominance of negative ("light") δ values. This is due to kinetic fractionations in bacterial sulfate reduction in which "heavy" sulfate reacts to give "light" hydrogen sulfide[35, 36].

Meanwhile[37, 38], this concept has been proved invalid in the above simple form. Whereas the ore minerals were formerly always assumed to have the same isotopic composition as the ore-transporting solution, *Ohmoto*[38] has shown that the isotopic composition can depend upon the following factors:

1) Isotopic composition of the total sulfur in the ore-forming solution; 2) temperature of the solution; 3) oxygen fugacity of the solution; 4) pH value of the solution.

For instance, at 250 °C a change in the oxygen fugacity by a factor of ten or a change in the pH value by one unit can give rise to a $20\,^0/_{00}$ change in the isotopic composition of the sulfides deposited. However, these considerations are based on the assumption that the dissolved sulfur compounds and the precipitated sulfides are in equilibrium, a condition which certainly may not always be fulfilled in Nature.

7. Extraterrestrial Material

Variations in the isotopic composition of meteorites and lunar samples can provide evidence for differing nuclear syntheses. The fractionation pathways described so far are characterized by a dependence of fractionation upon the relative mass difference $\Delta m/m$. With elements having more than two isotopes, *e.g.* oxygen, the fractionation effect for ^{17}O is therefore only half as great as that for ^{18}O. A plot of $\delta^{17}O$ *versus* $\delta^{18}O$ should therefore be a straight line having a slope of

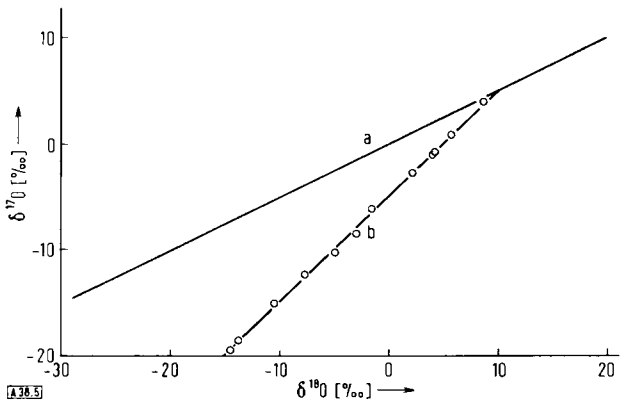


Fig. 5. Relation between ^{17}O and ^{18}O contents in terrestrial samples and lunar samples (a), and in minerals from carbonaceous meteorites (b) [40].

$+\frac{1}{2}$, provided that all samples have arisen *via* the same nuclear synthesis. *Kaplan* and *Hulston*[39] obtained similar results for sulfur in meteorites. In contrast, *Clayton et al.*[40] have obtained a line having a slope of $+1$ (see Fig. 5) for several anhydrous minerals from carbonaceous chondrites. This could be due to the admixture of almost pure ^{16}O, which may not have come from our planetary system.

8. Outlook

In conclusion we might attempt to forecast the future development of isotope geochemistry, neglecting further instrumental and methodological improvements. Our present knowledge of the isotopic composition of the elements present in terrestrial material is good. In order to gain further insight into the origin of minerals, rocks, and other interesting objects it will be necessary, on the one hand, to combine isotopic studies on the various elements and, on the other, to attempt simulations of natural fractionation processes in the laboratory.

Received: June 10, 1974 [A 38 IE]
German version: Angew. Chem. *87*, 104 (1975)

[1] *H. C. Urey, F. G. Brickwedde,* and *G. M. Murphy,* Phys. Rev. *40*, 1 (1932).

[2] *A. O. Nier, E. P. Ney,* and *M. G. Inghram,* Rev. Sci. Instrum. *18*, 294 (1947).

[3] *J. Bigeleisen,* Science *147*, 463 (1965).

[4] *A. E. Brodsky:* Isotopenchemie. Akademieverlag, Berlin 1961.

[5] *L. Melander:* Isotope Effects on Reaction Rates. Ronald Press, New York 1960.

[6] *S. S. Roginsky:* Theoretische Grundlagen der Isotopenchemie. VEB Deutscher Verlag der Wissenschaften, Berlin 1962.

[7] *H. C. Urey,* J. Chem. Soc. *1947*, 562.

[8] *H. Craig,* Science *133*, 1702 (1961).

[9] *J. Hoefs:* Stable Isotope Geochemistry. Minerals, Rocks, and Inorganic Materials. Vol. 9. Springer, Berlin 1973.

[10] *H. Craig,* Proc. Spoleto Conf. on Nuclear Geology, Spoleto 1963.

[11] *J. N. Weber,* Geochim. Cosmochim. Acta *32*, 33 (1968).

[12] *J. N. Weber* and *D. M. Raup,* Geochim. Cosmochim. Acta *30*, 681 (1966).

[13] *J. N. Weber* and *P. M. Woodhead,* Chem. Geol. *6*, 93 (1970).

[14] *K. Bandel* and *J. Hoefs,* Neues Jahrb. Mineral Monatsh., in press.

[15] *M. L. Keith* and *J. N. Weber,* Geochim. Cosmochim. Acta *28*, 1787 (1964).

[16] *C. Spaeth, J. Hoefs,* and *U. Vetter,* Geol. Soc. Amer. Bull. *82*, 3139 (1971).

[17] *G. D. Garlick* and *S. Epstein,* Geochim. Cosmochim. Acta *31*, 181 (1967).

[18] *H. P. Taylor* and *S. Epstein,* Geol. Soc. Amer. Bull. *73*, 675 (1962).

[19] *H. Friedrichsen,* Neues Jahrb. Mineral. Monatsh. *1971*, 26.

[20] *H. P. Taylor* and *R. G. Coleman,* Geol. Soc. Amer. Bull. *79*, 1727 (1968).

[21] *Y. N. Shieh* and *H. P. Taylor,* J. Petrol. *10*, 307 (1969).

[22] *H. P. Schwarcz, R. N. Clayton,* and *T. K. Mayeda,* Geol. Soc. Amer. Bull. *81*, 2299 (1970).

[23] *R. Park* and *S. Epstein,* Geochim. Cosmochim. Acta *21*, 110 (1960).

[24] *B. N. Smith* and *S. Epstein,* Plant Physiol. *47*, 380 (1971).

[25] *E. T. Degens, R. R. Guillard, W. M. Sackett,* and *J. A. Hellebust,* Deep-Sea Res. *15*, 1 (1968).

[26] *J. C. Lerman* and *J. Raynal,* C. R. Acad. Sci. *D 275*, 1391 (1972).

[27] *P. H. Abelson* and *T. C. Hoering,* Proc. Nat. Acad. Sci. USA *47*, 623 (1961).

[28] *E. T. Degens* in *G. Eglinton* and *M. T. Murphy:* Organic Geochemistry. Springer, Berlin 1969.

[29] *S. R. Silverman,* J. Amer. Oil Chem. Soc. *44*, 691 (1967).

[30] *F. Buschendorf, H. Nielsen, H. Puchelt,* and *W. Ricke,* Geochim. Cosmochim. Acta *27*, 501 (1963).

[31] *E. Dechow* and *M. L. Jensen,* Econ. Geol. *60*, 894 (1965).

[32] *A. Sasaki,* Geochem. J. *4*, 41 (1970).

[33] *D. E. White,* Econ. Geol. *63*, 301 (1968).

[34] *G. Anger, H. Nielsen, H. Puchelt,* and *W. Ricke,* Econ. Geol. *61*, 511 (1966).

[35] *M. Hartmann* and *H. Nielsen,* Geol. Rundsch. *58*, 621 (1969).

[36] *A. L. Kemp* and *H. G. Thode,* Geochim. Cosmochim. Acta *32*, 71 (1968).

[37] *H. Sakai,* Geochim. J. *2*, 29 (1968).

[38] *H. Ohmoto,* Econ. Geol. *67*, 551 (1972).

[39] *I. R. Kaplan* and *J. R. Hulston,* Geochim. Cosmochim. Acta *30*, 479 (1966).

[40] *R. N. Clayton, L. Grossman,* and *T. K. Mayeda,* Science *182*, 485 (1973).

Fixation of Atmospheric Nitrogen by Microorganisms

By Diethelm Kleiner[*]

In Memory of Artturi Ilmari Virtanen

Research on the enzymatic assimilation of molecular nitrogen (N_2 fixation) has made decisive advances in recent years. Both the purely scientific aspects of this process and its industrial implications are assuming ever-increasing interest. Some of the results most important from the biochemical point of view have been collected in the present report.

1. Introduction

The fixation of atmospheric nitrogen by microorganisms is a process whose importance is exceeded only by photosynthesis. The pioneering contributions to its study are closely connected with the names of *D. Burk*, *P. W. Wilson*, and *A. I. Virtanen*, but biochemical elucidation of the enzymatic processes involved took a leap forward only when, in 1960, it became possible to prepare cell-free extracts capable of fixing nitrogen[1].

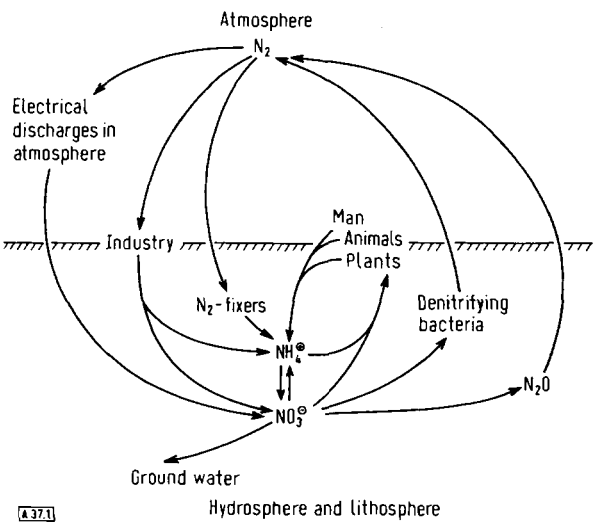


Fig. 1. Nitrogen cycle in Nature (after [2]).

Figure 1 shows the nitrogen cycle existing in nature in which part of the inorganic nitrogen present in the soil is washed out into the ground water and a further part is lost to the air by the action of denitrifying bacteria (reduction of nitrate to N_2). These losses are generally balanced by three processes: formation of nitrogen oxides by atmospheric electrical discharges (a few percent), industrial fertilizer production (*ca.* 30%), and microbial activity (*ca.* 70%)[2].

Many of the microorganisms capable of fixing nitrogen remain to be discovered. Those organisms that are known to have this action—whether existing free or in symbiosis—belong exclusively to the domain of the procaryotes (bacteria and blue-green algae) (Table 1). Of the sporadic reports that continually appear about N_2 fixation by fungi, not one could be confirmed on reinvestigation by means of the very sensitive acetylene-reduction method (see Section 3.2)[3].

[*] Dr. D. Kleiner
Chemisches Laboratorium der Universität
78 Freiburg, Albertstrasse 21 (Germany)

Free-living N_2-fixing agents are widely distributed in nature, being found in many soils[4–8], in lakes and seas[9–13], on Antarctic rocks[14], in hot springs[15], in the wood of dying

Table 1. N_2-fixing organisms.

a)	Free-living
	1. Bacteria (*e.g. Clostridium, Azotobacter*)
	2. Blue-green algae (*e.g. Anabaena, Tolypothrix*)
b)	Symbionts
	1. Blue-green algae in lichens
	2. Blue-green algae or bacteria in leaves (leaf symbionts)
	3. Rhizobia in leguminous plants
	4. Several mainly unknown microorganisms (Actinomycetes?) in the roots of angiosperms

trees[16], and in the gut of termites[17], mammals[18], and man[18]. More important agriculturally and ecologically, however, are the symbionts, particularly the bacteria that occur in nodules on the roots of higher plants.

2. Inertness of the N_2 Molecule

Nitrogen is known to be an unreactive element. Comparison of some of the physical properties and the molecular parameters of the isoelectronic compounds N_2, CO, and C_2H_2 (Table 2) shows that the main reason for this lack of activity lies in the great increase in bond energy occurring on transition from the double to the triple bond[19].

Table 2. Physical properties of the isoelectronic molecules N_2, CO, and C_2H_2 (after [19]).

	:N≡N:	:C≡O:	HC≡CH
Bond length [Å]	1.098	1.128	1.208
Ionization energy [eV]	15.6	14.0	11.4
Dissociation energy [kcal/mol]	225	235	200
Bond energy [kcal/mol] of the			
1st bond	38	84	83
2nd bond	100	170	147
3rd bond	225	235	200

Although the reaction

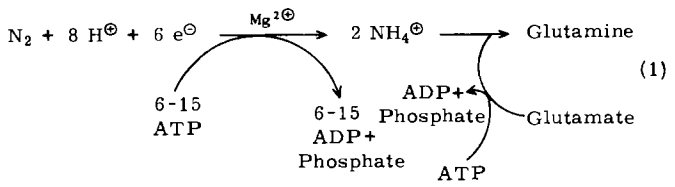
$$3\,H_2 + N_2 = 2\,NH_3$$

is exergonic with $\Delta G_0 = -12$ kcal/mol[19], it is immeasurably slow at room temperature even in the presence of industrial iron catalysts (Haber-Bosch process). In industry temperatures of at least 400 °C and pressures of about 200 atm are necessary to afford worthwhile conversion[20].

3. Biochemistry of Microbial N_2 Fixation

3.1. Reaction Path

In N_2-fixing microorganisms the assimilation is catalyzed by the binary enzyme complex nitrogenase. In this process the nitrogen is reduced according to eq. (1) to ammonium ions[21], which are probably bound to glutamate with the aid of the



(1)

enzyme glutamine synthetase[22]; ferredoxin is presumably responsible for the electron transport[23-27]. As in the Haber-Bosch process, the reaction can be induced only with a considerable expenditure of energy, which is here made available in the form of ATP[28-32]. The number of ATP molecules consumed in conversion of each N_2 molecule is not known exactly; in experiments *in vitro* it changes with the experimental conditions[33-35].

3.2. Determination of the Nitrogenase Activity[36]

In the oldest and most direct method the reaction is followed by means of heavy nitrogen. After incubation the tissue or enzyme preparation is subjected to *Kjeldahl* digestion, the NH_3 is oxidized to N_2, and the ^{15}N content of the nitrogen is determined by mass spectrometry. This method is used mainly for the determination of the activity *in vivo*.

Ammonia can also be measured directly by colorimetry if the enzyme preparations under study cannot induce its further reaction. In such cases the cofactors shown in eq. (1) (Mg^{2+}, ATP, and an electron donor, for which dithionite[37] has proved very suitable) must be added to the (usually cell-free) preparations.

In the simplest and most sensitive method, which is therefore most frequently used, acetylene is reduced to ethylene, this reduction also being catalyzed by nitrogenase (see Section 3.3). The two compounds can be readily determined by gas chromatography. The method is so sensitive that the fixation activity of no more than two blue-green algae colonies can still be determined[38].

3.3. Specificity of Nitrogenase

The active site of nitrogenase is not very substrate specific. To date the compounds listed in Table 3 have been reduced *in vitro* under the influence of the enzyme. If no substrate is added, the enzyme reduces protons and molecular hydrogen is evolved. It is remarkable that the acetylene is reduced only to ethylene[40]. In D_2O *cis*-$C_2H_2D_2$ is formed exclusively[40].

Except for the complicated reactions of cyanides and isocyanides, the relative reaction rates are in approximately inverse proportion to the number of electrons transferred, and it is therefore assumed that activation of the electrons

Table 3. Compounds reduced by nitrogenase (after [39]) n = Number of electrons transferred, V_{rel} = relative reaction rate.

Substrate	Product	n	V_{rel}
N_2	$2\ NH_3$	6	1
$N_3^{\ominus}$	$NH_3 + N_2$	2	3
N_2O	$H_2O + N_2$	2	3
C_2H_2	C_2H_4	2	3—4
HCN	CH_4, C_2H_4, C_2H_6, NH_3	6	0.6
	CH_3NH_2	4	
CH_3CN	C_2H_6, NH_3	6	0.2
CH_3NC	CH_3NH_2, CH_4	6	0.8
	C_2H_4, C_2H_6	8, 10	
	C_3H_6, C_3H_8	12, 14	
$2\ H^{\oplus}$	H_2	2	4

is the rate-determining step. Kinetic analysis of the mutual influence of the substrates has led to the hypothesis of a flexible active site capable of binding substrates with various structures[41]. All the reactions except evolution of hydrogen are inhibited by CO[41, 42]; inhibition of the reaction by the product ADP is of physiological importance[43] (see Section 4), but it is not yet clear whether this is due only to product inhibition or also to a regulatory inhibition of the enzyme[39, 44, 45]. Oxygen denatures the enzyme irreversibly.

3.4. Enzyme Purification

Denaturation by oxygen provides the chief difficulty in the preparation of pure nitrogenase, so that all the procedures must be conducted in oxygen-free atmosphere (under N_2, H_2, or argon).

In 1966 *Bulen* and *Le Comte*[46] discovered that nitrogenase is a complex of two easily separable proteins which, in the absence of systematic names, are designated component I (Mo—Fe-protein, molybdoferredoxin, azofermo) and component II (Fe-protein, azoferredoxin, azofer). A general purification scheme with the following principal steps has evolved in the course of time:

1) Preparation of a crude extract;
2) Preliminary purification (mainly fractional precipitations);
3) Chromatography on diethylaminoethyl cellulose. Elution with solvents of different ionic strengths can lead to separation of the two components in impure form;
4) Further purification of the isolated components (gel filtration, electrophoresis, fractional precipitations, heat denaturation).

This separation of the two components and their purification have been described for several microorganisms. However, in each case it has been shown that neither of the two proteins alone is able to catalyze the reduction of N_2, even in the presence of all the cofactors.

Suggestions that a third protein is necessary for full nitrogenase activity[47, 48] could not be confirmed[49].

3.5. Physicochemical Characterization of the Components

Table 4 shows the physical and chemical properties of the nitrogenase components of several organisms. In spite of the differing origins of the components, their properties are very similar. The occurrence of molybdenum in component I and the cold lability of component II in many organisms are remarkable. In accord with the low isoelectric points the

amino-acid analyses carried out so far on I and II from all the organisms show a predominance of acidic amino acids[54–56, 63, 64]; the absence of tryptophan from II is remarkable. According to *Marchalonis* and *Weltman*[65], the amino-acid composition of components I from *C. pasteurianum*, *K. pneumoniae*, *A. vinelandii*, and *Rh. japonicum* indicates their evolution from a common precursor; similarly, components II from *C. pasteurianum*, *A. vinelandii*, and *K. pneumoniae* may have evolved from a single ancestral protein.

Table 4. Properties of the nitrogenase components from microorganisms.

Component I	Component II	Organism [a]	Ref.
Molecular weight:			
220000	—	C.p.	[50]
—	55000	C.p.	[51]
210000	56000	C.p.	[52]
270—300000	—	A.v.	[53]
216000	64000	A.v.	[54]
218000	66800	K.p.	[55]
200000	—	Rh.j.	[56]
Subunits:			
2 × 60000 + 2 × 51000	2 × 27500	C.p.	[52]
2 × 60000 + 2 × 50000	—	C.p.	[50]
—	2 × 27500	C.p.	[51]
4 × 70000	—	A.v.	[57]
4 × 56000	2 × 33000	A.v.	[54]
2 × 50000 + 2 × 60000	2 × 34600	K.p.	[55]
4 × 50000	—	Rh.j.	[56]
2 species	—	Chr.	[58]
Isoelectric point:			
5.0	4.6	C.p.	[52]
5.2	4.7	A.v.	[54]
5.5	4	K.p.	[55]
Content of Mo [atoms per molecule]:			
1—1.5	—	C.p.	[52]
1.73	—	C.p.	[59]
1.8	—	A.v.	[53]
1.54	0	A.v.	[54]
1.04	0	K.p.	[55]
1.3	—	Rh.j.	[56]
1—2	—	Chr.	[58]
Content of Fe [atoms per molecule]			
—	4	C.p.	[51]
12—18	3—4	C.p.	[52]
22—24	—	C.p.	[59]
34—38	—	A.v.	[53]
24	3.5	A.v.	[54]
18	4	K.p.	[55]
29	—	Rh.j.	[56]
Content of $S^{2\ominus}$ [atoms per molecule]			
—	4	C.p.	[51]
8—15	3—4	C.p.	[52]
22—24	—	C.p.	[59]
26—28	—	A.v.	[53]
20	3	A.v.	[54]
16.7	3.82	K.p.	[55]
26	—	Rh.j.	[56]
Cold lability:			
−	+	C.p.	[60]
−	+	A.v.	[61]
−	−	K.p.	[55]
−	+	M.f.	[62]

[a] Abbreviations: C.p.—*Clostridium pasteurianum*; A.v.—*Azotobacter vinelandii*; K.p.—*Klebsiella pneumoniae*; Rh.j.—*Rhizobium japonicum*; Chr.—*Chromatium spp.*; M.f.—*Mycobacterium flavum*.

It could be shown by Mössbauer spectroscopy that the Fe atoms in I belong to three distinct groups with differing spectra, while in II they are bound in the same way[66]. The occurrence of iron and sulfide-sulfur in approximately equal amounts, the characteristic EPR signals (see Section 3.7), the absorption spectra in the visible and near UV regions[45], and the evolution of H_2S on acidification classify both nitrogenase components as iron-sulfur proteins[67]. Many members of this class, which is widely distributed among the procaryotes, are characterized by very low electron-transfer potentials.

3.6. Combination of the Components from Different Organisms

Although the nitrogenase components from different organisms are very similar, they cannot be combined at will to give active complexes. In particular, those that are only remotely related taxonomically show little readiness to cooperate[39, 68, 69]. For example, neither the combination of I from *A. vinelandii* (obligately aerobic) with II from *C. pasteurianum* (obligately anaerobic) nor the reciprocal mixture is capable of N_2 fixation[69]. Closer relatives give more positive results; for example, all "cross-reactions" of the nitrogenase proteins from *B. polymyxa* and *K. pneumoniae* (both facultatively anaerobic) are almost as active as the homologous combinations[69]. It is not yet known what causes these differences, because neither the amino-acid sequence nor the tertiary structure of any nitrogenase protein has so far been elucidated.

3.7. Electron Transport and Reaction Mechanism

Only very recently have the roles of the two components in the overall process been established, by means of EPR spectroscopy[70–75]. Fig. 2 shows the EPR spectra of the two components from *C. pasteurianum*, alone and in admixture, at 13 K, with and without cofactors. It is assumed that the signals at $g = 4.29$, 3.77, and 2.01 belong to half-reduced I, whereas reduced I shows no signal. In contrast, oxidized II is assumed not to display any signal but after reduction to show the signals at $g = 4.3$, 2.05, 1.94, and 1.88. Thus, in the presence of dithionite, I exists in the half-reduced form (a) and II in the reduced form (b). The signal of the mixture (c) shows weak interactions between the components, but no electron transfer. Addition of MgATP has no effect on

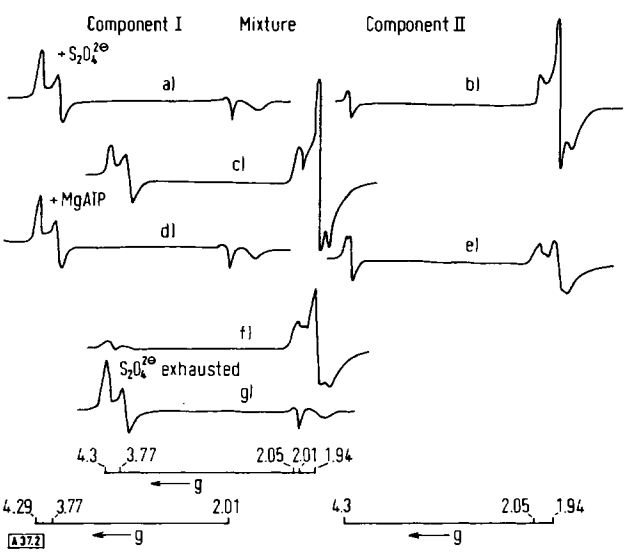
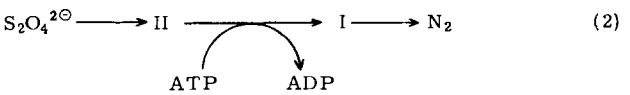


Fig. 2. EPR spectra of nitrogenase components I and II from *C. pasteurianum* under various conditions. a)—g) see text (after [70]).

the spectrum of I (d), but changes the spectrum of II (e). Hence it is concluded that MgATP is bound to II, and this finding has been confirmed by binding studies[76, 77] and other experiments[78]. The complex of II with MgATP is now in a position to reduce I completely with hydrolysis of ATP, whereupon the signal of the latter largely disappears (f). ATP can thus effect electron activation or conformational change of II, after which electron transfer can take place.

When the electron source is exhausted, II is oxidized and I is half-reduced, and only the signals of I are observed (g). Accordingly an electron flow as in eq. (2) may be postulated for the enzymatic reduction of N_2.



(2)

Although the electron transport in the enzyme complex has been largely elucidated by these investigations, they provide no information about the composition of the active site or the mechanism of the N_2 reduction. The oldest and most widely accepted proposal[79] assumes reduction of the N_2 in three steps, by way of diimine and hydrazine to ammonia. However, in spite of intensive search neither of these intermediates could be discovered, and furthermore, neither hydrazine nor diimine can be reduced by nitrogenase[80, 81]. In two other proposed mechanisms the ability of Mo^{III} and Mo^{VI} to form stable compounds is emphasized[82, 19]. Also, in analogy to inorganic N_2 complexes[82a], end-on binding of the N_2 has been postulated[82]. However, none of these theories has yet been supported by experimental evidence[*].

4. Regulation of Nitrogenase Activity *in Vivo*

As already mentioned, microbial reduction of N_2 is possible only because energy in the form of ATP is consumed for the activation of the unreactive N_2 molecule, so that this assimilation process is very expensive for the organism. A regulatory system has therefore been developed in many N_2-fixing organisms, in which the nitrogenase synthesis is repressed by $NH_4^{\oplus}$[83–90]. The extracellular $NH_4^{\oplus}$ concentration effecting this repression can be very low for many organisms (*e.g. ca.* 10 µmol/l in *A. vinelandii*[91]). If there is an adequate external supply of $NH_4^{\oplus}$ (and $NO_3^{\ominus}$) ions, this crude regulatory mechanism slows down the expensive N_2 assimilation that is then no longer necessary. Induction of the synthesis by the substrate N_2 probably does not occur; indeed, from the standpoint of evolution it would be useless since there is hardly any biotope on the Earth that is free from N_2[89].

A second and more sensitive regulatory mechanism, also mentioned above, is based on inhibition of the enzyme by ADP[43]. The organism is thus unable to use up its ATP completely for N_2 fixation unless the ADP produced in this reaction is immediately reconverted to ATP. Even though a low level of ATP decreases the rate of the N_2 fixation, ADP amplifies this signal to the nitrogenase. AMP has no inhibitory activity[43].

5. Possible Industrial Applications

Implications of the industrial application of N_2 assimilation abound in agriculture, environmental protection, and food technology.

5.1. Agriculture and the Environment

5.1.1. Symbionts

It has long been known that cultivation of leguminous plants increases the subsequent yield of other crops (green manuring)[92]. This is due to the N_2 assimilation by nodular bacteria (rhizobia), which can impart 80—90% of their nitrogen to the host plants[93]. To *Virtanen* in particular belongs the credit for the development of very active strains of rhizobia, which are used for the inoculation of leguminous seeds and which have led to considerably increased harvests.

However, it is still unclear what factors enable rhizobia to form a symbiotic association with leguminous plants in particular. Extensive investigations are now in progress[94, 95] on the clarification of this problem, in the hope that it will be possible to induce other plants also to undergo symbiosis with rhizobia[95]; the recent discovery of symbiosis between a non-leguminous plant (*Trema aspera*) and a bacterium of the genus *Rhizobium*[96] is encouraging.

In addition to leguminous plants there are other N_2-assimilating symbioses of ecological importance, *e.g.* among the lichens and in the roots of some angiosperms and gymnosperms[97, 98]. In the last case it has not yet been possible to isolate the endophyte (probably an actinomycete[99]). Both groups are extremely important for the colonization of washed out, arid soils, as these are poor in readily soluble nitrates and ammonium salts[92, 93].

5.1.2 Free-Living Microorganisms

The free-living N_2 fixers excrete up to 80%[13] of their assimilated nitrogen in bound forms, *inter alia* as NH_3[100, 101], hydroxylamine derivatives[102], amino acids[103, 104], peptides[105] growth substances[106], and fungicides[106]. These excretions can in turn be taken up and utilized by higher plants[107, 108].

In most soils the number of free-living N_2 fixers is small in comparison with the number of other soil bacteria[109], but it is assumed that, as a result of their wide distribution, the free-living N_2 fixers make a significant, though small, contribution to the fertility of the soil (5—20 kg of N per hectare per year, compared with 100—300 from leguminous plants[39, 94]. This contribution can be increased in two ways:

a) by transfer of the genetic material for N_2 fixation ('nif-genes') to soil bacteria that occur frequently;

b) by optimization of the living conditions of free-living N_2 fixers.

As regards a), it has recently been possible by conjugation to transfer nif-genes from *K. pneumoniae* to *E. coli*[110], which otherwise cannot assimilate atmospheric nitrogen. This success has given rise to great hopes but it has not yet led to large-scale

[*] Editorial comment: *G. N. Schrauzer* will shortly comment upon the most recent views concerning the mechanism of nitrogen reduction in this journal.

application, and the transfer of nif-genes to human hereditary material, envisaged by some journalists, belongs for the present to the realm of science fiction.

As regards b), the number of N_2 fixers can be increased by favorable ecological conditions to such an extent that almost the entire nitrogen demand of a biotope can be met by their activity. This is the case if in nitrogen-poor soils the amount of energy required for the assimilation of N_2 is available. This energy is ultimately provided by sunlight and is conserved in the form of ATP either by photophosphorylation or by photosynthesis (formation of carbohydrates) and oxidative phosphorylation. Bacteria capable of photophosphorylation and blue-green algae find particularly good living conditions in the warm, well-illuminated flooded areas of rice fields[111]; their large contribution to the nitrogen balance has been confirmed by measurements of N_2 fixation *in situ*[112, 113], and it has also been found in numerous experiments that the rice yield can be increased by inoculating the fields with these organisms[114–117].

Other favorable biotopes exist in the root zones of some plants if the roots excrete large amounts of organic compounds. (The reduction of 10 mg of N_2 requires *ca.* 1 g of carbohydrate.) The rhizospheres of cane sugar and bahia grass (*Paspalum*[118, 119]) have been investigated most widely. These plants excrete so much carbohydrate that some cane sugar fields have been cultivated for more than 100 years without nitrogen-manuring, yet without any decrease in yield[119].

Attempts have also been made to increase the yields of other cultivated plants (maize, wheat, oats, potatoes, *etc.*) by inoculating the fields with N_2 fixers, particularly *Azotobacter*[106, 120–123]. In most cases the application of these "bacterial manures" has resulted in a small increase in yield, but ironically this is probably ascribable less to an increase in the N content (because of the energy deficiency) than to the above-mentioned bacterial production of growth substances and fungicides[106, 121]. Becauses of the effort involved, the use of "bacterial manuring" has decreased greatly in recent years[106]. This technology could, however, attract renewed attention if questions of environmental protection and the dependence of agriculture on industry come to the fore. Only a small part of the nitrogen in artificial manures is utilized by the plants, the remainder being washed out into the ground water[109, 124, 125]. This in turn contributes to nutrient enrichment of the water and its eutrophication. However, nitrogen-containing secretions from microorganisms are released continuously and are probably better retained in the soil. The major problem remains the provision of a cheap source of energy. It has already been shown that the nitrogen content of soil can be increased under certain conditions by the addition of straw (cellulose) because of a stimulating interaction between N_2-fixing and cellulose-decomposing bacteria[126, 127].

It should also be noted that, owing to their high carbohydrate consumption, free-living N_2 fixers could be useful in the biotechnological purification of effluents having a high content of organic compounds[128, 129].

5.2. Food Technology

Provision of carbohydrates and proteins for the world's population is one of the most urgent problems of our time. Although this is primarily a political problem[130], yet in the long view new methods of providing food must be developed. Here mention will be made only of two unorthodox solutions of the protein problem.

In New Guinea there is a race of Papuans whose daily food consists almost exclusively of *ca.* 2 kg of sweet potatoes together with leaves, and in spite of the resulting permanent protein deficiency the district is densely populated and the adults can perform heavy work[131]. The solution of this riddle may lie in the significant activity of N_2 fixers recently discovered in the intestinal flora of these people.

When investigating an Indian maize mash ("Pozol"), a group of Mexican research workers[132] found that its nitrogen content increased by 30—60% during the 5 to 10 days fermentation period customary in that area; they attributed this enrichment to the activity of N_2 fixers. This conclusion should be tested by the acetylene-reduction method, but in this connection it is remarkable how widely the fermentation of food is encountered among many non-European peoples[133].

The author is grateful to Prof. K. Wallenfels for critical perusal of the manuscript and for stimulating discussions.

Received: May 27, 1974 [A 37 IE]
German version: Angew. Chem. 87, 97 (1975)
Translated by Express Translation Service, London

[1] *J. E. Carnahan, L. E. Mortenson, H. F. Mower,* and *J. E. Castle,* Biochim. Biophys. Acta *38,* 188 (1960).

[2] *C. C. Delwiche,* Sci. Amer. *223,* No. 9, p. 136 (1970).

[3] *J. R. Postgate:* The Chemistry and Biochemistry of Nitrogen Fixation. Plenum Press, London 1971, p. 161.

[4] *M. F. Jurgensen* and *C. B. Davey,* Can. J. Microbiol. *14,* 1179 (1968).

[5] *U. Granhall,* Oikos *21,* 330 (1970).

[6] *L. E. Henriksson, P. H. Enckell,* and *E. Henriksson,* Oikos *23,* 420 (1972).

[7] *A. N. McGregor* and *D. E. Johnson,* Soil Sci. Amer. Proc. *35,* 843 (1971).

[8] *E. N. Mishustin* and *V. T. Yemtsev,* Soil Biol. Biochem. *5,* 97 (1973).

[9] *R. Dugdale, V. Dugdale, J. Neess,* and *J. Goering,* Science *130,* 859 (1959).

[10] *J. S. Bunt, K. E. Cooksey, M. A. Heeb, C. C. Lee,* and *B. F. Taylor,* Nature *227,* 1163 (1971).

[11] *W. D. P. Stewart, T. Mague, G. P. Fitzgerald,* and *R. H. Burris,* New Phytol. *70,* 497 (1971).

[12] *A. J. Horne* and *A. B. Viner,* Nature *232,* 417 (1971).

[13] *W. D. P. Stewart,* Annu. Rev. Microbiol. *27,* 283 (1973).

[14] *O. Holm-Hansen,* Science *139,* 1059 (1963).

[15] *W. D. P. Stewart,* Phycologia 9, 261 (1970).

[16] *R. J. Seidler, P. E. Aho, P. N. Raju,* and *H. C. Evans,* J. Gen. Microbiol. *73,* 413 (1972).

[17] *J. A. Breznak, W. J. Brill, J. W. Mertins,* and *H. C. Coppel,* Nature *244,* 577 (1973).

[18] *F. J. Bergersen* and *E. H. Hipsley,* J. Gen. Microbiol. *60,* 61 (1970).

[19] *G. J. Leigh* in [3], p. 19.

[20] *A. Nielsen,* Advan. Catal. Relat. Subj. *5,* 1 (1953).

[21] *R. H. Burris,* Annu. Rev. Plant Physiol. *17,* 155 (1966).

[22] *H. Nagatani, M. Shimizu,* and *R. C. Valentine,* Arch. Mikrobiol. *79,* 164 (1971).

[23] *L. E. Mortenson,* Biochim. Biophys. Acta *81,* 473 (1964).

[24] *D. C. Yoch, J. R. Benemann, R. C. Valentine,* and *D. I. Arnon,* Proc. Nat. Acad. Sci. USA *64,* 1404 (1969).

[25] *D. C. Yoch* and *D. I. Arnon,* Biochim. Biophys. Acta *197,* 180 (1970).

[26] *R. V. Smith, R. J. Noy,* and *M. C. W. Evans,* Biochim. Biophys. Acta *253,* 104 (1971).

[27] *Y. I. Shethna, N. A. Stombaugh,* and *R. H. Burris,* Biochem. Biophys. Res. Commun. *42,* 1108 (1971).

[28] *J. E. McNary* and *R. H. Burris,* J. Bacteriol. *84,* 598 (1962).

[29] *R. W. F. Hardy* and *A. J. D'Eustachio,* Biochem. Biophys. Res. Commun. *15,* 314 (1964).

[30] *L. E. Mortenson*, Proc. Nat. Acad. Sci. USA *52*, 272 (1964).

[31] *W. A. Bulen, R. C. Burns*, and *J. R. Le Comte*, Biochem. Biophys. Res. Commun. *17*, 265 (1964).

[32] *B. Koch, H. J. Evans*, and *S. Russell*, Proc. Nat. Acad. Sci. USA *58*, 1343 (1967).

[33] *H. C. Winter* and *R. H. Burris*, J. Biol. Chem. *243*, 940 (1968).

[34] *K. L. Hadfield* and *W. A. Bulen*, Biochemistry *8*, 5103 (1969).

[35] *T. Ljones* and *R. H. Burris*, Biochim. Biophys. Acta *275*, 93 (1972).

[36] *R. H. Burris* in *S. P. Colowick* and *N. O. Kaplan*: Methods in Enzymology. Academic Press, New York 1972, Vol. 24, p. 415.

[37] *W. A. Bulen, R. C. Burns*, and *J. R. Le Comte*, Proc. Nat. Acad. Sci. USA *53*, 532 (1965).

[38] *W. D. P. Stewart, G. P. Fitzgerald*, and *R. H. Burris*, Proc. Nat. Acad. Sci. USA *58*, 2071 (1967).

[39] *H. Dalton* and *L. E. Mortenson*, Bacteriol. Rev. *36*, 231 (1972).

[40] *M. J. Dilworth*, Biochim. Biophys. Acta *127*, 285 (1966).

[41] *J. C. Hwang, C. H. Chen*, and *R. H. Burris*, Biochim. Biophys. Acta *292*, 256 (1973).

[42] *C. J. Lind* and *P. W. Wilson*, J. Amer. Chem. Soc. *63*, 3511 (1941).

[43] *E. Moustafa* and *L. E. Mortenson*, Nature *216*, 1241 (1967).

[44] *I. R. Kennedy*, Biochim. Biophys. Acta *222*, 135 (1970).

[45] *T. Ljones*, Biochim. Biophys. Acta *321*, 103 (1973).

[46] *W. A. Bulen* and *J. R. Le Comte*, Proc. Nat. Acad. Sci. USA *56*, 979 (1966).

[47] *L. E. Mortenson*, Biochim. Biophys. Acta *127*, 18 (1966).

[48] *K. B. Taylor*, J. Biol. Chem. *244*, 171 (1969).

[49] *D. Y. Jeng, T. Devanathan*, and *L. E. Mortenson*, Biochem. Biophys. Res. Commun. *35*, 625 (1969).

[50] *T. C. Huang, W. G. Zumft*, and *L. E. Mortenson*, J. Bacteriol. *113*, 884 (1973).

[51] *G. Nakos* and *L. E. Mortenson*, Biochemistry *10*, 455 (1971).

[52] *M. Y. Tso*, Arch. Microbiol. *99*, 71 (1974).

[53] *R. C. Burns, R. D. Holsten*, and *R. W. F. Hardy*, Biochem. Biophys. Res. Commun. *39*, 90 (1970).

[54] *D. Kleiner* and *C. H. Chen*, Arch. Microbiol. *98*, 93 (1974).

[55] *R. R. Eady, B. E. Smith, K. A. Cook*, and *J. R. Postgate*, Biochem. J. *128*, 655 (1972).

[56] *D. W. Israel, R. L. Howard, H. J. Evans*, and *S. A. Russell*, J. Biol. Chem. *249*, 500 (1974).

[57] *J. T. Stasny, R. C. Burns, B. D. Korant*, and *R. W. F. Hardy*, J. Cell Biol. *60*, 311 (1974).

[58] *M. C. W. Evans, A. Telfer*, and *R. V. Smith*, Biochim. Biophys. Acta *310*, 344 (1973).

[59] *W. G. Zumft, W. C. Cretney, T. C. Huang, L. E. Mortenson*, and *G. Palmer*, Biochem. Biophys. Res. Commun. *48*, 1525 (1972).

[60] *E. Moustafa, L. E. Mortenson*, and *P. T. Bui*, Bacteriol. Proc. *1968*, 132.

[61] *E. Moustafa*, Biochim. Biophys. Acta *206*, 178 (1970).

[62] *D. R. Biggins, M. Kelly*, and *J. R. Postgate*, Eur. J. Biochem. *20*, 140 (1971).

[63] *R. C. Burns* and *R. W. F. Hardy* in *S. P. Colowick* and *N. O. Kaplan*: Methods in Enzymology. Academic Press, New York 1972, Vol. *24*, p. 480.

[64] *J. S. Chen, J. S. Multani*, and *L. E. Mortenson*, Biochim. Biophys. Acta *310*, 51 (1973).

[65] *J. J. Marchalonis* and *J. K. Weltman*, Comp. Biochem. Physiol. *38 B*, 609 (1971).

[66] *B. E. Smith* and *G. Lang*, Biochem. J. *137*, 169 (1974).

[67] *R. W. F. Hardy* and *R. C. Burns* in *W. Lovenberg*: Iron-Sulfur Proteins. Academic Press, New York 1973, Vol. 1, p. 65.

[68] *R. H. Burris* in [3], p. 105.

[69] *R. W. Detroy, D. F. Witz, R. A. Parejko*, and *P. W. Wilson*, Proc. Nat. Acad. Sci. USA *61*, 537 (1968).

[70] *W. H. Orme-Johnson, W. D. Hamilton, T. Ljones, M. Y. W. Tso, R. H. Burris, V. K. Shah*, and *W. J. Brill*, Proc. Nat. Acad. Sci. USA *69*, 3142 (1972).

[71] *B. E. Smith, D. J. Lowe*, and *R. C. Bray*, Biochem. J. *130*, 641 (1972).

[72] *B. E. Smith, D. J. Lowe*, and *R. C. Bray*, Biochem. J. *135*, 331 (1973).

[73] *G. Palmer, J. S. Multani, W. C. Cretney, W. G. Zumft*, and *L. E. Mortenson*, Arch. Biochem. Biophys. *153*, 325 (1972).

[74] *W. G. Zumft, G. Palmer*, and *L. E. Mortenson*, Biochim. Biophys. Acta *292*, 413 (1973).

[75] *L. E. Mortenson, W. G. Zumft*, and *G. Palmer*, Biochim. Biophys. Acta *292*, 413 (1973).

[76] *P. T. Bui* and *L. E. Mortenson*, Proc. Nat. Acad. Sci. USA *61*, 1021 (1968).

[77] *M. Y. W. Tso* and *R. H. Burris*, Biochim. Biophys. Acta *309*, 263 (1973).

[78] *G. A. Walker* and *L. E. Mortenson*, Biochem. Biophys. Res. Commun. *53*, 904 (1973).

[79] *G. E. Hoch, K. C. Schneider*, and *R. H. Burris*, Biochim. Biophys. Acta *37*, 273 (1960).

[80] *R. H. Burris, H. C. Winter, T. O. Munson*, and *J. Garcia-Rivera* in *A. San Pietro*: Non-Heme Iron Proteins—Role in Energy Conversion. Antioch Press, Yellow Springs, Ohio 1965, p. 315.

[81] *J. Garcia-Rivera* and *R. H. Burris*, Arch. Biochem. Biophys. *119*, 167 (1967).

[82] *J. Chatt* and *R. L. Richards* in [3], p. 57.

[82a] *D. Sellmann*, Angew. Chem. *86*, 692 (1974); Angew. Chem. internat. Edit. *13*, 639 (1974).

[83] *G. W. Strandberg* and *P. W. Wilson*, Can. J. Microbiol. *14*, 25 (1968).

[84] *M. C. Mahl* and *P. W. Wilson*, Can. J. Microbiol. *14*, 33 (1968).

[85] *R. A. Parejko* and *P. W. Wilson*, Can. J. Microbiol. *16*, 681 (1970).

[86] *D. C. Yoch* and *R. M. Pengra*, J. Bacteriol. *92*, 618 (1966).

[87] *V. K. Shah, L. C. Davis*, and *W. J. Brill*, Biochim. Biophys. Acta *256*, 498 (1972).

[88] *R. S. Tubb* and *J. R. Postgate*, J. Gen. Microbiol. *79*, 103 (1973).

[89] *G. Daesch* and *L. E. Mortenson*, J. Bacteriol. *110*, 103 (1972).

[90] *D. Gadkari* and *H. Stolp*, Arch. Microbiol. *96*, 135 (1974).

[91] *D. Kleiner*, Arch. Microbiol. *101*, 153 (1974).

[92] *A. I. Virtanen*, Angew. Chem. *65*, 1 (1953).

[93] *A. I. Virtanen* and *J. K. Miettinen* in *F. C. Steward*: Plant Physiology Academic Press, New York 1963, Vol. 3, p. 539.

[94] *D. Werner*, Naturwiss. Rundsch. *27*, 177 (1974).

[95] *R. D. Holsten, R. C. Burns, R. W. F. Hardy*, and *R. R. Hebert*, Nature *232*, 173 (1971).

[96] *M. J. Trinick*, Nature *244*, 459 (1973).

[97] *W. D. P. Stewart*, Science *158*, 1426 (1967).

[98] *W. S. Silver* in [3], p. 244.

[99] *J. H. Becking*, Plant Soil *32*, 611 (1970).

[100] *I. Zelitch, E. D. Rosenblum, R. H. Burris*, and *P. W. Wilson*, J. Biol. Chem. *191*, 295 (1951).

[101] *G. E. Fogg* and *H. Pattnaik*, Phykos *5*, 58 (1966).

[102] *N. E. Saris* and *A. I. Virtanen*, Acta Chem. Scand. *11*, 1438 (1957).

[103] *A. Watanabe*, Arch. Biochem. Biophys. *34*, 50 (1951).

[104] *W. D. P. Stewart*, Nature *200*, 1020 (1963).

[105] *G. E. Fogg*, Proc. Roy. Soc. *B 139*, 372 (1952).

[106] *E. N. Mishustin*, Plant Soil *32*, 545 (1970).

[107] *H. F. Mayland* and *T. H. McIntosh*, Nature *209*, 421 (1966).

[108] *W. D. P. Stewart*, Nature *214*, 603 (1967).

[109] *T. Beck*: Mikrobiologie des Bodens. Bayerischer Landwirtschaftsverlag, München 1968, pp. 371 ff.

[110] *R. A. Dixon* and *J. R. Postgate*, Nature *237*, 102 (1972).

[111] *A. Watanabe* and *Y. Yamamoto*, Plant Soil Spec. Vol. 403 (1971).

[112] *I. C. McRae* and *T. F. Castro*, Soil Sci. *103*, 277 (1967).

[113] *G. Rinaudo, J. Balandreau*, and *Y. Dommergues*, Plant Soil Spec. Vol. 471 (1971).

[114] *A. Watanabe, S. Nishigaki*, and *C. Konishi*, Nature *168*, 748 (1951).

[115] *M. B. Allen*, Sci. Mon. Aug. 1956, 100.

[116] *A. N. Ibrahim, M. Kamel*, and *M. El-Sherbeny*, Agrokem. Talajtan *20*, 389 (1971).

[117] *M. Kobayashi* and *M. Z. Haque*, Plant Soil Spec. Vol. 443 (1971).

[118] *J. Döbereiner, J. M. Day*, and *P. J. Dart*, J. Gen. Microbiol. *71*, 103 (1972).

[119] *J. Döbereiner, J. M. Day*, and *P. J. Dart*, Plant Soil *37*, 191 (1972).

[120] *F. E. Allison*, Soil Sci. *64*, 413 (1947).

[121] *R. Cooper*, Soils Fert. *22*, 327 (1959).

[122] *M. Sulaiman*, Beitr. Trop. Subtrop. Landwirt. Tropenveterinärmed. *9*, 139 (1971).

[123] *D. Bertrand*, C. R. Acad. Sci. *D 275*, 2131 (1972).

[124] *W. V. Bartholomew*, Soils Humid Trop. *1972*, 63.

[125] *W. Vaughan*, Compost Sci. *14*, 26 (1973).

[126] *C. C. Delwiche* and *J. Wijler*, Plant Soil *7*, 113 (1956).

[127] *W. A. Rice* and *E. A. Paul*, Can. J. Microbiol. *18*, 715 (1971).

[128] *O. Vejbora, D. Sokol*, and *V. Jozefy*, Listy Cukrov. *85*, 288 (1969); Chem. Abstr. *72*, 82767 (1970).

[129] *R. V. Finn* and *A. L. Tannahill*, Biotechnol. Bioeng. *15*, 413 (1973).
[130] *G. Myrdal:* Politisches Manifest über die Armut in der Welt. Suhrkamp, Frankfurt 1970.
[131] *R. Luyken, F. W. M. Luyken-Koning, N. A. Pikaar*, and *A. Blom*, Amer. J. Clin. Nutr. *14*, 13 (1964).
[132] *M. Ulloa, T. Herrera*, and *G. de la Lanza*, Rev. Latinoamer. Microbiol. Parasitol. *13*, 113 (1971).
[133] *C. W. Hesseltine*, Mycologia 57, 149 (1965).

Preparation, Structure, and Reactions of Halomalondialdehydes[1]

New synthetic methods (8)

By Christian Reichardt and Klaus Halbritter[*]

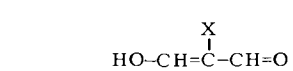
Dedicated to Professor Karl Dimroth

The present progress report provides a survey of the synthesis, structure, and reactions of halomalondialdehydes, including "cyanomalondialdehyde" (diformylacetonitrile), the only pseudohalogen compound so far known in this series. Halomalondialdehydes are reactive compounds, applicable in a variety of ways, and are characterized particularly by their cyclizations with bifunctional compounds. Many of the reactions discussed below can be applied to substituted malondialdehydes other than those specified.

1. Introduction

The chemical properties of saturated aliphatic dialdehydes of the general formula OCH—$(CH_2)_n$—CHO ($n>1$) do not differ fundamentally from those of simple monoaldehydes, for they act as bifunctional monoaldehydes; however, the first two members of this homologous series—glyoxal ($n=0$) and malondialdehyde ($n=1$)—are exceptional, since in the former compound the two carbonyl groups interact conjugatively and in the latter there is a possibility of keto-enol tautomerism. Glyoxal and malondialdehyde can be regarded as the initial members of a homologous series of unsaturated dialdehydes, and it is then useful to distinguish those with an even number of carbons from those with an odd number. Unsaturated aliphatic dialdehydes with an even number of carbons and of general formula OCH—$(CH{=}CH)_m$—CHO, being vinylogs of glyoxal, can be assigned to the series of polyene dyes. Unsaturated dialdehydes of the general formula OCH—$(CH{=}CH)_{m-1}$—CH_2—CHO⇌OCH—$(CH{=}CH)_m$—OH are enolized and are thus vinylogs of formic acid; the anions (and cations) of these dialdehydes belong to the polymethinoxonol class of dyes[2].

Because of its low stability, malondialdehyde *(1)*, the parent compound of this homologous series, could not be obtained in crystalline state until 1941 (*Hüttel*[3]), although as early as 1903 *Claisen*[4] had obtained it in aqueous solution by hydrolysis of 3-ethoxyacrolein diethyl acetal[5].



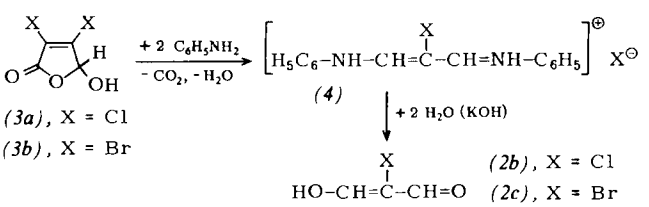
(1), X = H
(2), X = alkyl, cycloalkyl, aryl, heteroaryl, CHO, COR, CO_2R, CN, NH_2, NR_2, $N_2^{\oplus}$, N=N-R, NO_2, OH, OR, OCOR;
(2a), X = F; *(2b)*, X = Cl; *(2c)*, X = Br; *(2d)*, X = I;
(2e), X = CN

On the other hand, some of the substituted malondialdehydes *(2)*, *e.g.* nitro-[6] and bromomalondialdehyde *(2c)*[7, 8], were prepared and studied in depth long ago. Only the halo- and pseudohalomalondialdehydes *(2a)* to *(2e)* are treated in detail below, but they should be regarded as characteristic representatives of a large number of accessible substituted malondialdehydes.

2. Preparation of Monohalomalondialdehydes

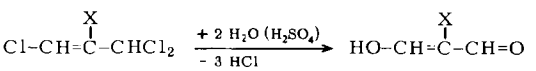
2.1. General Methods

Mucochloric acid *(3a)* and mucobromic acid *(3b)* react with aniline to afford, with decarboxylation, the halomalondialdehyde dianil hydrogen halides *(4)*, from which alkaline hydrolysis leads by way of the monoanils and potassium salts to the free halomalondialdehydes *(2b)* and *(2c)*[7, 9]. In this way chloromalondialdehyde *(2b)* was first obtained[9].



(3a), X = Cl
(3b), X = Br
(4)
(2b), X = Cl
(2c), X = Br

Hydrolysis of the 1,2,3,3-tetrahalo-1-propenes *(5a)* and *(5b)* with conc. sulfuric acid leads, according to the nature of the halogen on C-2, to chloro-[10-14] or bromomalondialdehyde[11]. Compounds *(5a)* and *(5b)* are readily accessible by $AlCl_3$-catalyzed addition of chloroform to the 1,2-dihaloethylene followed by dehydrohalogenation.

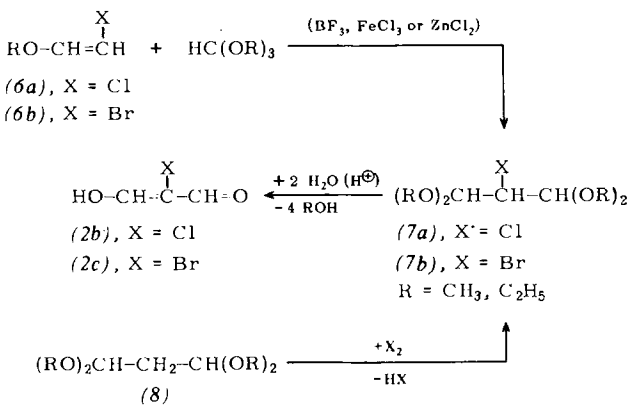


(5a), X = Cl
(5b), X = Br
(2b), X = Cl
(2c), X = Br

The electrophilic addition of orthoformic esters to suitably β-substituted enol ethers *(6)* is of particular importance, since

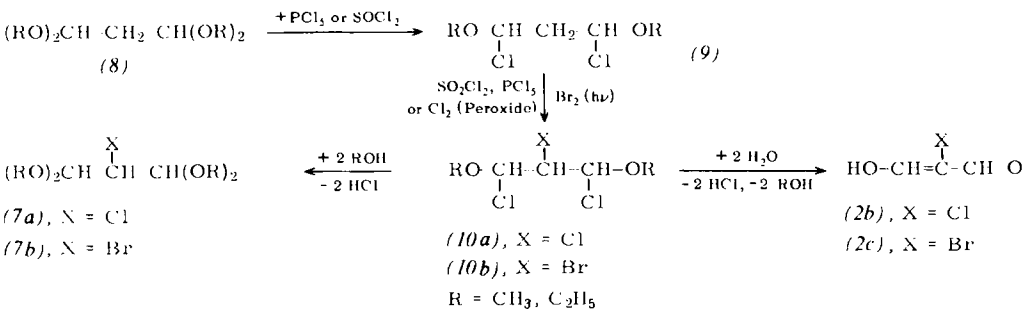
[*] Prof. Dr. C. Reichardt and Doz. Dr. K. Halbritter
Fachbereich Chemie der Universität
335 Marburg, Lahnberge (Germany)

it can be used for the synthesis of many substituted malondialdehydes; in case of *(6a)* and *(6b)* this reaction gives 70—80% yields of the readily hydrolyzable tetraalkyl acetals *(7a)* and *(7b)* of chloro-[15, 16] and bromomalondialdehyde[15–17], respectively. The reaction is catalyzed by Lewis acids and includes the addition of a dialkoxycarbenium ion formed from the orthoester to the double bond of the enol ether[18, 19].



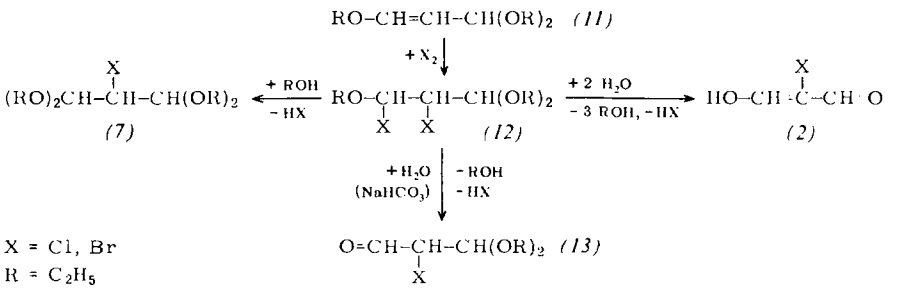
The tetraalkyl acetals *(7a)* and *(7b)* are also accessible by cautious direct halogenation of the malondialdehyde diacetal *(8)*[20–23, 23a].

Although halogens substitute the malondialdehyde diacetals *(8)* directly at C-2, the first product formed on treatment of *(8)* with phosphorus pentachloride or thionyl chloride is 1,3-dialkoxy-1,3-dichloropropane *(9)*, which can then also be halogenated at C-2, thus giving *(10a)* or *(10b)*[24]. These 1,2,3-trihalo compounds can be converted by alcohols into the diacetals *(7a)* and *(7b)* and by water into chloro- *(2b)* and bromomalondialdehyde *(2c)*[24].



(2b) can also be prepared from an intermediate (X=Cl, R=$COCH_3$) similar to *(10a)* which is obtained from trimethylene diacetate by photochemical chlorination[25].

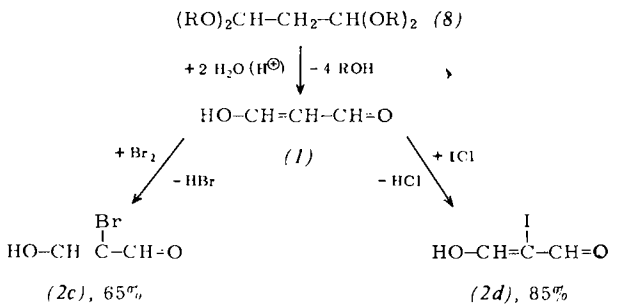
According to the method used, working up the products *(12)* of the addition of chlorine or bromine to 3-ethoxyacrolein



diethyl acetal *(11)*, R=C_2H_5, may yield the halomalondialdehyde *(2b)* or *(2c)* or alternatively their tetraalkyl acetals *(7a)* or *(7b)* or even the 1,1-dialkyl acetals *(13)*[9, 26–30].

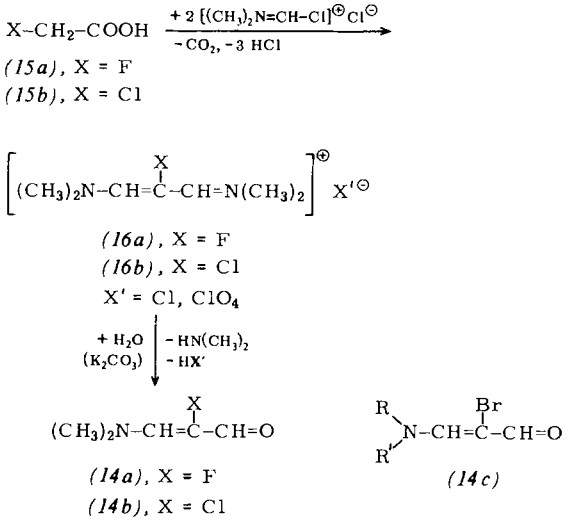
In an essentially similar manner, addition of bromine to 1,3-diethoxy-3-chloro-1-propene leads to bromomalondialdehyde *(2c)*[31].

A further route to halomalondialdehydes is provided by direct substitution of free malondialdehyde *(1)* [prepared by acid-catalyzed hydrolysis of malondialdehyde tetraalkyl diacetals *(8)*] by bromine or iodine(I) chloride. The former reaction is the simplest method of preparing bromomalondialdehyde *(2c)*[32] and the latter is the only route so far known to iodomalondialdehyde *(2d)*[33].



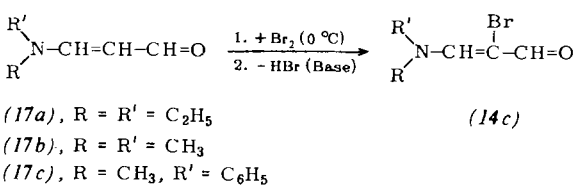
The 3-(dimethylamino)-2-haloacroleins *(14a)*[33–35], *(14b)*[34] and *(14c)*, R=R'=CH_3[36, 37], are important derivatives of the halomalondialdehydes, because as vinylogous formamides they can be readily hydrolyzed to the free halomalondialdehydes. By a process worked out by *Arnold*[34], and also applicable for the synthesis of other substituted malondialdehydes, Vilsmeier formylation of halogenated acetic acids *(15)* affords satisfactory yields of the aminohaloacroleins *(14a)* and *(14b)*. The course of the first reaction step is complicated and not yet fully understood[33, 34].

Fluoromalondialdehyde *(2a)* has only recently become known. Its synthesis by the route *(15a)*→*(14a)* involves a 37% yield of 3-(dimethylamino)-2-fluoroacrolein *(14a)*,



which is hydrolyzed by aqueous sodium hydroxide to the sodium salt of fluoromalondialdehyde, whence the free dialdehyde is obtained by means of ethereal hydrogen chloride[33, 35]. Alkylation of *(14a)* by triethyloxonium tetrafluoroborate followed by treatment with dimethylamine permitted the trimethinium salt *(16a)* to be isolated as tetrafluoroborate[38].

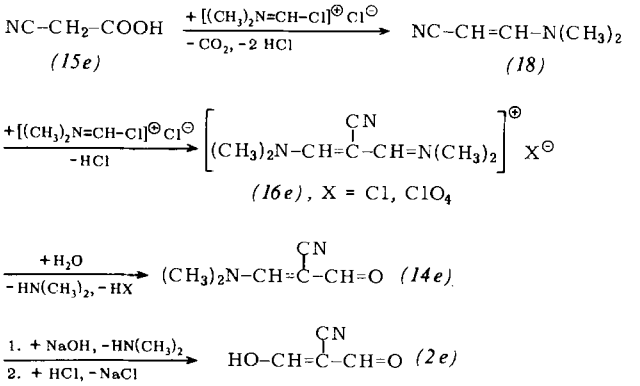
Vilsmeier formylation of bromoacetic acid led, however, not to 2-bromo-3-(dimethylamino)acrolein *(14c)*, but to a derivative of formylmalondialdehyde by the introduction of a third dimethylaminomethylene group[34]. 2-Bromo-3-(dialkylamino)acroleins can nevertheless be obtained by cautious direct bromination of the 3-(dialkylamino)acroleins *(17a)*—*(17c)* in inert solvents (benzene, chloroform, or dichloromethane)[36, 37]; the hydrogen bromides formed initially are converted into *(14c)* by treatment with bases (triethylamine or sodium carbonate solution).



Bromination of *(17b)* in aqueous solution at room temperature and subsequent heating at 100 °C lead directly to bromomalondialdehyde *(2c)*[39]. From the reaction conditions described in ref.[39] it can be deduced that the primary product is not the free malondialdehyde [obtainable by hydrolysis of *(17b)*] but instead the hydrogen bromide of *(14c)*, R = R′ = CH_3, which is hydrolyzed to bromomalondialdehyde *(2c)* at 100 °C.

The 1,3-bis(dimethylamino)-2-halotrimethinium salts *(16)* arising on Vilsmeier formylation of substituted acetic acids are also valuable halomalondialdehyde derivatives and can be obtained either, like *(16b)*, by suitable work up directly from chloroacetic acid[34, 40] or, like the bromine derivative, by bromination of the unsubstituted trimethinium salt with *N*-bromosuccinimide[41].

Vilsmeier formylation of haloacetic acids can be extended to cyanoacetic acid *(15e)*[42, 43]. Reaction of *(15e)* with dimethylformamide/oxalyl chloride in the presence of triethylamine gives, however, a 50% yield of 3-(dimethylamino)acrylonitrile *(18)* which must be again formylated in order to produce the trimethinium salt *(16e)*; according to the mode of work up, the isolated product may be the trimethinium perchlorate[41] (83%) or, after hydrolysis, 3-(dimethylamino)-2-formylacrylonitrile *(14e)* (79%)[43]. Further hydrolysis of *(14e)* is the simplest route so far to cyanomalondialdehyde *(2e)*[43].

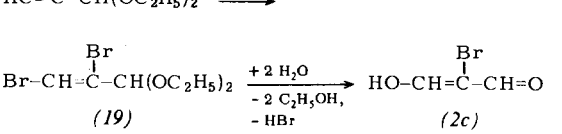


Surprisingly, the carboxyl group of *(15e)* is not needed to activate the CH_2 group in the Vilsmeier formylation: even acetonitrile reacts with dimethylformamide/$POCl_3$ to give *(14e)* in 32% yield[42, 43].

2.2. Special Methods

Whereas the more general methods described in Section 2.1 can all be used for the synthesis of at least two halomalondialdehydes, the present section gives synthetic routes that have not yet been generalized.

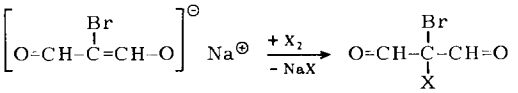
The first synthesis of bromomalondialdehyde *(2c)* was achieved by *Lespieau*[8] by the addition of bromine to 1,2-dibromo-2-methoxy-1-propene. *(2c)* can also be obtained from propargylaldehyde diethyl acetal by the addition of bromine (in chloroform) and hydrolysis of the unisolated intermediate *(19)*[44].



The first synthesis of cyanomalondialdehyde *(2e)* was accomplished by condensation of 3,3-diethoxypropionitrile with ethyl formate and hydrolysis of the intermediate 2-formyl derivative, which yields the sodium salt of *(2e)*[45, 46]. Catalytic hydrogenation of cyanoform (dicyanoketenimine) leads to 3-amino-2-formylacrylonitrile in 50% yield among other products, and alkaline hydrolysis then affords the sodium salt of cyanomalondialdehyde[47, 48].

3. Preparation of Dihalomalondialdehydes

Dibromomalondialdehyde *(20a)* is formed in 76% yield on bromination of the sodium salt of bromomalondialdehyde (in CCl_4)[32]. Chlorination gives bromochloromalondialdehyde *(20b)*[32].



(20a), X = Br
(20b), X = Cl

The tetraethyl diacetal of *(20a)* can be prepared in 60% yield from bromomalondialdehyde tetraethyl diacetal *(7b)*, R = C_2H_5, by reaction with the pyridine-bromine addition compound[28]. Attempted double dehydrohalogenation of this compound to yield carbon suboxide tetraethyl acetal was unsuccessful[28].

4. Fine Structure of Halomalondialdehydes

Halomalondialdehydes can exist as crystals and in solution in one of the three tautomeric forms *(A)* to *(C)*. An X-ray structure analysis of bromomalondialdehyde *(2c)* has been carried out[49, 50], and its results are collected in Figure 1[50]. It is found that, in the crystal, *(2c)* assumes the (*Z*)-enol form *(B)* stabilized by intermolecular hydrogen bonding[51].

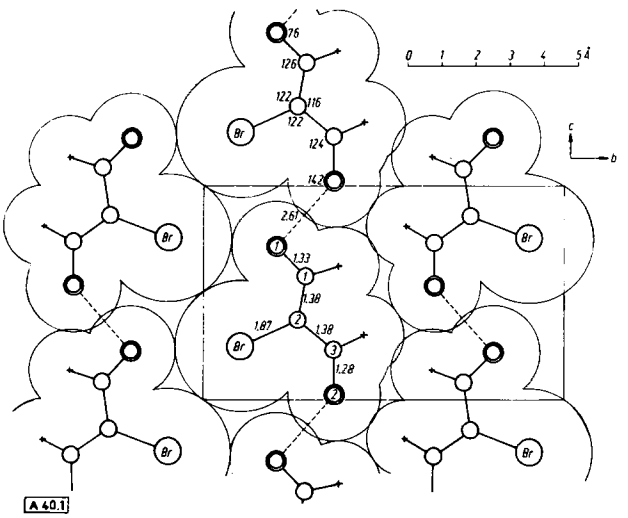
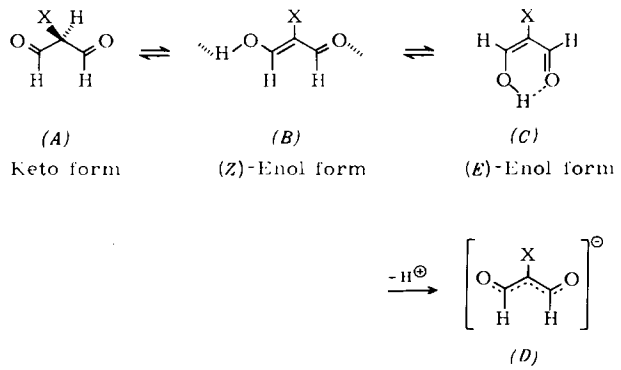


Fig. 1. Bond lengths, bond angles, and packing of the planar molecules of bromomalondialdehyde *(2c)* in the crystal [50]. Cell constants: $a = 6.490(4)$ Å; $b = 10.830(6)$ Å; $c = 6.392(3)$ Å; space group $Cmc2_1$.

Occurrence of the enol form *(B)* also in solution is indicated by the following chemical and spectroscopic findings: a) With aqueous iron(III) chloride solution, solutions of halomalondialdehydes give the reddish-violet coloration characteristic of enolized 1,3-dicarbonyl compounds. b) Aqueous solutions of halomalondialdehydes are acidic; CO_2 is liberated from sodium carbonate. c) The IR spectra of the various halomalondialdehydes are very similar[33, 43, 52]. A detailed analysis has been carried out for the IR spectrum of bromomalondialdehyde, and this is in accord with the enol form *(B)*[52]. The IR spectrum of the bromomalondialdehyde anion indicates the conformation *(D)* with C_{2v} symmetry[52], which has also been demonstrated for the anion of unsubstituted malondialdehyde *(1)*[53]. d) The ^{1}H-NMR spectra of halomalondialdehydes (measured for *ca.* 0.2 M solutions in trideuterioacetonitrile) contain a singlet for the hydroxyl proton at *ca.* 5.5—9.5 ppm and just one signal for the two other protons at *ca.* 8.1—8.9 ppm, the intensity ratio being 1 : 2[33, 43, 54]. The OH signal is shifted downfield with increasing concentration of the solution measured[33, 43]. Such association shifts are characteristic of intermolecular hydrogen bonding. Because of the rapid exchange of position of the hydroxyl proton the two H atoms on C-1 and C-3 are equivalent and give rise to only one signal, which in the case of fluoromalondialdehyde is split to a doublet by coupling with the fluorine ($^3J_{FH} = 21$ Hz). The size of this coupling is in the region typical of vicinal *trans*-^{19}F-^{1}H couplings in fluoroalkenes[33].



(A) Keto form — *(B)* (*Z*)-Enol form — *(C)* (*E*)-Enol form

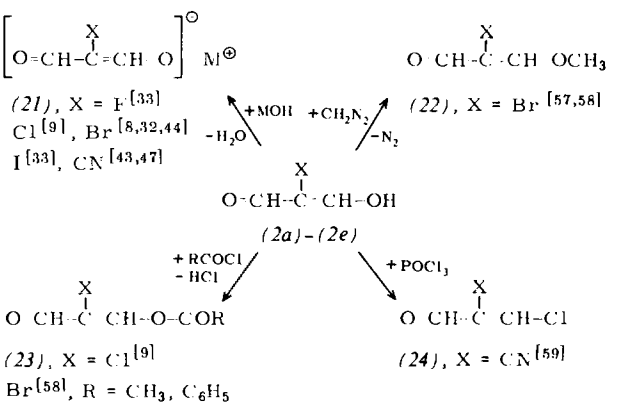
(D)

For malondialdehyde *(1)*, which occurs in the form *(C)* in apolar solvents (CCl_4, $CHCl_3$, CH_2Cl_2) but in form *(B)* in polar solvents (H_2O)[55], CNDO/2 calculations favor form *(C)* with unsymmetrical intramolecular hydrogen bonds as the energetically most favorable state[56].

5. Uses of Halomalondialdehydes in Syntheses

5.1. Preparation of Open-Chain Compounds

The fact that it is not only formally that halomalondialdehydes can be regarded as vinylogous formic acids is shown by their typical carboxylic acid reactions, such as those with metal hydroxides to give salts *(21)*, with diazomethane to give vinylogous esters *(22)*, and with acid halides (in pyridine) or phosphoryl chloride to give vinylogous carboxylic anhydrides *(23)* or formyl chlorides *(24)*, respectively.



(21), X = F[33], Cl[9], Br[8,32,44], I[33], CN[43,47]

(22), X = Br[57,58]

(2a)–(2e)

(23), X = Cl[9], Br[58], R = CH_3, C_6H_5

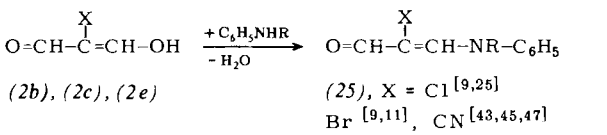
(24), X = CN[59]

However, halomalondialdehydes undergo typical aldehyde reactions such as ready acetalization [*(2b)*[13], *(2c)*[32]] and many of the reactions in the following sections.

5.1.1. Reactions with Amines

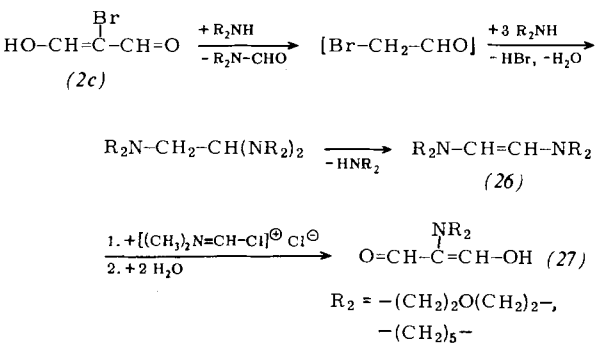
Halomalondialdehydes react with primary or secondary aromatic amines to give, according to the reaction conditions,

either the vinylogous formamides *(25)* (monoanils) or the dianils; the hydrogen halides of the latter are, however, more advantageously prepared from the mucohalic acids *(3)* and aniline (see Section 2.1). Investigation of the fine structure of the potentially tautomeric monoanils (and dianils) of cyanomalondialdehyde in solution shows their exclusive existence in the lactam form *(25)*, R = H, with intramolecular hydrogen bonding[43], in agreement with the results obtained for malondialdehyde anils[60-63].



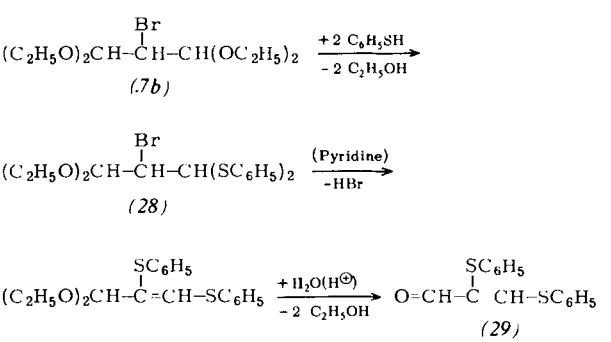
(2b), (2c), (2e) *(25)*, X = Cl[9,25], Br[9,11], CN[43,45,47]; R = H, CH_3

Surprisingly the reaction of bromomalondialdehyde *(2c)* with secondary aliphatic (cyclic) amines (morpholine, pyrrolidine) takes a different course, providing a simple route to vinylenebis(dialkylamines) *(26)*[64] which can be converted, again by Vilsmeier formylation, into the (dialkylamino)malondialdehydes *(27)*[65].

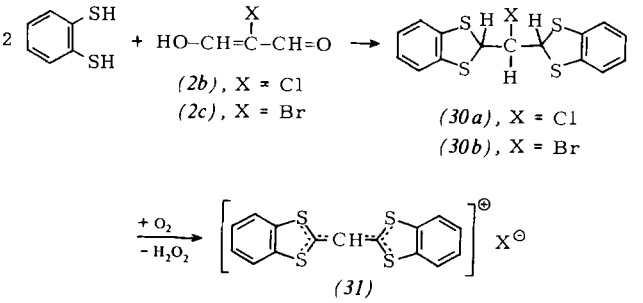


5.1.2. Reactions with Thiols

Interaction of thiophenol with bromomalondialdehyde tetraethyl acetal *(7b)* affords first the acetal-thioacetal *(28)*, which is not converted by pyridine into the ketene dithioketal by normal elimination of HBr[29] but instead gives a derivative *(29)* of (phenylthio)malondialdehyde by migration of a phenylthio group[66].



With sodium *p*-nitrophenyl sulfide chloromalondialdehyde reacts by nucleophilic substitution, yielding (*p*-nitrophenylthio)malondialdehyde[67]. With dithiopyrocatechol chloro- *(2b)* and bromomalondialdehyde *(2c)* give the bis(dithioacetals) *(30a)* and *(30b)*, respectively, both of which afford the methine dye *(31)* when air is passed through their solutions in moist chloroform[68].



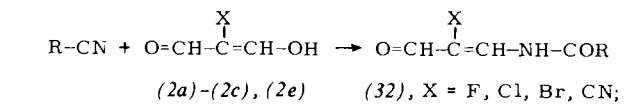
(2b), X = Cl; *(2c)*, X = Br

(30a), X = Cl; *(30b)*, X = Br

(31)

5.1.3. Reactions with Nitriles

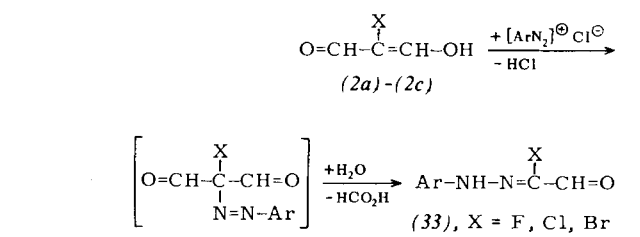
The reaction of aliphatic nitriles with halomalondialdehydes occurs analogously to that of aliphatic carboxylic acids with nitriles[48], thus providing simple access to *N*-(2-formyl-2-halovinyl)carboxamides *(32)*[54].



(2a)-(2c), (2e) *(32)*, X = F, Cl, Br, CN; R = CH_3, C_2H_5

5.1.4. Reactions with Diazonium Salts

When applied to halomalondialdehydes, the Japp-Klingemann reaction, *i.e.*, treatment of 1,3-dicarbonyl compounds with aromatic diazonium salts, leads to 1-haloglyoxal 1-phenylhydrazones *(33)*[69-72], which possess insecticidal and acaricidal properties[70].

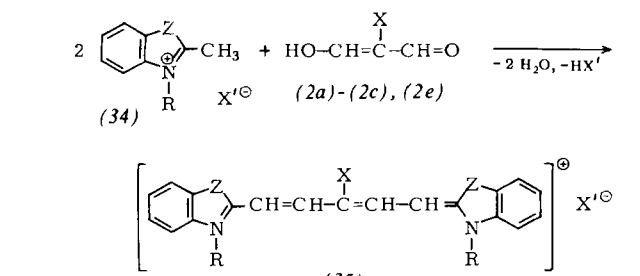


(2a)-(2c) *(33)*, X = F, Cl, Br

The potentially tautomeric compounds *(33)* exist in solution exclusively in the open phenylhydrazone form shown in the formula[72].

5.1.5. Reactions with CH-Acidic Compounds

Condensation of halomalondialdehydes *(2)*, their dianils *(4)*, their sodium salts *(21)*, or their acetals *(7)* with the heterocyclic immonium salts *(34)* customarily used in cyanine chemistry leads to γ-substituted pentamethine cyanine dyes *(35)*[73-81],



(34) *(2a)-(2c), (2e)*

(35)

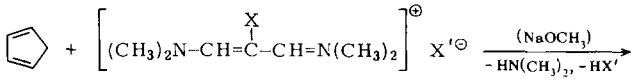
R = CH_3, C_2H_5;

X = F[80], Cl[73,79], Br[74-76,78,79,81], CN[77,79];

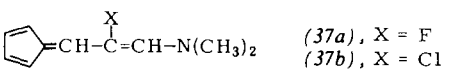
Z = $C(CH_3)_2$, CH=CH, O, S, Se

which have assumed importance as sensitizers of photographic silver halide emulsions[82] and as models for investigating the influence of substituents on the UV and visible spectra of polymethine dyes[79, 80, 83].

In condensations of halomalondialdehydes it is often advantageous to employ the 2-halotrimethinium salts *(16)* instead of the free dialdehydes, since the higher electrophilic potential of the former frequently makes reaction possible even with only weakly CH-acidic reactants. For example, the 6-[2-(dimethylamino)-1-halovinyl]fulvenes *(37)* thus become easily accessible from *(16)* and cyclopentadiene[38, 84].



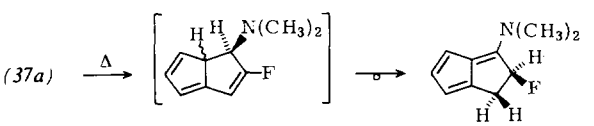
(36) *(16a)*, X = F; *(16b)*, X = Cl



(37a), X = F; *(37b)*, X = Cl

5.2. Preparation of Carbocyclic Compounds

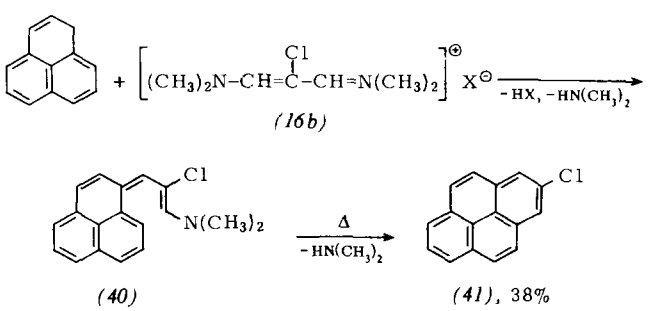
When heated for a short time in piperidine the 6-[2-(dimethylamino)-1-fluorovinyl]fulvene *(37a)* mentioned in Section 5.1.5 undergoes a presumably conrotatory electrocyclic reaction yielding the non-isolable intermediate *(38)*, which then affords 3-(dimethylamino)-2-fluoro-1,2-dihydropentalene *(39)* by a double sigmatropic [1.5]-shift of hydrogen[38, 85].



(37a) *(38)* *(39)*

In the corresponding reaction of the chloro compound *(37b)* nucleophilic replacement of the chlorine leads to the 2-piperidino derivative[54] which, like *(39)*, should be useful for the preparation of simpler pentalenes.

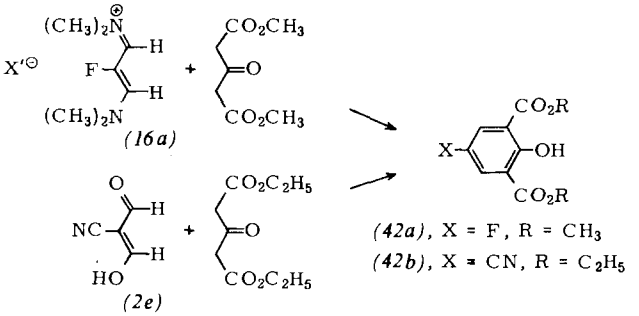
An electrocyclic ring closure with subsequent elimination of dimethylamine leading to the 2-chloropyrene *(41)* has been observed when the intermediate product *(40)* obtained from phenalene and the 2-chlorotrimethinium salt *(16b)* was heated[40]—a reaction that is capable of considerable generalization[86].



(16b) *(40)* *(41)*, 38%

On treatment of 1,2,3,3-tetrachloro-1-propene *(5a)* with anthrone in conc. sulfuric acid the intermediate chloromalondialdehyde formed from *(5a)* (cf. Section 2.1) undergoes ring closure to 2-chlorobenzanthrone[11].

The elegant Hill synthesis of *p*-nitrophenol from nitromalondialdehyde and acetone[6] has been applied to halomalondialdehydes in only two cases: interaction of cyanomalondialdehyde *(2e)* or the 2-fluorotrimethinium salt *(16a)* and acetonedicarboxylic ester gives the phenols *(42a)*[38] and *(42b)*[43], respectively.



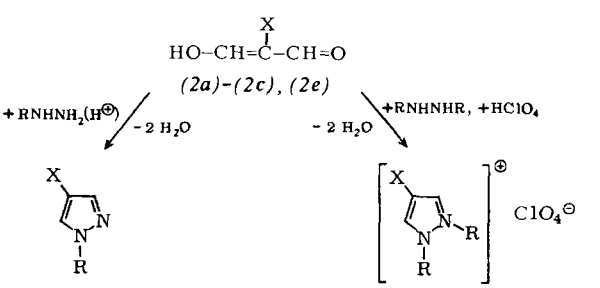
(16a) *(2e)* *(42a)*, X = F, R = CH_3; *(42b)*, X = CN, R = C_2H_5

5.3. Preparation of Heterocyclic Compounds

The synthetic potential of the halomalondialdehydes (and other substituted malondialdehydes), which is by no means yet exhausted, lies particularly in their heterocyclization with bifunctional reactants, such reactions often making it possible to prepare by simple routes pharmacologically valuable halogen-substituted heterocycles that are in many cases difficult to prepare by other methods.

5.3.1. Synthesis of Five-Membered Heterocycles

Interaction of halomalondialdehydes with hydrazine or phenylhydrazine gives good yields of 4-halopyrazoles *(43)*. It is only with iodomalondialdehyde *(2d)* that the use of hydrazine leads to unsubstituted pyrazole; here, as in almost all other cases, reactions of iodomalondialdehyde with nucleophiles are accompanied by an immediate formation of iodine[54].



(43), 50-95%
X = F[38,87], Cl[9,24,25], Br[8,9,24], CN[43,47];
R = H, C_6H_5, 4-NO_2–C_6H_4

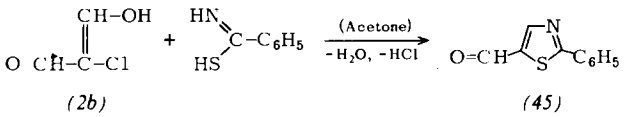
(44), 50-60%
X = F[38,87], Br[54], CN[43];
R = CH_3, $C_6H_5CH_2$

The method discovered by *Elguero et al.*[88] for the preparation of 1,2-dialkyl-substituted pyrazolium salts *(44)* can also be applied to halomalondialdehydes[38, 43, 54, 87]. 1,2-Diphenylpyrazolium salts *(44)*, R = C_6H_5, however, cannot be obtained in this way since in acid solution hydrazobenzene undergoes the benzidine rearrangement. Nevertheless, the 4-bromo-1,2-diphenylpyrazolium salt can be prepared by oxidative ring

closure of bromomalondialdehyde dianil with *N*-bromosuccinimide[89].

With sulfanes H_2S_x ($x=2$ or 3) chloro- and bromomalondialdehyde give 4-halo-1,2-dithiolium salts, analogous to *(44)*, in 10% yield[90].

Although in the preceding reactions the bifunctional nucleophile reacts with both carbonyl groups, treatment of chloromalondialdehyde *(2b)* with thiobenzamide gives an almost quantitative yield of 2-phenyl-5-thiazolecarbaldehyde *(45)*, which arises by the reaction of only one carbonyl group and nucleophilic replacement of the chlorine atom[91].

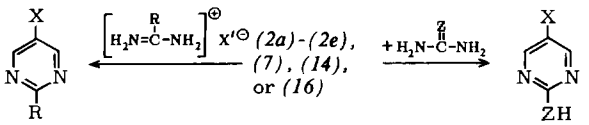


(2b) *(45)*

Similarly, 5-aminoimidazo[1,2-*a*]pyridine-2-carbaldehyde is formed from 2,6-diaminopyridine and chloro- or bromomalondialdehyde in 10 or 17% yield, respectively[92].

5.3.2. Synthesis of Six-Membered Heterocycles

Halomalondialdehydes are of special importance for the synthesis of substituted pyrimidines *(46)* and *(47)*. In condensations with amidinium salts[99] or urea derivatives the free halomalondialdehydes *(2a)—(2e)*[24, 38, 87, 93, 94] or their acetals *(7)*[24] are introduced in an acid reaction medium, or the 3-(dimethylamino)-2-haloacroleins *(14)*[38, 87] or 2-halotrimethinium salts *(16)*[43, 95, 96] are used in a basic reaction medium. The yields vary between 20 and 95%.



(46) *(47)*

X = F[38,87], Cl[95], CN[43];
R = CH_3, C_6H_5

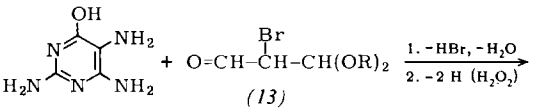
X = F[38,87], Cl[24,93-96], Br[24,96], CN[43,96], I[54];
Z = NH, S, O

By a process described by *Bredereck et al.*[97], 5-halopyrimidines which are unsubstituted at C-2, such as 5-bromo- (63%)[22] and 5-fluoropyrimidine (52%)[38, 87] can also be synthesized from halomalondialdehyde derivatives and formamide.

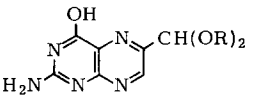
Novel types of heterocycles such as 3-fluoropyrimido[1,2-*b*]indazole[38] and 6-chloroselenazolo[3,2-*a*]pyrimidinium salts[98] are formed from 3-aminoindazole and fluoromalondialdehyde or 2-aminoselenazolium salts and chloromalondialdehyde, respectively.

The pteridine derivative *(48)*, which is formed on reaction of bromomalondialdehyde diethyl acetal *(13)*, X=Br, with 2,5,6-triamino-4-pyrimidinol, is a valuable intermediate for the synthesis of folic acid (pteroylglutamic acid)[27, 30].

The monoanils *(25)*, X=CN, R=H[43, 45, 47] obtainable from aromatic amines and cyanomalondialdehyde *(2e)* can be cyclized under drastic conditions to yield 3-quinolinecarbonitriles[45, 100, 101]; thus, when heated at 300 °C with anhydrous zinc chloride, the monoanil that is readily obtainable from

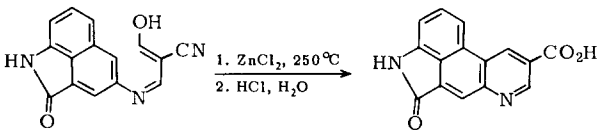


(13)



(48), R = C_2H_5

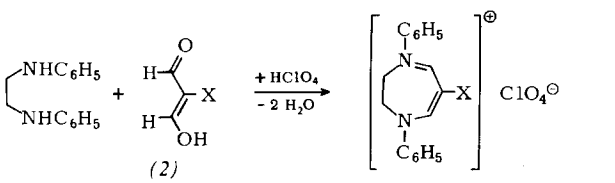
(2e) and aniline affords a mixture of 3-quinoline-carbonitrile and -carbamide[45]. Application of this reaction to the monoanil *(49)* arising from cyanomalondialdehyde and 2-aminonaphthostyril[45] and other complicated amines[100, 101] leads to quinoline derivatives such as *(50)*, which have become important intermediates for the synthesis of some lysergic acid derivatives.



(49) *(50)*

5.3.3. Synthesis of Seven-Membered Heterocycles

When 1,2-dianilinoethane, introduced by *Wanzlick* and *Löchel*[102] as a reagent for the detection of aldehydes, reacts with substituted malondialdehydes, it does not lead, as expected, to imidazolidines; instead, the 2,3-dihydro-1*H*-1,4-diazepinium salts *(51)* are formed (see also ref.[104]).



(2)

(51), X = F[38,87], Cl[54], Br[103], CN[43]

Bromomalondialdehyde reacts analogously with *o*-phenylenediamine, yielding a 3-bromo-1,5-benzodiazepine[105, 106].

Received: July 30, 1974 [A 40 IE]
German version: Angew. Chem. *87*, 124 (1975)
Translated by Express Translation Service, London

[1] Syntheses with substituted malondialdehydes. Part 21.—Part 20: *C. Reichardt* and *E.-U. Würthwein*, Chem. Ber. *107*, 3454 (1974).

[2] *S. Dähne*, Z. Chem. *5*, 441 (1965).

[3] *R. Hüttel*, Ber. Deut. Chem. Ges. *74*, 1825 (1941).

[4] *L. Claisen*, Ber. Deut. Chem. Ges. *36*, 3664 (1903).

[5] Recent reviews of malondialdehyde: a) *F. Mashio* and *Y. Kimura*, Yuki Gosei Kagaku Kyokai Shi *19*, 647 (1961); Chem. Abstr. *55*, 25747 (1961); b) *T. W. Kwon*, Hwahak Kwa Kongop Ui Chinbo *8*, 137 (1968); Chem. Abstr. *70*, 67472u (1969).

[6] *H. B. Hill* and *C. R. Sanger*, Ber. Deut. Chem. Ges. *15*, 1906 (1882); *H. B. Hill* and *J. Torrey*, *ibid. 28*, 2597 (1895); for a recent review of nitromalondialdehyde see: *P. E. Fanta* and *R. A. Stein*, Chem. Rev. *60*, 261 (1960).

[7] *H. Simonis*, Ber. Deut. Chem. Ges. *34*, 509 (1901).

[8] *R. Lespieau*, C. R. Acad. Sci. *133*, 538 (1901); Chem. Zbl. *1901*, II, 1044; Bull. Soc. Chim. Fr. *25*, 1062 (1901).

[9] *W. Dieckmann* and *L. Platz*, Ber. Deut. Chem. Ges. *37*, 4638 (1904).

[10] *H. J. Prins*, DRP 261689 (1912); Chem. Zbl. *1913* II, 394; J. Prakt. Chem. [2] *89*, 414 (1914); cf. also Houben-Weyl-Müller: Methoden der organischen Chemie. 4th Edit., Vol. 7/1, Thieme, Stuttgart 1954, p. 119.

[11] *I. M. Heilbron, R. N. Heslop*, and *F. Irving*, J. Chem. Soc. *1936*, 781.

[12] *G. R. Clemo* and *N. Legg*, J. Chem. Soc. *1947*, 539.

[13] *J. W. Cornforth, E. Fawaz, L. J. Goldsworthy*, and *R. Robinson*, J. Chem. Soc. *1949*, 1549.

[14] *H. Khalaf*, Tetrahedron Lett. *1971*, 4239.

[15] *E. Kobayashi*, Jap. Pat. 2169 (1956); Mitsubishi Chemical Industries Co.; Chem. Abstr. *51*, 9677g (1957).

[16] *S. Hattori, T. Minagawa, A. Yusawa*, and *E. Kobayashi*, Yakugaku Zasshi *82*, 265 (1962); Chem. Abstr. *58*, 439 (1963).

[17] *L. A. Janovskaja, S. S. Jufit*, and *V. F. Kučerov*, Izv. Akad. Nauk SSSR *1960*, 1246; Chem. Abstr. *54*, 24452 (1960).

[18] *L. S. Povarov*, Usp. Khim. *34*, 1489 (1965); Russ. Chem. Rev. *34*, 639 (1965); further literature cited therein.

[19] *V. V. Mežerickij, E. P. Olechnovič*, and *G. N. Dorofeenko*, Usp. Khim. *42*, 896 (1973); Russ. Chem. Rev. *42*, 392 (1973).

[20] *R. F. Kleinschmidt*, French Pat. 980968 (1949); General Aniline and Film Corp.; Chem. Zbl. *1952*, 3405; cf. also the improved procedure of *B. Eistert* and *F. Haupter*, Chem. Ber. *93*, 264 (1960).

[21] *E. Kobayashi* and *A. Yusawa*, Yakugaku Zasshi *82*, 451 (1962); Chem. Abstr. *58*, 4552f (1963).

[22] *H. Bredereck, F. Effenberger*, and *E. H. Schweizer*, Chem. Ber. *95*, 803 (1962).

[23] *P. Pino, F. Piacenti*, and *G. Fatti*, Gazz. Chim. Ital. *90*, 356 (1960).

[23a] Cf. also the preparation of 2-bromo-3-alkoxyacroleins by bromination of 1,1,3,3-tetraalkoxypropanes and subsequent heating: *J. A. Kirby*, DBP 2351376 (1974), Eli Lilly and Co.; Chem. Abstr. *81*, 13116q (1974).

[24] *A. P. Skoldinov* and *T. V. Protopopova*, USSR-Pat. 121444 (1959); Chem. Abstr. *54*, 5474 (1960); Zh. Obshch. Khim. *29*, 3982 (1959); Chem. Abstr. *54*, 20869 (1960); *T. V. Protopopova, V. T. Klimko*, and *A. P. Skoldinov*, Khim. Nauka Prom. *4*, 805 (1959); Chem. Abstr. *54*, 11036 (1960).

[25] *S. Olsen, L. Kühn*, and *C.-D. Friedberg*, Chem. Ber. *81*, 540 (1948).

[26] Merck and Co., Inc., Brit. Pat. 785351 (1957); Chem. Abstr. *52*, 5452 (1958).

[27] *M. Sletzinger, D. Reinhold, J. Grier, M. Beachem*, and *M. Tishler*, J. Amer. Chem. Soc. *77*, 6365 (1955); *M. Sletzinger* and *M. Tishler*, US-Pat. 2821527 (1958) and 2821558 (1958); both Merck and Co., Inc.; Chem. Abstr *52*, 11972 (1958).

[28] *S. M. McElvain* and *L. R. Morris*, J. Amer. Chem. Soc. *73*, 206 (1951).

[29] *E. Rothstein* and *R. Whiteley*, J. Chem. Soc. *1953*, 4012.

[30] *J. N. Wells* and *M. S. Strahl*, J. Pharm. Sci. *60*, 533 (1971); Chem. Abstr. *74*, 141701u (1971).

[31] *A. N. Stavrovskaja, T. V. Protopopova, R. Ja. Popova*, and *A. P. Skoldinov*, Zh. Org. Khim. *4*, 1194 (1968); Chem. Abstr. *69*, 66856q (1968).

[32] *S. Trofimenko*, J. Org. Chem. *28*, 3243 (1963).

[33] *C. Reichardt* and *K. Halbritter*, Liebigs Ann. Chem. *737*, 99 (1970).

[34] *Z. Arnold*, Collect. Czech. Chem. Commun. *26*, 3051 (1961); *30*, 2125 (1965).

[35] *C. Reichardt* and *K. Halbritter*, DBP 2017010 (1971), Schering AG; Chem. Abstr. *76*, 24691w (1972).

[36] *H. R. Hensel*, Chem. Ber. *97*, 96 (1964).

[37] *K. Hafner* and *M. Neuenschwander*, Angew. Chem. *80*, 443 (1968); Angew. Chem. internat. Edit. *7*, 459 (1968); *H.-J. Gais, K. Hafner*, and *M. Neuenschwander*, Helv. Chim. Acta *52*, 2641 (1969).

[38] *C. Reichardt* and *K. Halbritter*, Liebigs Ann. Chem. *1975*, in press; *K. Halbritter, W.-D. Kermer*, and *C. Reichardt*, Angew. Chem. *84*, 68 (1972); Angew. Chem. internat. Edit. *11*, 62 (1972).

[39] *N. V. Kuznecov* and *I. I. Krasavcev*, USSR-Pat. 403666 (1973); Chem. Abstr. *80*, 47458x (1974).

[40] *C. Jutz, R. Kirchlechner*, and *H.-J. Seidel*, Chem. Ber. *102*, 2301 (1969).

[41] *J. Kučera* and *Z. Arnold*, Collect. Czech. Chem. Commun. *32*, 1704 (1967).

[42] *C. Reichardt* and *W.-D. Kermer*, Synthesis *1970*, 538.

[43] *C. Reichardt* and *W.-D. Kermer*, unpublished; *W.-D. Kermer*, Dissertation, Universität Marburg 1972.

[44] *J. Grard*, C. R. Acad. Sci. *190*, 187 (1930); Chem. Zbl. *1930* I, 2389; Ann. Chim. Phys. [10] *13*, 336 (1930); Chem. Zbl. *1930* II, 542.

[45] *F. C. Uhle* and *W. A. Jacobs*, J. Org. Chem. *10*, 76 (1945); cf. improved procedure of *G. A. Swan* and *D. Wright*, J. Chem. Soc. *1956*, 1549.

[46] Sandoz Ltd., Brit. Pat. 759105 (1956); Chem. Abstr. *51*, 10590 (1957).

[47] *S. Trofimenko*, J. Org. Chem. *28*, 2755 (1963).

[48] *F. C. Schaefer* in *Z. Rappoport*: The Chemistry of the Cyano Group. Interscience, New York 1970, p. 246.

[49] *B. Aurivillius* and *G. Lundgren*, Acta Chem. Scand. *9*, 912 (1955); *18*, 1642 (1964); for a critique of this X-ray structure analysis see *O. Kennard et al.*: Molecular Structure and Dimensions. International Union of Crystallography 1972, Vol. A 1, p. 44, No. 5.2.

[50] *R. Allmann* and *A. Kutoglu*, Marburg 1974, unpublished.

[51] Hydroxymalondialdehyde has an analogous crystal structure: *D. Semmingsen*, Acta Chem. Scand. *B 28*, 141 (1974).

[52] *W. O. George* and *V. G. Mansell*, Spectrochim. Acta *A 24*, 145 (1968).

[53] *N. Bacon, W. O. George*, and *B. H. Stringer*, Chem. Ind. (London) *1965*, 1377.

[54] *C. Reichardt* and *K. Halbritter*, unpublished.

[55] *W. O. George* and *V. G. Mansell*, J. Chem. Soc. *B 1968*, 132.

[56] *P. Schuster*, Chem. Phys. Lett. *3*, 433 (1969); Z. Chem. *13*, 41 (1973).

[57] *B. Eistert*, Ark. Kemi *2*, 129 (1950).

[58] *M. F. Šostakovskij, N. V. Kuznecov*, and *C. M. Yang*, Izv. Akad. Nauk SSSR *1961*, 1685; Chem. Abstr. *56*, 5808 (1962).

[59] *K. Friedrich* and *H. K. Thieme*, Synthesis *1973*, 111.

[60] *J. Dabrowski*, J. Mol. Struct. *3*, 227 (1969).

[61] *E. Daltrozzo* and *K. Feldmann*, Ber. Bunsenges. Phys. Chem. *72*, 1140 (1968).

[62] *J. S. Walia, A. S. Walia*, and *L. J. Guillot*, Chem. Ind. (London) *1972*, 933.

[63] *H.-H. Limbach* and *W. Seiffert*, Tetrahedron Lett. *1972*, 371; Ber. Bunsenges. Phys. Chem. *78*, 532 (1974).

[64] *L. Duhamel, P. Duhamel*, and *V. Truxillo*, C. R. Acad. Sci. *C 275*, 225 (1972).

[65] *C. Reichardt* and *K. Schagerer*, Angew. Chem. *85*, 346 (1973); Angew. Chem. internat. Edit. *12*, 323 (1973).

[66] *W. E. Parham* and *J. Heberling*, J. Amer. Chem. Soc. *77*, 1175 (1955).

[67] *M. Yanagita* and *R. Futaki*, Yakugaku Zasshi *72*, 236 (1952); Chem. Abstr. *47*, 6424 (1953).

[68] *O. Neunhoeffer* and *A. Nowak*, Naturwissenschaften *45*, 491 (1958).

[69] *W. Dieckmann* and *L. Platz*, Ber. Deut. Chem. Ges. *38*, 2986 (1905).

[70] *W. Draber, K. H. Büchel, I. Hamann*, and *G. Unterstenhöfer*, South African Pat. 6903968 (1970), Bayer AG; Chem. Abstr. *73*, 45130r (1970).

[71] *M. O. Lozinskij* and *A. A. Geršković*, Zh. Org. Khim. *8*, 785 (1972); Chem. Abstr. *77*, 19303n (1972).

[72] *C. Reichardt* and *K. Halbritter*, Chem. Ber. *106*, 1661 (1973).

[73] *I. M. Heilbron* and *F. Irving*, Brit. Pat. 353889 (1930), Imperial Chemical Industries, Ltd.; Chem. Zbl. *1931* II, 3669; *S. Beattie, I. M. Heilbron*, and *F. Irving*, J. Chem. Soc. *1932*, 260.

[74] *Z. P. Sytnik* and *B. S. Steingardt*, J. Appl. Chem. SSSR *9*, 1842 (1936); Chem. Abstr. *31*, 2609 (1937).

[75] *A. T. Troščenko*, J. Gen. Chem. SSSR *9*, 1661 (1939); Chem. Abstr. *34*, 3739 (1940).

[76] *L. G. S. Brooker*, US-Pat. 2189599 (1940), Eastman Kodak Co.; Chem. Abstr. *34*, 4003 (1940).

[77] *F. P. Doyle*, Brit. Pat. 640127 (1950), Ilford Ltd.; Chem. Abstr. *45*, 6519 (1951).

[78] *M. Koral, A. Leifer, D. Bonis, M. Collins, P. Dougherty, A. J. Fusco*, and *J. E. LuValle*, J. Chem. Eng. Data *10*, 67 (1965); Chem. Abstr. *62*, 7901 (1965).

[79] *C. Reichardt*, Liebigs Ann. Chem. *715*, 74 (1968).

[80] *C. Reichardt* and *K. Halbritter*, Chem. Ber. *104*, 822 (1971).

[81] *E. P. Ščelkina* and *A. V. Kazymov*, Zh. Org. Khim. *8*, 635 (1972); Chem. Abstr. *77*, 50119f (1972).

[82] *F. M. Hamer* in *A. Weissberger*: The Chemistry of Heterocyclic Compounds. Vol. 18, Interscience, New York 1964.

[83] *C. Reichardt* and *W. Mormann*, Chem. Ber. *105*, 1815 (1972).

[84] *C. Reichardt*, Lecture on May 19, 1972 in Vienna; cf. Allg. Prakt. Chem. *23*, 90 (1972).

[85] Similar intramolecular ring closures leading to dihydropentalene derivatives have also been recorded for other 6-(2-aminovinyl)fulvene derivatives: a) *R. Kaiser* and *K. Hafner*, Angew. Chem. *82*, 877 (1970); Angew. Chem. internat. Edit. *9*, 892 (1970); b) *C. Reichardt* and *P. Miederer*, Liebigs Ann. Chem. *1973*, 750.

[86] *C. Jutz* and *R. M. Wagner*, Angew. Chem. *84*, 299 (1972); Angew. Chem. internat. Edit. *11*, 315 (1972); *C. Jutz* and *E. Schweiger*, Chem. Ber. *107*, 2383 (1974).

[87] *C. Reichardt* and *K. Halbritter*, DBP 2016990 (1971), Schering AG; Chem. Abstr. *76*, 46229d (1972).

[88] *J. Elguero, R. Jacquier*, and *D. Tizané*, Bull. Soc. Chim. Fr. *1969*, 1687.

[89] *B. Hirsch* and *W.-D. Kaiser*, Z. Chem. *7*, 364 (1967).

[90] *M. Schmidt* and *H. Schulz*, Z. Naturforsch. *23b*, 1540 (1968).

[91] *A. Silberg, A. Benkö,* and *G. Csávássy,* Chem. Ber. *97,* 1684 (1964).

[92] *O. Ceder, K. Rosen,* and *J. F. Witte,* Acta Chem. Scand *27,* 1817 (1973).

[93] *M. E. Hultquist, R. O. Roblin, P. S. Winnek,* and *J. P. English,* J. Amer. Chem. Soc. *64,* 570 (1942); *M. E. Hultquist,* US-Pat. 2436360 (1948); American Cyanamide Corp.; Chem. Abstr. *42,* 3438 (1948).

[94] *S. Yanagita,* Jap. Pat. 6728 (1951); Chem. Abstr. *47,* 11262c (1953).

[95] *R. M. Wagner* and *C. Jutz,* Chem. Ber. *104,* 2975 (1971).

[96] *A. Holý* and *Z. Arnold,* Collect. Czech. Chem. Commun. *38,* 1371 (1973).

[97] *H. Bredereck, R. Gompper, H. G. v. Schuh,* and *G. Theilig* in *W. Foerst:* Neuere Methoden der präparativen organischen Chemie. Vol. III, Verlag Chemie, Weinheim 1961, p. 163.

[98] *V. I. Šeiko* and *V. A. Čuiguk,* Ukr. Khim. Zh. *39,* 956 (1973); Cheminform 1973-50-382.

[99] For a review see *M. Miocque, C. Fauran,* and *A. Y. Le Cloarec,* Ann. Chim. (Paris) *7,* 89 (1972); Chem. Abstr. *77,* 61847t (1972).

[100] *W. G. H. Edwards* and *V. Petrow,* J. Chem. Soc. *1954,* 2853.

[101] Sandoz Ltd., Brit. Pat. 759105 (1956); Chem. Abstr. *51,* 10590 (1957).

[102] *H.-W. Wanzlick* and *W. Löchel,* Chem. Ber. *86,* 1463 (1953).

[103] *B. Eistert* and *F. Haupter,* Chem. Ber. *93,* 264 (1960).

[104] *C. Reichardt,* Liebigs Ann. Chem. *746,* 207 (1971).

[105] *W. Ruske* and *E. Hüfner,* J. Prakt. Chem. *18,* 156 (1962).

[106] For a review see *G. A. Archer* and *L. H. Sternbach,* Chem. Rev. *68,* 747 (1968).

The Replacement of Phosphates in Detergents—Possibilities and Limits[**]

By Peter Berth, Günter Jakobi, Edmund Schmadel, Milan J. Schwuger, and Carl Heinrich Krauch[*]

Elimination of phosphates from detergents alone, is insufficient to solve the eutrophication problem. Nevertheless, the endeavors of the detergent industry are aimed at finding phosphate substitutes. Novel approaches for at least a partial replacement of detergent phosphates have been found by using water-soluble organic complexing agents as well as heterogeneous organic or inorganic ion exchangers. So far, a large-scale replacement is not possible. It is not justifiable until all technical requirements are met with and safety with regard to man, animals, plants and drinking water has been established.

1. Introduction

While several years ago, the term "eutrophication" was familiar only to a number of specialists, it now belongs to the vocabulary of the daily press. In connection with phosphate eutrophication, detergents are among the targets of criticism, because of their content of pentasodium triphosphate (STP)[***].

What are the issues?

Undisturbed natural waters are frequently characterized by a stationary state—with regard to their content of biomass—of producers, consumers and decomposers.

The *producers* build up the biomass from minerals (phosphate, *etc.*), CO_2 and light. This is to say that they do not depend on organic carbon as a nutrient. The producers are used up by the *consumers* (mainly fish), forming a food chain up to the species man. The metabolic products are then mineralized and thus recycled by the *decomposers*.

This balance may be disturbed by excessive addition of nutrients or harmful substances: additional matter entering the ecosystem may have different effects on the activity of decomposers and producers.

Organic matter is accumulated, if it cannot be degraded by the decomposers, and a stationary state cannot be achieved. If, however, the additional organic matter is decomposed, more oxygen is withdrawn than in the stationary state.

The presence of additional inorganic matter may lead to excessive fertilization and stimulate growth of the producers, thus contributing to eutrophication. This applies, for instance, to phosphates.

Phosphates are also part of natural waters, as they are released by soil erosion. Furthermore, they find their way into the waters by way of animal and human feces.

The share of phosphates originating from detergents in stagnant or slowly flowing waters—only in these are the high nutrient concentrations achieved which will result in eutrophication—can be estimated on the basis of statistical data on land use and population figures in the affected area, sales figures for detergents and calculation of the amount of phosphate entering domestic sewerage systems by way of metabolic products. These values vary from area to area depending on the density of population, industrial structure, development of canalization and sewage treatment plants, season, amount of rainfall, type of soil and limnological conditions. According to investigations by the joint pollution control commission for Lake Constance in 1972, about 1170 tons of phosphorus found its way into the lake. 470 tons of this amount (40%) came from washing and cleaning products[1]. In the case of the Haltern reservoir, the share of phosphates originating from domestic sewage (detergents and fecal matter) is calculated to amount to 35 to 40%[2]. More than half of the

[*] Dr. P. Berth, Dr. G. Jakobi, Dr. E. Schmadel, Dr. M. J. Schwuger, and Prof. Dr. C. H. Krauch
Henkel & Cie GmbH
4 Düsseldorf, Postfach 1100 (Germany)

[**] Based on a paper presented by *P. Berth* during the Detergent Chemistry Meeting of the "Gesellschaft Deutscher Chemiker"—Bamberg, October 11. 1974.

[***] Sodium triphosphate.

phosphate content of the Wahnbachtal impounding reservoir is thought to reach the water by way of soil erosion[3].

The situation is quite different if a large city without surroundings is considered. Investigations in Chicago (USA) showed communal sewage to contain up to 68 % of phosphate originating from washing and cleaning products[4]. The situation may be similar in other conurbation areas, such as, for instance, the Ruhr District.

Many attempts have been made to assess the phosphate load in surface waters. According to *Bucksteeg*, the human excretion of phosphorus is 1.65 g per inhabitant per day[5]. Assuming an average quantity of sewage of 0.374 m^3 per person and day to reach the surface waters *via* the public sewage system[6], then the fecal P-content in waste water is calculated to be about 4.4 mg per liter. Mechanical and biological treatment will eliminate an average of 35 % of this[7–10], so that about 2.86 mg of fecal phosphorus per liter remain in the sewage plant effluent.

Figures for the long-term average of the surface water effluent in the Federal Republic of Germany which is about 68.4×10^9 m^3/a[11], and the total amount of sewage (6.4×10^9 m^3/a in 1969)[6] yield a dilution ratio of 1 : 10.72 (sewage/receiving water).

Thus, the amount of phosphorus in the surface waters, which is of fecal origin, should be *ca.* 0.27 mg P per liter. According to *Nümann*[12] about one third of this, *i. e. ca.* 0.09 mg phosphorus per liter is available for plant growth in the form of soluble phosphate.

Vollenweider[13], on the other hand, gives a threshold value for *oligotrophic* waters of 0.01 mg available phosphorus per liter. This value—an independent determination is presently being carried out at the Ruhrverband, Essen[14]—cannot be met, even if no detergent phosphates at all were to go into the sewage.

Hence, phosphates must be eliminated from *all* sources in order to really solve the problem of phosphate eutrophication[*]. Extensive elimination can be achieved by leading the entire sewage into sewage treatment plants and adding a chemical precipitation step to the mechanical and biological purification. In this way heavy metals and biochemically difficultly degradable organic compounds are eliminated from the sewage together with phosphates.

Here, the bulk of experience has been collected in Sweden, where 90 % of the waters are stagnant or slowly flowing, and where over 500 sewage plants incorporating chemical precipitation have been built since 1968. This measure has resulted in considerable improvement of the quality of surface waters. The phosphorus content of the effluent on leaving the chemical precipitation plant is between 0.02 and 0.5 mg per liter, and is—at an initial concentration of 1.5 to 9 mg per liter—independent of the initial concentration[15]. Considering that the phosphorus is diluted and partially *immobilized* (by precipitation) on entering the receiving water, the threshold value of 0.01 mg per liter demanded by *Vollenweider* is reached.

In spite of these considerations, the detergent industry has been trying for years to find ways to reduce the phosphate content in detergents.

[*] Consensus by experts at the Hearing "Waschmittel/Gewässerschutz" before the Ministry of the Interior of the Federal Republic of Germany, Bonn, February 26–27, 1973.

Before going into the proposition of eliminating phosphates from modern detergents, let us first discuss the function and importance of phosphates as additives in detergents.

2. Functions and Properties of Phosphates in Detergents

Polyphosphates have a specific washing power of their own, which varies according to the type of fiber and the nature of the soil constituents, *i. e.* the washing performance of phosphate solutions is considerably better than that of pure water. In addition to these primary washing effects (effects on single application) phosphates show remarkable secondary washing properties (effects on repeated application of a detergent). The reason for this is that polyphosphates remove alkaline earth ions from the water, the textiles and the dirt; the precipitation of insoluble alkaline earth salts on textiles is prevented and the dirt is dispersed in the wash liquor. Thus—even after many washings—incrustations and graying of the laundered textiles are minimal. In the physicochemical interpretation of these properties, which are the most important properties of phosphates in the washing process, a distinction has to be made between non-specific effects and specific effects. The former can also be achieved with other additives by changing the pH-value or the ionic strength of the wash liquor, while the latter, the specific effects, reveal the chemical characteristics of phosphates.

2.1. Non-Specific Effects

2.1.1. Alkalinity

Pentasodium triphosphate (STP), the most important of the laundry phosphates and the most widely used, shows alkaline reaction in aqueous solutions. An increase in the pH-value of the wash liquor frequently accelerates the chemical degradation of the soil constituents; thus, removal of fatty soils, for example, is facilitated by partial hydrolysis of the ester linkages.

2.1.2. Increased Interfacial Activity of Ionic Surfactants

The increased interfacial activity of ionic surfactants caused by the presence of electrolytes is another non-specific effect. As shown in Fig. 1, STP exhibits the same behavior as other electrolytes: addition of STP lowers the interfacial tension between an aqueous solution of sodium dodecyl sulfate and

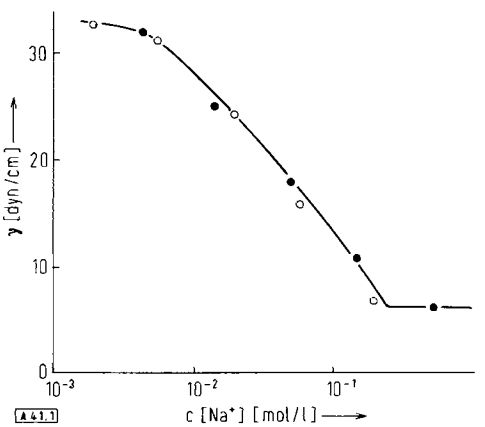


Fig. 1. Interfacial tension γ in the system sodium dodecylsulfate/water/paraffin oil as a function of Na^+-ion concentration, added as Na_2SO_4 (○) or STP (●). The concentration of dodecylsulfate was 1×10^{-3} mol/l.

paraffin oil to the same extent as the addition of an equivalent amount, with respect to the Na^+ concentration, of sodium sulfate.

2.1.3. Non-Specific Development of Electrostatic Surface Charges

Finally, the adsorption of hydroxide ions and other anions leads to the development of an electric potential at the dirt particle and fiber surfaces relative to the aqueous medium[16]. These surface charges lead to electrostatic repulsion between the dirt particles themselves and between dirt particles and fibers.

2.2. Specific Effects

It turns out—especially with cotton as the substrate—that STP shows a washing power which is too large to be explained by these non-specific effects. Furthermore, the specific washing performance of STP is further, and frequently synergistically, increased by combination with anionic surfactants (Fig. 2).

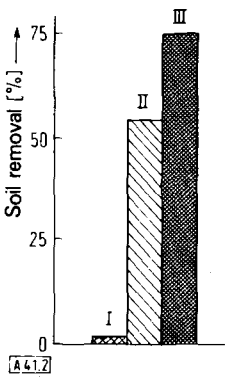


Fig. 2. Primary washing power of anionic surfactants and STP (cotton substrate). Column I: 1.0g anionic surfactant per liter + 2.0g Na_2SO_4 per liter. Column II: 2.0g STP per liter. Column III: 1.0g anionic surfactant per liter + 2.0g STP per liter. Linear alkylbenzenesulfonate as anionic surfactant.

Apparently, this specificity is connected with a specific adsorption of the laundry phosphates on certain types of fibers and soils: electrophoretic studies (determination of zeta-potentials) on soil pigments have shown that STP is strongly adsorbed at surfaces such as those of hematite and γ-Al_2O_3, which show localized concentrations of charge[*], but not at graphite or soot surfaces. Similarly, cotton differs from other fibers in that carboxy groups, which are practically totally ionized in the wash liquor, are present at the surface in addition to hydroxy groups.

The consequences of specific STP-adsorption during the washing process at interfaces with marked concentrations of charge are twofold: interfacial potentials are altered, and anionic surfactants are displaced from solid matter surfaces.

2.2.1. Influences on Interfacial Potentials

The electrostatic repulsions between the individual soil pigment particles and between these and the fibers are increased as a consequence of the increased potential at the pigment particle and fiber surfaces[18]. This effect is also responsible for the distinct ability of STP to disperse hydrophilic soil pigments: clay minerals, *e.g.* are significantly better dispersed by STP than by surfactants (Fig. 3)[18a].

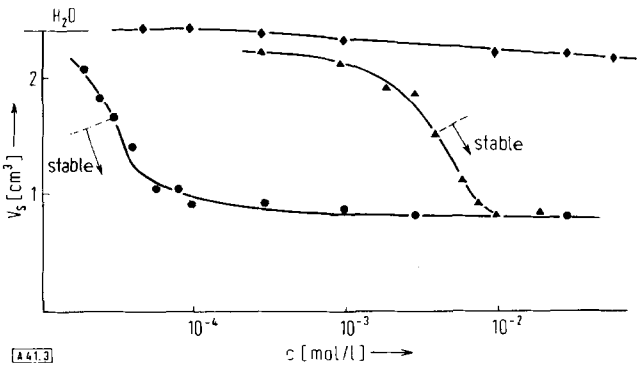


Fig. 3. Sedimentation V_S of kaolin in the presence of anionic surfactants (▲) (example: sodium dodecylsulfate), non-ionic surfactants (♦) (example: dodecyl nonaglycol ether), and STP (●).

2.2.2. Displacement of Anionic Surfactants from Solid Matter Surfaces

Because of specific adsorption, phosphates may reduce the extent of adsorption of anionic surfactants at certain surfaces[17] (Fig. 4). Thus, phosphate adsorption leads to the liberation of adsorbed surfactants "for other duties". The synergy between STP and anionic surfactants observed especially in the case of cotton is probably related to this effect.

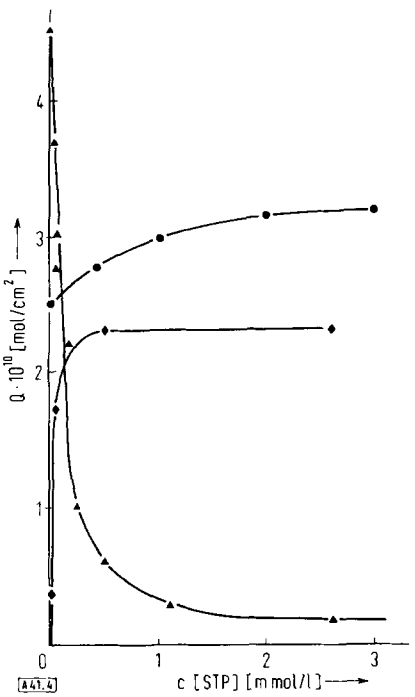


Fig. 4. Competitive adsorption Q of STP and anionic surfactants on soot and γ-Al_2O_3. On soot, STP increases the adsorption of *n*-dodecyl sulfate (●), while on γ-Al_2O_3 adsorption of *n*-decylbenzenesulfonate (▲) is suppressed by STP. The adsorption of STP (♦) on γ-Al_2O_3 is shown for comparison.

In contrast, the adsorption of anionic surfactants is increased in the case of surfaces without marked concentrations of charge, *e.g.* in the case of synthetic fibers or soot. Therefore, surfactant effects prevail in such cases.

[*] Differences encountered in textile fiber and soil pigment interfaces are frequently characterized using the terms 'polar' and 'non-polar'. While the use of these terms is well-established, they do not characterize the chemical differences with sufficient precision.

2.2.3. Binding of Alkaline Earth Ions

A further, very important property of polyphosphates is their binding capacity for alkaline earth ions, the hardening constituents of water. In general, the presence of free alkaline earth ions—introduced with the tap water, and also as constituents of soil—is generally detrimental to the washing process. Removal of the alkaline earth ions prevents precipitation of their compounds with detergent components and the formation of lime deposits in washing equipment and on textiles. Furthermore, polyphosphates remove alkaline earth ions from the soil particle surfaces; thus, the soil is literally "broken up".

In addition, the removal of alkaline earth ions is desirable for another reason: use of the most common types of surfactant at normal dosage levels leads to adsorptive saturation[*] at the interfaces. However, increasing concentration of electrolyte then leads to a decrease in thickness of the electrical double-layer at the interfaces, and thus to decreased electrostatic repulsion between fiber and soil. In principle, increasing the electrolyte concentration by addition of STP has the same effect; it is much more pronounced, however, in the case of the divalent alkaline earth cations than in the case of the monovalent cations, which are freed by the dissociation of STP.

3. Possibilities of Lowering the Phosphate Content in Detergents

As shown in the preceding paragraphs, phosphates are valuable ingredients of laundry detergents. Furthermore, manufacturing, packaging and storage are uncomplicated, and corrosion problems are absent. The environmental behavior of phosphates is particularly impressive: phosphates are toxicologically safe in every respect; there are no adverse effects on sewage or drinking water treatment. A reduction of the phosphate content of laundry detergents—or even a total elimination without replacement—would have the following consequences:

a) a deterioration of the primary washing performance: impact on cleanness and hygiene[19]

b) deterioration of the secondary washing performance: deterioration of wear properties and durability of the laundered textiles because of increasing degree of incrustation[19]

c) formation of lime deposits in the washing machines: reduction of service life[19, 20].

In order to avoid these shortcomings, external measures, such as central water softening, as well as a replacement of detergent phosphates in favor of other compounds have been considered.

3.1. External Measures

The alkaline earth ions present in ordinary tap water may be eliminated by water softening appliances before the washing process. However, alkaline earth ions are also introduced by dirt as well as textile incrustations in amounts that may result in increases of water hardness in the order of 10 to 15° German hardness[21–24]. Therefore, the problem cannot be solved by the use of softened water in the washing machine, but at best be somewhat reduced. Furthermore, there are hygienic objections against the provision of ion exchangers in washing machines: ion exchange resins can become growth media for microorganisms, especially fungi[25–28].

3.2. The Replacement of Detergent Phosphates by Other Substances

The search for phosphate substitutes appears more promising; on a worldwide basis, some 500 million DM has been invested into this particular approach.

There are numerous factors limiting the chances of success: it is not only required that phosphate substitutes take over the functions of detergent phosphates to the greatest possible extent, but also acceptable phosphate substitutes must be toxicologically safe to humans and unobjectionable with regard to sewage biology. Furthermore, they should be biologically degradable—or removable by other means—and should not contribute to eutrophication, nor interfere with the preparation of drinking water *etc.*[29] (Tables 1 and 2).

3.3. Water-Soluble Inorganic Substances

One possibility of phosphate replacement is to use strongly alkaline substances, in order to at least partially compensate for the loss of primary washing power. Among the compounds

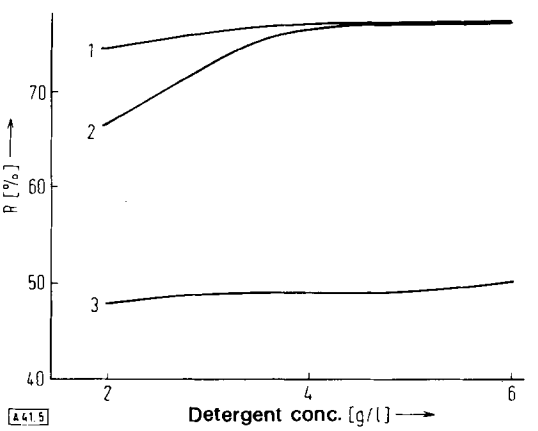


Fig. 5. Primary washing power (quoted as remission R) of STP (1), STP/Na_2SO_4 (2), and Na_2CO_3 (3) in a heavy duty laundry detergent formulation at 90 °C on resin-finished cotton. For definition of R see legend to Fig. 6.

of this class, soda and sodium silicate have been subjected to the most detailed studies. Both compounds contribute to the primary washing performance of a detergent only by their alkalinity, *i.e.* by non-specific effects; the primary washing performance, as shown in Fig. 5, is quite inferior to that of STP. Also the secondary washing behavior is unsatisfactory due to the lack of binding capacity for calcium and magnesium ions: this leads to the formation of incrustations on textiles and lime deposits in the washing machines. Finally, the incorporation of strongly alkaline substances in laundry detergents increases their skin irritancy.

[*] As long as adsorptive saturation has not been reached, increases in the concentration of electrolytes—including hardening constituents of water—lead to increased adsorption and thus to increased washing power of the surfactants. Such conditions may be found, for example at low dosage levels of short-chain surfactants.

Table 1. Checklist: environmental behavior of detergents in technical systems.

Sewerage	Sewage treatment	Sludge treatment	Reclamation of drinking water
corrosive action sediments	biodegradation temperature dependence metabolism foaming properties	anaerobic digestion heavy-metal transport	soil filtration flocculation, precipitation, filtration active carbon treatment chlorination, ozonization ion exchange

Table 2. Checklist: environmental behavior of detergents in natural systems.

Surface waters	Toxicological effects acute and chronic	Accumulation	Eutrophication
biodegradation, aerobic and anaerobic metabolism remobilization of heavy metals foaming properties	bacteria algae zooplankton fish aquatic and terraneous plants	sludges and sediment algae fish crustaceae birds aquatic and terraneous plants	stimulation of algae growth stimulation of aquatic plants

3.4. Replacement by Water-Soluble Organic Substances

Because of the difficulties just mentioned, the search for phosphate substitutes has been focused on water-soluble organic complexing agents during the last ten years. Both low molecular weight as well as high molecular weight organic substances have been studied[30–42].

Table 3, which lists only a small selection of the compounds already studied, compares the calcium binding capacity, acute toxicity, and biological degradability of some technologically interesting organic complexing agents with the values for STP.

Figures 6a to 6d show the results obtained with laundry detergents based on these complexing agents at various dosage levels. The primary washing performance has been determined using three different textile substrates, cotton, highly finished cotton and cotton/polyester blends.

3.4.1. Organic Complexing Agents Containing Nitrogen or Phosphorus

At first sight, the consideration of phosphonic acids and compounds containing nitrogen as potential substitutes for laundry detergent phosphates might appear paradoxical: after all, one wishes to avoid the addition of nitrogen, and especially of phosphorus, to stagnant waters. However, it is quite conceivable that nitrogen or phosphorus containing phosphate substitutes can be found which contribute less to eutrophication than STP at the dosage levels required.

Of all the organic phosphonic acids examined—Table 3 lists some examples—hydroxyethanediphosphonic acid (HEDP)

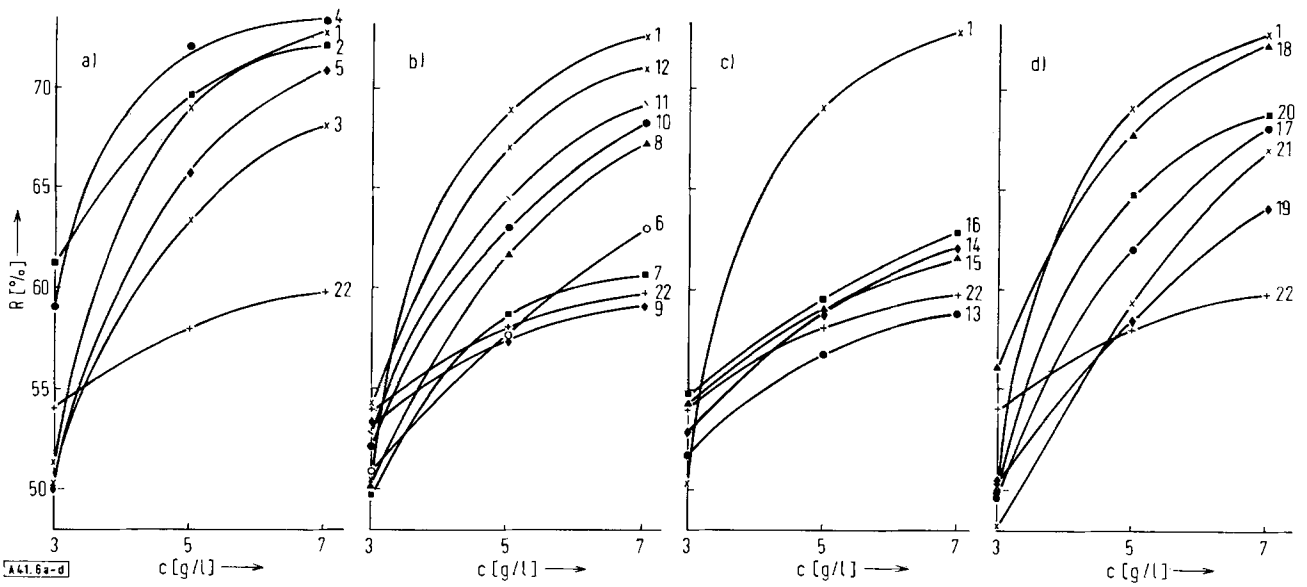


Fig. 6. Primary washing power (quoted as remission R) of water-soluble organic complexing agents in a heavy duty laundry detergent formulation on three textile substrates (cotton, highly finished cotton, cotton/polyester blend) as a function of concentration compared to STP (1) and Na_2SO_4 (22). a) Compounds 2—5; b) compounds 6—12; c) compounds 13—16; d) compounds 17—21. Numbering as in Table 3. The primary washing performance is determined as the (light) remission (R [%]) of standard test cloths which had been soiled and washed under standard conditions. The potential phosphate substitutes were tested in detergent formulations, which closely corresponded to commercially available detergents, the phosphate content (40% STP) being replaced by equal amounts of the substitutes.

Table 3. Calcium-binding capacity, acute toxicity and biodegradability of water-soluble organic complexing agents. For primary washing performance, see Fig. 6.

No. [a]	Substance	Calcium binding capacity [b] [mg CaO/g] 20 °C	90 °C	Toxicity LD_{50} [c] [g/kg]	Biological degradability BOD_{30} in % of theory [d] [%]
1	Pentasodium triphosphate (STP)	158	113	rat, oral 4.1	—[e]
2	1-Hydroxyethane-1,1-diphosphonic acid	394	378	mouse, oral 1.8	2—21
3	2-Phosphonobutane-1,2,4-tricarboxylic acid	383	277	mouse, oral >5	5—11
4	Nitrilotriacetic acid	285	202	rat, oral 1.1 –1.6	3—74
5	*N*-(2-Hydroxyethyl)iminodiacetic acid	145	91		49—78
6	1,2,3,4-Cyclopentanetetracarboxylic acid	280	235	mouse, oral 10	0—17
7	Mellithic acid	141	49		10—20
8	1,2,3,4,5,6-Cyclohexanehexacarboxylic acid	157	117	mouse, oral 6.9	0
9	Tartaric acid	43	28		64—67
10	*O*-(Carboxymethyl)tartaric acid	189	116		5—10
11	Bis(*O*-carboxymethyl)tartaric acid	138	98		24—30
12	*O*-(Carboxymethyl)tartronic acid	247	123	rat, oral 3.6	25—33
13	Gluconic acid	70	28	rat, intra-peritoneal 0.09	91—97
14	Citric acid	195	30	mouse, intra-peritoneal 1.05	85—93
15	Diglycolic acid	112	—	rat, oral 0.5	88—96
16	*O*-(Carboxymethyl)malic acid	368	54		50
17	Polyacrylic acid	307	259	rat, oral 2.5	0—6
18	Poly(α-hydroxyacrylic acid)	228	182	rat, oral 10	2—7
19	Poly[3-(hydroxymethyl)hexamethylene-1,3,5-tricarboxylic acid]	254	138		25—30
20	Poly[4-methoxytetramethylene-1,2-dicarboxylic acid]	223	250		0—20
21	Poly[tetramethylene-1,2-dicarboxylic acid]	243	235		0

[a] The numbering corresponds to the numbers in Figures 6a to 6d.
[b] The *calcium binding capacity* is given as mg CaO/g of the potential phosphate substitute at 20 and 90 °C, determined at pH 10.
[c] The acute *toxicity* is given as LD_{50} in g/kg for rats and mice.
[d] The *biological degradability* is given as biochemical oxygen demand (BOD) in percent of theory after 30 days. The biochemical oxygen demand is a quantitative measure of the rate of aerobic microbial degradation of chemical compounds. The theoretical oxygen demand corresponds to complete mineralization [43].
[e] Irrelevant.

(No. 2) gave the best results in the washing tests. At low dosage levels, HEDP is even better than STP.

Among nitrogen containing complexing agents—generally aminopolycarboxylic acids with triply substituted nitrogen—nitrilotriacetic acid (NTA) (No. 4) has turned out to be the most interesting compound. NTA shows a somewhat better primary washing performance than STP on weight for weight replacement; it counts among the best phosphate substitutes studied so far. However, the toxicological and ecological properties of nitrogen-containing complexing agents have not yet been fully elucidated. In any case, it is important that nitrogen-containing complexing agents do not contain secondary amines, for these may be converted into nitrosamines in oxidizing media or in the presence of nitrous acid, and nitrosamines are carcinogenic. Moreover, objections against NTA have been raised with respect to the possible mobilization of heavy metals from river sediments.

As it is still unclear whether the results of extensive toxicological as well as ecological studies will suffice to remove these doubts, present research and development work is focused on phosphorus and nitrogen free complexing agents.

3.4.2. Low Molecular Weight Nitrogen-free and Phosphorus-free Compounds

Some cyclic polycarboxylic acids (Table 3) show pronounced washing performance in addition to high calcium binding capacity. Hydroxypolycarboxylic acids, and the etherpolycarboxylic acids obtainable from them by carboxymethylation of the hydroxy groups, are particularly interesting. *O*-(Carboxymethyl)tartronic acid (No. 12) shows excellent properties in the washing process even at low dosage levels.

While citric acid (No. 14) is toxicologically unobjectionable, its washing properties above 30 °C are poor, since its calcium binding capacity decreases strongly with increasing temperature. Consequently, a replacement of STP by citric acid is out of the question in Europe[*].

[*] There are marked differences between European and American washing processes. Thus, American laundry detergents do not contain perborate, and the US home washer has no heating system, but is connected to a central hot water system. American washing machines are therefore not suited for washing at close to boiling temperatures.

3.4.3. Higher Molecular Weight Nitrogen-free and Phosphorus-free Polycarboxylic Acids

Numerous oligomeric as well as polymeric water-soluble organic complexing agents containing many carboxy groups are accessible by homopolymerization of unsaturated carboxylic acids or carboxylic acid precursors, or by copolymerization with other monomers. Many of these polymeric polycarboxylic acids have outstanding calcium binding capacities, and some—polycarboxylic acids without other substituents as well as polymers with additional hydroxy and/or ether functions—show marked primary washing performances and quite satisfactory secondary washing properties.

The biological degradability of polymeric carboxylic acids is generally poor; under certain conditions, however, these compounds may be eliminated at least partially by sludge adsorption in biological sewage treatment plants. This type of elimination is, for example, observed in the case of poly(α-hydroxyacrylic acid), (No. 18), which corresponds to STP in its washing performance at all dosage levels, and is even somewhat better than STP at very low dosage.

3.4.4. The Mode of Action of Water-soluble Organic Phosphate Substitutes

Mellithic acid as well as HEDP correspond to STP in increasing the zeta-potential of hematite (Fig. 7). Also, in competitive adsorption experiments with organic complexing agents and

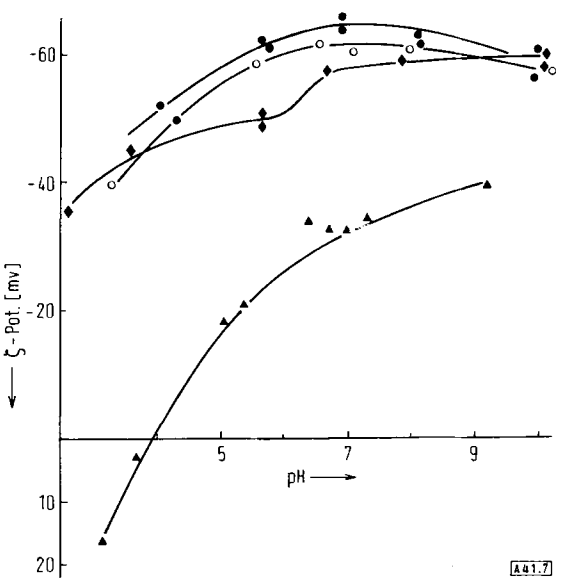


Fig. 7. pH-dependence of the zeta potential of hematite in the presence of STP (●), benzenehexacarboxylic acid (○) 1-hydroxyethane-1,1-diphosphoric acid (◆), and sodium chloride ▲.

anionic surfactants, similar results were obtained as with STP and anionic surfactants, which implies that the organic complexing agents show specific adsorption similar to the one found in the case of STP at interfaces with marked concentrations of charge.

4. Water-insoluble ("Heterogeneous") Systems

The use of water-*in*soluble phosphate substitutes deserves a separate chapter since an entirely different approach from that commonly used is involved. The laundry detergents in common use are water-soluble, so it is not surprising that the search for phosphate substitutes was first focused on water-soluble organic complexing agents. However, any additional organic compounds introduced into the ecosystem water would present a basically undesirable burden. The problem may be circumvented by the use of water-insoluble phosphate substitutes, which may be removed from the wash liquor after the washing process. The concept of removing the constituents of water hardness by means of water-insoluble inorganic ion exchangers is of biblical age[44]. The finely dispersed mineral bentonite, which is capable of ion exchange, has been used as a washing aid for probably thousands of years. In more recent years, bentonite was used in "war soaps" during both world wars because of the shortage of fats and oils. By modern standards, however, the washing performance of bentonite is unsatisfactory[45, 46].

A few years ago, the use of water-insoluble organic ion-exchangers in laundry detergents was proposed. However, neither the standard products nor a special ion-exchanging cotton cloth (phosphorylated cellulose) gave satisfactory results in the washing process[47, 48]. Common organic ion-exchangers tend to form deposits on the laundered textiles and in both cases the washing performance was quite inferior to that of STP, in a weight-to-weight comparison.

On the other hand, poromeric fleeces[49, 50], which contain carboxy groups and are manufactured by a special process show considerable washing power in a weight-by-weight comparison with STP[51, 52]. Such a "washcloth" may be separated from the laundry after the washing process and discarded together with other household refuse. Only CO_2, H_2O and $CaCO_3$ would be formed on incineration of the refuse.

However, not until all refuse is subjected to incineration, will the washcloth approach prove ideal with respect to its environmental impact. Moreover, the washcloth is not perfectly satisfactory because of its expensive petroleum basis (polyacrylate)..

Despite the fact that washing with insoluble inorganic ion-exchangers has so far not gained acceptance, except in times of need, we have reinvestigated this field in recent years.

Alkali-metal aluminum silicates of the following composition were found to be particularly promising[53]:

$$M_{2/n}O : Al_2O_3 : x\,SiO_2 : y\,H_2O$$

$M = Li, Na, K$

$n = 1$

$x \approx 2$

y = variable

In contrast to the behavior of water-soluble complexing agents, the calcium binding capacity of these silicates increases with increasing temperature (Fig. 8), quite a desirable novel feature for washing at higher temperatures. In addition, the calcium binding capacity depends on the duration of the exposure, the pH value of the wash liquor, the particle size of the silicates, and the concentration.

Table 4 compares the washing performances of detergent formulations with normal and low phosphate contents, where part of the normal phosphate content is replaced by a sodium aluminum silicate. Tests were carried out on three different

textile substrates at various temperatures. It can be seen that the laundry detergent containing sodium aluminum silicate is comparable to the laundry detergents commonly used today. A similar finding is observed on comparison of secondary washing properties.

Before any particular phosphate substitute is chosen, not only have hygienic, toxicological and ecological factors to be considered, but also the impact on industrial as well as national economics. In the latter respect, sodium aluminum silicates offer a particularly promising alternative, inasmuch as they

Table 4. Primary washing power of detergents, based on 40% STP, 20% STP+20% sodium aluminum silicate (HAB) and 20% STP, on artificially soiled textiles.

Washing temperature	Fabric	Dosage (g/l)	Primary washing effect in % remission at 460 nm		
			40% STP	20% STP 20% HAB	20% STP
95°C	Unfinished cotton	6.6	81	79	63
		10	83	81	69
60°C	Resin finished cotton	6.6	64	62	56
		10	66	65	59
60°C	Polyester/cotton blend	6.6	63	62	59
		10	65	64	61

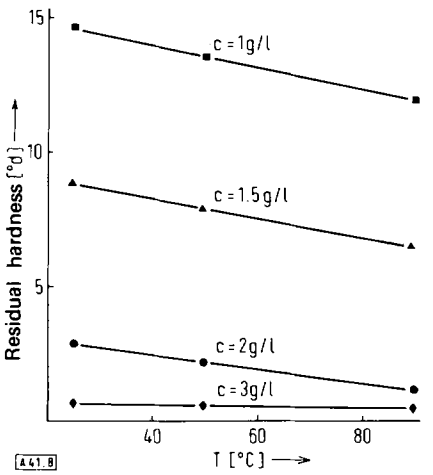


Fig. 8. Temperature-dependence of calcium binding capacity—change of residual hardness (given as °d = °German hardness) of sodium aluminum silicates.

can be manufactured from domestic raw materials. The extensive study program instituted to test their environmental behavior is outlined in Table 5. In many respects, this program differs from the testing programs used in the evaluation of water-soluble organic phosphate substitutes. While in the case of organic materials the question of biological degradability and the resulting intermediates formed in the process is of prime importance, this question is irrelevant in the case of inorganic substances such as sodium aluminum silicates. Sodium aluminum silicates occur in large quantities in the lithosphere; they are natural constituents of lake and river sediments, and therefore it is hoped that there is very little ecological risk involved. Nevertheless, these risks must be assessed most carefully.

Some preliminary results support our expectations: thus, laundry detergents containing sodium aluminum silicates are comparable to detergents containing phosphates with respect to their toxicological properties. The acute toxicity of sodium

Table 5. Environmental behavior of sodium aluminum silicate—an assessment of individual measures.

Criteria	Laboratory testing	Pilot plant testing	Field testing
1. binding and remobilization of heavy metals Cu, Cd, Zn, Hg, Ni, Co, Mn, Pb, Fe, Cr	laboratory model under variation of • time • pH • water hardness • temperature • soluble complexing agents		in sewage and river water
2. sedimentation	laboratory model • in sewage • in river water • with and without current	in sewerage models in sewage treatment models	in house and urban sewerage systems in sewage treatment plants
3. toxicology	animal experiments irritancy potential to skin and mucous membranes acute and chronic toxicity silicosis potential		clinical studies
4. other effects on biological systems	toxicity to water organisms • fish • plankton • sludge organisms eutrophication potential impact on sludge digestion	in sewage treatment models in sludge digestion models ecological effects in open air basins	in various types of sewage treatment plants ecological effects on surface waters

aluminum silicates is given as $LD_{50} > 10\,g/kg$ (mouse, oral intake). The toxicity to water organisms (Daphnia: $LC_0 > 100\,mg/l$[*]) and fish (golden orfe: $LC_0 > 250\,mg/l$) is also very low. According to model experiments, the presence of sodium aluminum silicates does not interfere with the biological degradation of linear alkylbenzenesulfonate. Their influence on the various types of mechanical and biological sewage treatments remains to be assessed in extensive experimental studies. Sodium aluminum silicates have a high binding capacity for transition metal ions (copper, cadmium, zinc, nickel, cobalt, manganese). This feature is presently believed to be an advantage; however, the consequences for the various sewage treatment processes must be studied. The same applies to questions of sedimentation. Here, preliminary studies have shown that sodium aluminum silicates tend to form aggregates with other sewage constituents and are largely eliminated in the pre-sedimentation of sewage treatment; thus they do not reach the surface waters.

We are indebted to BASF, Bayer, Hoechst, Chemische Werke Hüls, Gelsenberg, VEBA Chemie, GAF, Monsanto, and Solvay for sample chemicals as well as useful suggestions. The studies concerning the development of suitable sodium aluminum silicates were carried out jointly with Degussa.

Received: October 16, 1974 [A 41 IE]
German version: Angew. Chem. *87*, 115 (1975)
Translated by *Dagmar Schenck*, Düsseldorf

[*] LC_0: maximum concentration at which all organisms survived the duration of the test.

[1] Written report by Federal Minister *Genscher* in reply to the questions asked in writing by Mr. *Biechele*, Member of the Bundestag (Printed Matter VI/3016); Minutes of the German Bundestag, 6th term, 164th Session, Jan 21, 1972.

[2] *F. J. Springer*, Vom Wasser *34*, 146 (1967) and *35*, 137 (1968).

[3] *H. Bernhardt, W. Such*, and *A. Wilhelms*, Münchener Beitr. zur Abwasser-Fischerei- und Flussbiol. *16*, 60 (1969).

[4] Chicago Daily News, January 16, 1973.

[5] *W. Bucksteeg*, Vortragsveröffentlichung Nr. 83, Haus der Technik, Essen 1966.

[6] Umweltschutz, Nr. 18, Abwasseranfall, -Behandlung und -Beseitigung in Gemeinden und Industriebetrieben in der Bundesrepublik Deutschland, Federal Ministry of the Interior of the Federal Republic of Germany, Bonn, Nov. 1972.

[7] *H. Bernhardt*, Vom Wasser *39*, 53 (1972).

[8] *W. Bucksteeg*, Abwassertechnik *17*, 3, I—II (1966); *17*, 4, III—IV (1966).

[9] *L. Huber*, Münchner Beitr. zur Abwasser-, Fischerei- und Flussbiol. *12*, 149 (1965).

[10] *K. Wuhrmann*, Schweizerische Zeitschrift für Hydrologie *26*, 520 (1964).

[11] *W. Triebel*: Lehr- und Handbuch der Abwassertechnik. 2nd edition, Verlag Wilhelm Ernst & Sohn, Berlin 1973, Vol. 1, p. 21.

[12] *W. Nümann*, Arch. für Hydrobiol. *26*, 377 (1964).

[13] *R. A. Vollenweider*: The scientific fundamentals of the eutrophication of lakes and flowing waters with particular reference to nitrogen and phosphorus as factors in eutrophication, OECD-report DAS/CSJ/68.27 (1968).

[14] Dr. *Koppe*, Ruhrverband Essen, personal communication.

[15] *R. Nilsson*, Städtehygiene *24*, 210 (1973).

[16] *E. J. W. Verwey* and *J. T. G. Overbeck*: Theory of the Stability of Lyophobic Colloids. Elsevier, Amsterdam 1948.

[17] *D. Balzer* and *H. Lange*, unpublished.

[18] *J. C. Harris*, Text. Res. J. *28*, 912 (1958).

[18a] *H. Lange*, Chimie, Physique et Applications Pratiques des Agents de Surface. Reports of the V International Congress for Surface-Active Substances 1968. Ediciones Unidas, Barcelona 1969, Vol. II, p. 41.

[19] *W. Kling*, Münchner Beitr. zur Abwasser-, Fischerei und Flussbiol. *12*, 38 (1965).

[20] *O. Oldenroth*, Fette, Seifen, Anstrichm. *68*, 203 (1966).

[21] *H. Krüssmann* and *A. Barbu*, Reiniger Wäscher *27*, 10, 34 (1974).

[22] *H. Dreyer*, Fette, Seifen, Anstrichm. *66*, 97 (1964).

[23] *O. Oldenroth*, Fette, Seifen, Anstrichm. *61*, 1142 (1959).

[24] Henkel & Cie GmbH, Düsseldorf—unpublished work.

[25] *H. Reploh* and *H. Bösenberg*, Wäschereitechnik u. -chemie *22*, 223 (1969).

[26] *D. Botzenhart* and *E. Thofern*, Krankenhaus *61*, 24 (1969).

[27] *E. Thofern* and *D. Botzenhart*, Reiniger Wäscher *24*, 8, 19 (1971).

[28] *G. Müller*, Bundesgesundheitsblatt *14*, 1 (1971).

[29] *G. K. Ashforth* and *G. Calvin*, Water Res. *7*, 309 (1973).

[30] *Th. A. Downey*, Soap Chem. Spec. *42*, Nr. 2 (1966).

[31] *R. W. Cummins*, Detergent Age *5*, Nr. 3 (1968).

[32] *R. P. Langguth*, Deterg. Spec. *7*, 11, 28 (1970).

[33] *C. A. Wilham, T. A. McGuire, A. M. Mark*, and *C. L. Mehltretter*, J. Amer. Oil Chem. Soc. *47*, 522 (1970).

[34] Chem. Week *108*, 3. March 1971, 15 (1971).

[35] *P. Berth, G. Jakobi*, and *E. Schmadel*, Chem.-Ztg. *95*, 548 (1971).

[36] *P. Berth* and *W. K. Fischer*, Tenside *8*, 1 (1971).

[37] Chem. Week *111*, 19. July 1972, 45 (1972).

[38] *G. P. Lauhus*, Seifen, Öle, Fette, Wachse *98*, 26, 869 (1972).

[39] *H. Haschke, G. Morlock*, and *P. Kuzel*, Chem.-Ztg. *96*, 199 (1972).

[40] *E. A. Matzner, M. M. Crutchfield, R. P. Langguth*, and *R. D. Swisher*, Tenside Deterg. *10*, 119, 239 (1973).

[41] *G. Zeit*, Chem.-Ztg. *96*, 685 (1972).

[42] *K. Merkenich, K. Henning*, and *H. Gudernatsch*, Seifen, Öle, Fette, Wachse *100*, 18, 433 (1974).

[43] *W. K. Fischer, P. Gerike*, and *R. Schmid*, Wasser- u. Abwasserforsch. *7*, 99 (1974).

[44] The Book of Exodus, Ch. XV, v. 23ff.

[45] US Pat. 2411090 (1946), Pennsylvania Salt Manufacturing Comp.

[46] *V. Rimoldi* and *L. Vitiello*, Ital. Pat. 393604 (1942).

[47] DOS 2055423 (1972), Chem. Fabrik Budenheim.

[48] DOS 1617058 (1971), Colgate-Palmolive.

[49] *C. H. Krauch* and *A. Sanner*, Naturwissenschaften *55*, 539 (1968).

[50] DOS 1770543 (1968), BASF.

[51] DOS 2307923 (1973), BASF.

[52] *P. Krings, M. J. Schwuger*, and *C. H. Krauch*, Naturwissenschaften *61*, 75 (1974).

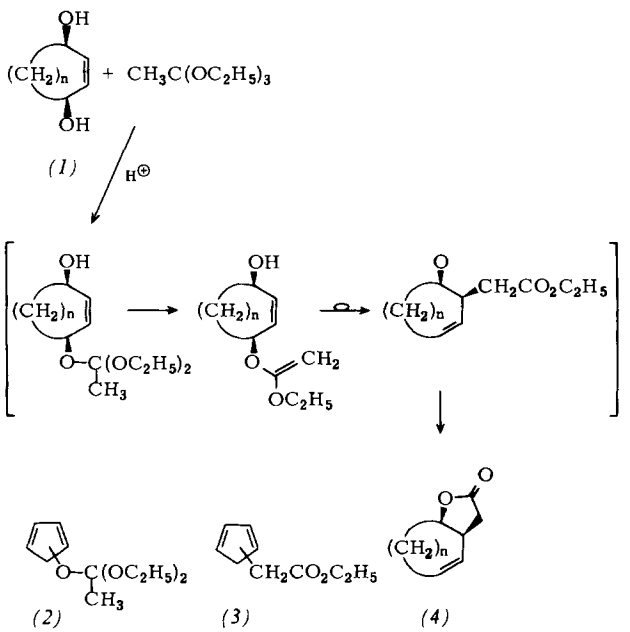
[53] DOS 2412837 (1974), Henkel & Cie GmbH.

Synthesis of Bicyclic γ-Lactones from 2-Cycloalkene-1,4-diols

By *Kiyosi Kondo*, *Masakatsu Matsumoto*, and *Fumio Mori*[*]

We have recently reported that the condensation of *trans*-2-alkene-1,4-diols with orthocarboxylic esters leads directly to γ-lactones bearing vinylic substituents in the β-position[1]. The reaction has now been extended to cyclic alkenediols *(1)* and found to be a simple and convenient method for the preparation of bicyclic γ-lactones. One of the products is the well-known precursor *(4a)* for the synthesis of prostaglandins and jasmones[2]. The starting 2-cycloalkene-1,4-diols *(1)* can easily be obtained by photosensitized oxygenation of cyclic 1,3-dienes followed by reduction of the resulting 1,4-endoperoxides with thiourea or $LiAlH_4$.

Thermal condensation of the diols *(1a)*—*(1d)* with triethyl orthoacetate in the presence of a catalytic amount of a weak acid, such as hydroquinone or phenol, and distillation of the reaction mixture leads directly to the lactones *(4a)*—*(4d)* (see Table 1). Though the distilled *(4a)* was essentially pure judging from its NMR spectrum, careful analysis by GC-MASS revealed that the cyclopentadienes *(2)* and *(3)* were present as contaminants.



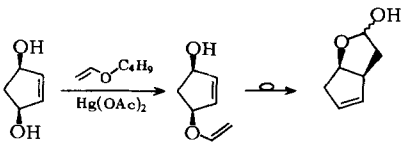
(a), n = 1; *(b)*, n = 2; *(c)*, n = 3; *(d)*, n = 4

Table 1. Bicyclic γ-lactones *(4)* from diols *(1)*. Hydroquinone was used as a catalyst.

	Reaction conditions		Yield	IR (film)	B.p.
	t [h]	*T* [°C]	[%]	[cm^{-1}]	[°C/torr]
(4a)	6	140—150	85	1780	74/0.3
(4b)	6	140—150	85	1775	78/0.16
(4c)	8	140—150	83	1775	95/0.28
(4d)	18	150—160	43	1780	103/0.22

[*] Dr. K. Kondo and Dr. M. Matsumoto
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa, 229 (Japan)
Dr. F. Mori
Central Research Laboratory, Kuraray Co. Ltd., Sakazu, Kurashiki, Okayama, 710 (Japan)

The analogous Claisen rearrangement followed by cyclization can also be performed with the vinyl ether *(5)*[3]. Heating of *(5)* in xylene under an argon atmosphere for 4 h afforded the bicyclic γ-lactol 2-oxabicyclo[3.3.0]oct-6-en-3-ol *(6)* directly in 63% yield; b.p. 49 °C/0.15 torr (44—45 °C/0.01 torr[2c]).



(1a) *(5)* *(6)*

2-Oxabicyclo[3.3.0]oct-6-en-3-one (4a)

A mixture of *cis*-2-cyclopentene-1,4-diol *(1a)* (3.0 g, 30 mmol) and triethyl orthoacetate (11.3 g, 70 mmol) was heated with hydroquinone (0.33 g, 3 mmol) at 140—150 °C for 6 h with continuous removal of the resulting ethanol. The reaction mixture was fractionally distilled under reduced pressure. The first fraction was unreacted orthoester, and the second one was the desired bicyclic γ-lactone *(4a)*; yield 3.08 g (85%); b.p. 74 °C/0.3 torr (70—71 °C/0.2 torr[2c]).

Received: September 23, 1974 [Z 122 IE]
German version: Angew. Chem. *87*, 109 (1975)

CAS Registry numbers:
(1a), 29783-26-4; *(1b)*, 53762-85-9; *(1c)*, 53762-86-0; *(1d)*, 37996-40-0; *(4a)*, 26054-46-6; *(4b)*, 34896-02-1; *(4c)*, 53762-87-1; *(4d)*, 53783-45-2; *(6)*, 53762-88-2; *(7)*, 34636-26-1; triethyl orthoacetate, 78-39-7.

[1] *K. Kondo* and *F. Mori*, Chem. Lett. *1974*, 741.

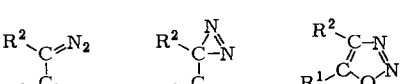
[2] a) *E. J. Corey* and *R. Noyori*, Tetrahedron Lett. *1970*, 311; b) *E. J. Corey* and *T. Ravindranathan*, *ibid. 1971*, 4753; c) *P. A. Grieco*, J. Org. Chem. *37*, 2363 (1972); d) *E. J. Corey* and *J. Mann*, J. Amer. Chem. Soc. *95*, 6832 (1973); e) *J. J. Partridge*, *N. K. Chadha*, and *M. R. Uskokovic*, *ibid. 95*, 7171 (1973); f) *E. J. Corey* and *B. B. Snider*, Tetrahedron Lett. *1973*, 3091.

[3] Refluxing of the diol *(1a)* in *n*-butyl vinyl ether in the presence of a catalytic amount of mercury(II) acetate for 2 h afforded a mixture of the monovinyl ether *(5)* (91%) and divinyl ether (9%), total yield 80%. The ether *(5)* could easily be separated by column chromatography on neutral alumina (Woelm, activity grade IV).

Diazirines as Photochromic Valence Isomers of α-Diazo Carbonyl Compounds[**]

By *Erika Voigt* and *Herbert Meier*[*]

As cyclic valence isomers, the diazirines *(2)* and the 1,2,3-oxadiazoles *(3)* should be discussed in the context of the α-diazo carbonyl compounds *(1)*.



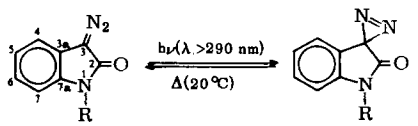
(1) *(2)* *(3)*

[*] Univ.-Doz. Dr. H. Meier and E. Voigt
Chemisches Institut der Universität
74 Tübingen, Auf der Morgenstelle (Germany)

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

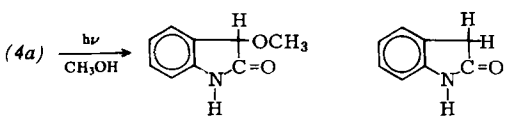
Whereas heterocycles of type *(3)* are so far unknown, numerous alkyl- or aryl-substituted diazirines are known to exist[1]. In contrast to the α-diazo carbonyl compounds, which are generally thermodynamically more stable than aliphatic diazo compounds, the stability of the diazirines is lowered by pseudoconjugation of the three-membered ring with a carbonyl function. Thus the half-life of 1-oxospiro[cyclohexane-2,3'-diazirine] with regard to elimination of nitrogen is found to be about one hour at room temperature[1-3].

The ready thermal or photochemical elimination of nitrogen from *(1)* and *(2)* imposes experimental limitations on the valence isomerization *(1)*⇌*(2)*. We have detected it for the first time in the case of the thermally reversible photochromic system 2-oxo-3-diazoindoline *(4)*/2-oxospiro[indoline-3,3'-diazirine] *(5)*.



(4) *(a)*, R = H; *(b)*, R = CH_3 *(5)*

Irradiation of *(4a)*[4-6] in methanol leads, by nitrogen elimination, *via* the carbene intermediate to the major products 3-methoxyoxindole *(6a)* and oxindole *(7a)*.



(6a) (30 : 25) *(7a)*

If the reaction is prematurely interrupted, a product can be isolated by column chromatography which is itself photolabile. On standing as the pure solid or in solution, the pale yellow to colorless crystals are transformed back to the red starting compound *(4a)*, even at room temperature.

According to cryoscopic molecular weight determination, the crystalline compound must be an isomer of *(4a)*. Spectroscopic data unequivocally indicate the structure *(5a)*. Compound *(4b)* behaves analogously. The UV spectra of *(4a)* and *(5a)* differ primarily in the absence of the longest-wave transition [λ_{max} = 440 nm (ε = 21.3)], responsible for the red color of the diazo compound *(4a)*, from the spectrum of *(5a)*. On complete retro-isomerization *(5a)* → *(4a)*, three isosbestic points can be observed. The characteristic IR bands of *(4a)* and *(5a)* are listed in Table 1.

Table 1. Characteristic stretching vibrations of *(4a)* and *(5a)* $\bar{\nu}$ [cm^{-1}].

	>N—H	—N≡N	—N=N—	>C=O
in KBr				
(4a)	3100	2085	—	1670
(5a)	3180	—	1630	1740/1690
in CH_2Cl_2				
(4a)	3430/3180	2110	—	1685
(5a)	3380/3145	—	1620	1720

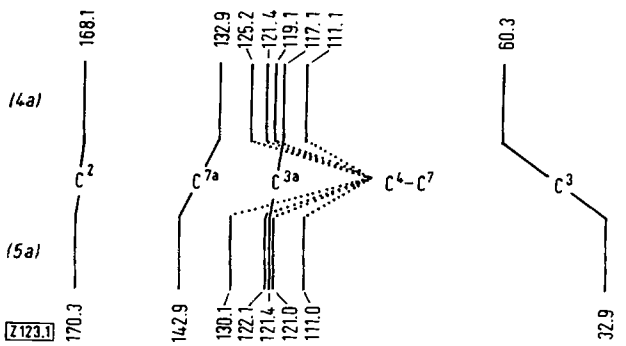


Fig. 1. ^{13}C-NMR signals of 2-oxa-3-diazoindoline *(4a)* and 2-oxospiro[indoline-3,3'-diazirine] *(5a)*. Data in ppm relative to TMS as internal standard.

Received: October 7, 1974 [Z 123 IE]
German version: Angew. Chem. 87, 109 (1975)

CAS Registry numbers:
(4a), 3265-29-0; *(5a)*, 53762-89-3.

[1] *E. Schmitz:* Dreiringe mit zwei Heteroatomen. Springer, Berlin 1967, pp. 114ff.
[2] *E. Schmitz, A. Stark,* and *Ch. Horig,* Chem. Ber. *98,* 2509 (1965).
[3] *E. Schmitz,* XIII. IUPAC-Congress, Boston 1971, Vol. 2, pp. 283ff.
[4] *E. J. Moriconi* and *J. J. Murray,* J. Org. Chem. *29,* 3577 (1964).
[5] *G. Lowe* and *J. Parker,* Chem. Commun. *1971,* 1135.
[6] *R. A. Franich, G. Lowe,* and *J. Parker,* J. C. S. Perkin I *1972,* 2034.

The Dimerization of Propylene to Linear Hexenes

By *G. Henrici-Olivé* and *S. Olivé*[*]

A homogeneous catalyst solution made up from pentanedionatopalladium, a tertiary phosphane, and ethylaluminum dichloride, in 1,2-dichloroethane, dimerizes propylene selectively (up to 95%) to linear hexenes, although at relatively low reaction rate (Table 1). Replacement of the phosphane by a phosphite increases the rate, but considerably lowers the selectivity. As in all systems containing a Lewis acid such as $C_2H_5AlCl_2$, special care must be taken to eliminate moisture from the reaction solution. Otherwise highly active cationic species will cause the polymerization of propylene.

Table 1. Dimerization of propylene with Pd/Al catalysts in the presence of phosphorus-containing additives. [$Pd(acac)_2$] = 2 × 10^{-3} mol/l; [$C_2H_5AlCl_2$] = 22 × 10^{-3} mol/l; [P]/[Pd] = 2; [propylene] = 1.3 mol/l; T = 20 °C; t = 3 h

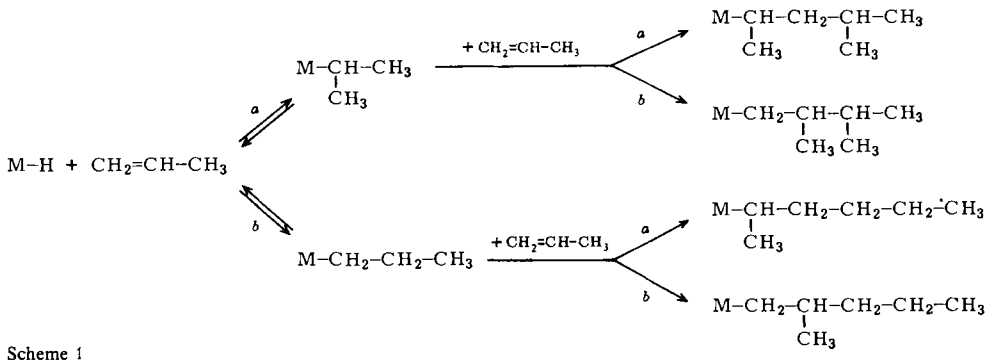
Phosphorus compound	Conversion [%]	Selectivity [%] linear hexenes	methyl-pentenes	dimethyl-butenes
Bu_3P	4	95.1	4.9	-
Ph_3P	4	81.8	18.2	—
$(PhO)_3P$	12	23.6	68.2	8.2

Four reaction modes are conceivable for the dimerization of propylene at a transition metal center M, depending upon the orientation of the monomer in the two insertion steps (Scheme 1).

The first step is reversible, since β-hydrogen abstraction regenerates a metal hydride and propylene. The second step is irreversible; β-hydrogen abstraction at this stage gives the product dimer and a metal hydride, which latter continues the kinetic chain.

[*] Dr. G. Henrici-Olivé and Prof. Dr. S. Olivé
Monsanto Research S.A.
CH-8050 Zürich, Eggbühlstrasse 36 (Switzerland)

The dimerization of propylene with Group VIII metal complexes (in particular those of nickel) in combination with alkylaluminum compounds has repeatedly been reported[1-3]. It appears from these literature data that, in the absence of steric effects, the route *aa* giving 4-methyl-2-pentene is



Scheme 1

by far the predominant one, indicating that the *a* mode of monomer incorporation is electronically favored. *Wilke, Bogdanović, et al.*[2], however, have shown that, in the case of the catalyst system π-allylnickel halide/alkylaluminum compound the addition of bulky phosphane ligands can force the reaction to adopt the route *ab* by steric influences.

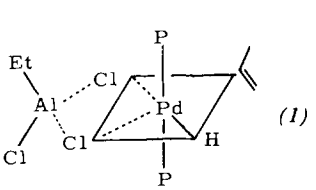
The presently reported formation of linear hexenes, on the other hand, requires the unusual reaction sequence *ba*. Evidently this must be also the consequence of a steric phenomenon, because an electronic tailoring of the catalyst center would influence both steps in the same manner. It is assumed that also in this system the first step occurs predominantly according to the electronically favored *a* mode, but that the combined bulk of the resulting isopropyl group plus the surrounding ligands impedes the second step. Because of the reversibility of the first step the less favorable (slower) *b* mode can then gain importance. The incorporation of the first monomer gives the less bulky *n*-propyl group which permits the second step to proceed according to electronic preferences, *i.e.* by route *a*.

Comparison of the data obtained with tributyl- and triphenylphosphane (Table 1) underlines the steric character of the influence of the phosphane. Differing considerably in the electron donor ability, the two phosphanes have comparable bulkiness. Reaction rate and isomer distribution are similar. The low reaction rate appears to indicate that the catalyst spends most of its time in the inactive form attached to the isopropyl group. The less bulky phosphite ligand, on the other hand, is not able to build up an efficient barrier.

The ratio P/Pd is critical; best results are obtained at P/Pd = 2; at lower ratios black colloidal Pd^0 is formed even at low concentration of alkylaluminum compound. At P/Pd $\geq$ 5 no catalytic activity is observed, presumably due to the blocking of free sites.

Relatively high ratios of Al/Pd are required, indicating that the catalytic species is formed in an equilibrium reaction. Activity is found for $5 \leq$ Al/Pd ≤ 25, with an optimum around 20. In this region an absorption peak at 25600 cm^{-1} is observed, indicating the presence of an alkylaluminum compound in the complex.

Based on these data, and in analogy to other Ziegler type catalyst systems[4, 5], we suggest structure *(1)* for the active site (P = phosphane).



(1)

Evidently the pentanedionate ligands of the palladium have to be displaced by chlorine (from the alkylaluminum chloride, as found formerly for $VO(acac)_2$ and $Cr(acac)_3$[5]). Subsequent exchange of one chlorine with an ethyl group forms an alkyl derivative of Pd which, on β-hydrogen abstraction, produces the hydride. The other chlorine is used for the aluminum bridge. The phosphanes keep the complex in solution[6].

Received: October 17, 1974 [Z 124 IE]
German version: Angew. Chem. 87, 110 (1975)

CAS Registry numbers:
Propylene, 115-07-1; hexene, 25264-93-1; methylpentene, 27236-46-0; dimethylbutene, 563-79-1; pentadionatopalladium, 14024-61-4; ethylaluminum dichloride, 563-43-9; Bu_3P, 998-40-3; Ph_3P, 603-35-0; $(PhO)_3P$, 101-02-0.

[1] *G. Wilke, B. Bogdanović, P. Hardt, P. Heimbach, W. Keim, M. Kröner, W. Oberkirch, K. Tanaka, E. Steinrücke, D. Walter*, and *H. Zimmermann*, Angew. Chem. *78*, 157 (1966); Angew. Chem. internat. Edit. *5*, 151 (1966); *J. Ewers*, Angew. Chem. *78*, 593 (1966); Angew. Chem. internat. Edit. *5*, 584 (1966); *B. Bogdanović* and *G. Wilke*, Proceedings of the 7th World Petroleum Congress 1967, p. 351.

[2] *B. Bogdanović, B. Henc, H.-G. Karmann, H.-G. Nüssel, D. Walter*, and *G. Wilke*, Ind. Eng. Chem. *62*, 34 (1970).

[3] Jap. Pat. 7224523 (1972); US Pat. 3651111 (1972).

[4] *G. Henrici-Olivé* and *S. Olivé*, Angew. Chem. *79*, 764 (1967); Angew. Chem. internat. Edit. *6*, 790 (1967).

[5] *G. Henrici-Olivé* and *S. Olivé*, Angew. Chem. *82*, 955 (1970); *83*, 782 (1971); Angew. Chem. internat. Edit. *9*, 957 (1970); *10*, 776 (1971).

[6] We thank Prof. *J. Halpern*, University of Chicago, for helpful discussions concerning the reaction mechanism.

Chemiluminescence of the Exhaust Gases of an Internal Combustion Engine

By *Joachim Stauff* and *Hartmut Fuhr*[*]

Only few publications[1, 2] have so far considered the possibility that atmospheric pollutants are emitted in electronically excited states. On the other hand, studies on "photochemistry without light"[3] describe effects occurring during the action of molecules that have been electronically excited by chemical reactions on other ground state molecules which normally only take place on irradiation of the reaction mixture with

[*] Prof. Dr. J. Stauff and Dr. H. Fuhr
Institut für physikalische Biochemie und Kolloidchemie
6 Frankfurt/M.-Niederrad 1, Sandhofstrasse 3 (Germany)

visible or ultraviolet light. We have now found that the exhaust of an internal combustion engine (Otto motor) contains electronically excited molecules.

We employed an auxiliary electrical generator driven by a Briggs and Stratton four-stroke engine of 164 cm^3 capacity fueled by gasoline having research octane number 90–92. The generator produced current up to 1500 watt. Varying loads could be produced by switching resistors of different sizes into the generator circuit. The exhaust passed first through the muffler fitted to the device and then through an observation system consisting of replaceable ground Pyrex tubes of 5-cm diameter. The chemiluminescence was recorded at right angles to the direction of flow of the gas by red-sensitive photomultiplier (RCA 7265) fitted to a direct current amplifier.

Only slight luminescence was observed directly after starting the engine. Its intensity increased with time as a function of the load. After switching the engine off, an afterglow persisted for 40 min. Flushing the Pyrex tube with N_2 or O_2 had no effect on the intensity and rate of decay. The intensity rises 10- to 20-fold if the exhaust is allowed to impinge on a glass plate positioned at 45° to the directions of flow and observation. The decay curve of the luminescence obeys first order kinetics with a rate constant of about $10^{-3} s^{-1}$ and a lifetime of 10^3 s (16 min). The luminescence intensity initially increases exponentially with the engine load, and then at a somewhat slower rate.

Most probably, the high-energy combustion product is present in the soot particles or tar droplets that precipitate on the walls of the tube or on the glass plate. No luminescence is observed if the exhaust aerosol is passed through a tube having six 90° bends.

A crude determination of the spectral distribution of the luminescence was accomplished with a set of cut-off filters. The emission maximum lies between 420 and 470 nm, thus indicating a remarkably high energy level of the luminescence reaction.

Extraction of the soot or tar deposits on the glass plate with *n*-heptane or benzene yields solutions displaying fluorescence maxima in the same region as those in the luminescence spectrum.

If the exhaust gas is passed through a solution of 9,10-diphenylanthracene in dibutyl phthalate the luminescence is intensified by a factor of 20 to 30. The same effect was observed with chlorophyll a in dibutyl phthalate and with rubrene in benzene.

These observations show that photodynamic effects warrant more attention, especially in view of the known fact that the carcinogenic action of electronically excited molecules is considerably greater than that of the corresponding ground states[4].

Received: October 24, 1974 [Z 128 IE]
German version: Angew. Chem. 87, 132 (1975)

[1] *J. Stauff, G. Reske,* and *I. Simo,* Z. Naturforsch. *28c,* 469 (1973).

[2] *H. H. Seliger, W. H. Biggley,* and *J. P. Hamman,* Science *185,* 253 (1974).

[3] *E. H. White, J. Wielko,* and *D. F. Roswell,* J. Amer. Chem. Soc. *91,* 5194 (1969).

[4] *L. Santamaria, G. G. Giordano, M. Alfisi,* and *F. Cascione,* Nature *210,* 824 (1966).

Reductive Dehydrohalogenation of β-Halogenated Fatty Acids and Stereoselective Hydrogenation of α-Halogenated α,β-Unsaturated Fatty Acids by *Clostridium kluyveri*[**]

By *Hironobu Hashimoto* and *Helmut Simon*[*]

We recently reported the hydrogenation of structurally very different α,β-unsaturated fatty acids by hydrogen[1] or cofermentation[2] with the aid of *Clostridium kluyveri.* We have now found that α,β-unsaturated β-halocarboxylic acids *(1)* are converted by *C. kluyveri* in presence of crotonate or butyrate, or hydrogen gas, into the halogen-free saturated carboxylic acids (Table 1).

R = H or CH_3; X = F, Cl or Br

Table 1. Reductive dehydrohalogenation of β-halocarboxylic acids of type *(1)* and *(2)* by *Clostridium kluyveri* in presence of hydrogen as reducing agent.

Exp.	Halocarboxylic Acid *(1)* or *(2)*	Product	Yield [%]
1	*E*-β-Chloroacrylic acid *(1a)*	Propionic acid	70
2	*Z*-β-Chloroacrylic acid *(1b)*	Propionic acid	30
3	*E*-β-Bromoacrylic acid *(1c)*	Propionic acid	100
4	*Z*-β-Chlorocrotonic acid *(1d)*	[a]	
5	*Z*-β-Fluorocrotonic acid *(1e)*	[a]	
6	β-Chloropropionic acid *(2a)*	Propionic acid	90
7	D,L-β-Chlorobutyric acid *(2b)*	[a]	
8	*E*-β-Chloroacrylic acid *(1a)* [b]	no reaction	
9	β-Chloropropionic acid *(2a)* [b]	β-Hydroxypropionic acid	100

[a] Quantitative conversion to butyric and acetic acid. Corresponds to the fermentation with crotonic acid.
[b] Without reducing agent.

Saturated β-halocarboxylic acids lead to the same products (Experiments 6 and 7). If incubation is carried out in the absence of reducing agent, the unsaturated acids *(1a)* do not react (Experiment 8), whilst the saturated acids *(2a)* eliminate HX and add water (Experiment 9). Clearly, the crotonases in *C. kluyveri* also facilitate elimination of haloacid instead of water. Particularly surprising is the fact that both enantiomeric forms of β-chlorobutyric acid are converted.

[*] Prof. Dr. H. Simon and Dr. H. Hashimoto
Lehrstuhl für Organische Chemie
und Biochemie der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[**] This work was supported by the Bundesministerium für Forschung und Technologie. We thank Dr. *H. Günther* and Frl. *S. Klüpfel* for cultivation of the microorganisms.

To our knowledge such activities have not previously been described.

$RHC{=}CX{-}COOH$ (3) $\qquad RCH_2{-}CHX{-}COOH$ (4)

R = H or CH_3; X = F, Cl, or Br

The behavior of unsaturated α-halocarboxylic acids is depicted in Table 2. With the exception of α-fluorobutyric acid the absolute configurations of the compounds obtained are known.

Table 2. Hydrogenation of α,β-unsaturated α-halocarboxylic acids *(3)* by *Clostridium kluyveri* in presence of hydrogen to α-halocarboxylic acids *(4)*.

Halocarboxylic acid *(3)*	Amount [mmol]	Product *(4)*	Yield [%]	$[\alpha]_{23}^{D}$ [°] in methanol	*c* [g/100 ml]	$[\alpha]_{23}^{D}$ [°] in methanol [3]
α-Chloroacrylic acid *(3a)*	2.0	(*R*)-α-Chloropropionic acid *(4a)*	91	17.3 ± 1.4	0.51	−13.9
α-Bromoacrylic acid *(3b)*	1.5	(*R*)-α-Bromopropionic acid *(4b)*	86	32.4 ± 3.6	0.49	−27.6
Z-α-Fluorocrotonic acid *(3c)*	2.6	α-Fluorobutyric acid *(4c)*	98	1.2 ± 0.1	2.0	—
Z-α-Chlorocrotonic acid *(3d)*	0.5	(*R*)-α-Chlorobutyric acid *(4d)*	83	12.7 ± 1.4	0.42	− 9.7
Z-α-Bromocrotonic acid *(3e)*	1.0	(*R*)-α-Bromobutyric acid *(4e)*	79	21.6 ± 0.9	1.1	−31.7

The hydrogenation system of *C. kluyveri* affords the *R* configuration. Most of the compounds exhibit a higher rotation than is given in the literature[3]. An exception is α-bromobutyric acid.

As a rule for each mmol of sodium salt of the carboxylic acids, 2.0 g of wet *C. kluyveri* sediment grown on crotonate was incubated in 10 ml 0.1 M phosphate buffer at pH = 7.0 for 10—25 h at 35 °C under hydrogen.

Received: November 11, 1974 [Z 126 IE]
German version: Angew. Chem. *87*, 111 (1975)

CAS Registry numbers:
(1a), 2345-61-1; *(1b)*, 1609-93-4; *(1c)*, 6213-89-4; *(1d)*, 6213-90-7; *(1e)*, 3791-42-2; *(2a)*, 107-94-8; *(2b)*, 625-68-3; *(3a)*, 598-79-8; *(3b)*, 10443-65-9; *(3c)*, 383-85-7; *(3d)*, 53993-41-2; *(3e)*, 5405-34-5; *(4a)*, 7474-05-7; *(4b)*, 10009-70-8; *(4c)*, 433-44-3; *(4d)*, 54053-45-1; *(4e)*, 2681-94-9.

[1] *H. Simon, B. Rambeck, H. Hashimoto, H. Günther, G. Nohynek*, and *H. Neumann*, Angew. Chem. *86*, 675 (1974); Angew. Chem. internat. Edit. *13*, 608 (1974).

[2] *H. Günther, H. Hashimoto, B. Rambeck*, and *H. Simon* in *H. Dellweg*: 3. Symposium Technische Mikrobiologie Berlin. Verlag Versuchs- und Lehranstalt für Spiritusfabrikation und Fermentationstechnologie, Berlin 1973, p. 329.

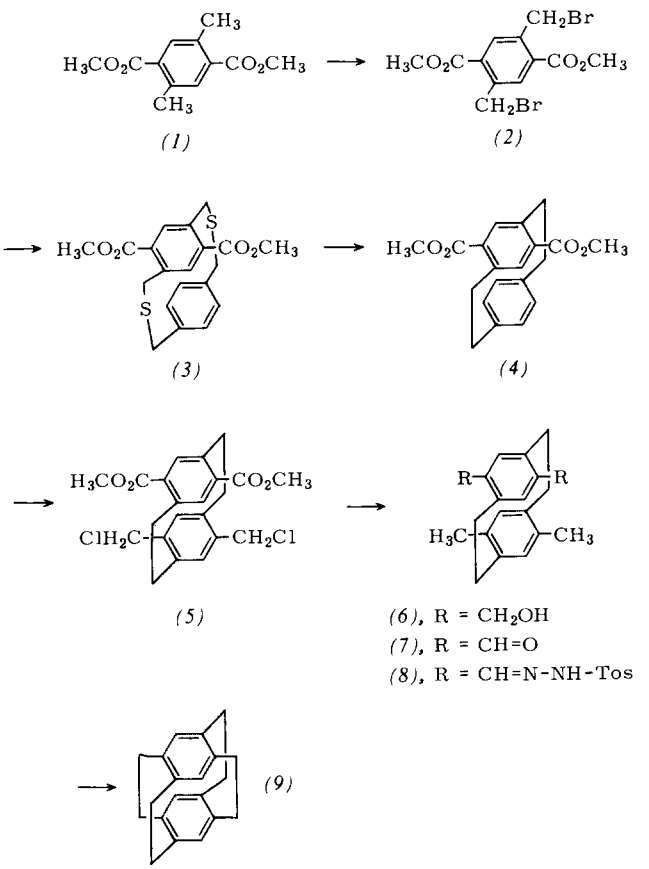
[3] *W. Gaffield* and *W. G. Galetto*, Tetrahedron *27*, 915 (1971).

[2.2.2.2](1,2,4,5)Cyclophane[***]

By *Richard Gray* and *V. Boekelheide*[*]

Although cyclophanes with multiple bridges having three or more linking atoms in the bridges are known[1], the tris-bridged cyclophanes having only two linking atoms in the bridges, [2.2.2](1,3,5)cyclophane and [2.2.2](1,2,4)cyclophane, have only been reported recently[2]. Because of the strong transannular interaction between the aromatic π-electron clouds in these molecules, as evidenced from their spectral and chemical properties, it is of interest to examine other, even more highly-bridged cyclophanes. We now report the synthesis of [2.2.2.2](1,2,4,5)cyclophane *(9)*.

Treatment of dimethyl 2,5-dimethylterephthalate *(1)*[3] with *N*-bromosuccinimide gave *(2)* (colorless needles, m. p. 169 to 171 °C; caution! *(2)* is a potent allergen)[4]. The coupling of *(2)* with 1,4-benzenebis(methanethiol) occurred in 59% yield to give *(3)* (colorless prisms, m. p. 158.5—159.5 °C). Irradiation of a solution of *(3)* in trimethyl phosphite, following the usual procedure for expulsion of sulfur from the molecule[5], gave *(4)* (colorless plates, m.p. 144—145 °C) in 69% yield. From the work of *Reich* and *Cram*[6], it is known that carbonyl groups attached to one deck of a [2.2]paracyclophane exert a strong influence directing electrophilic substitution to the pseudogeminal position of the opposite deck. Therefore, as anticipated, chloromethylation of *(4)* using chloromethyl methyl ether and aluminum chloride gave *(5)* (colorless plates, m. p. 189—192 °C) in 72% yield. Reduction of *(5)* with diisobutylaluminum hydride led to *(6)* (colorless powder, m. p. (dec) > 200 °C) in 98% yield. Oxidation of *(6)* with activated manganese dioxide[7] then gave the corresponding dialdehyde *(7)* (fine yellow needles, m.p. (dec) > 240 °C) in 85% yield. Transannular carbenoid insertion reactions of [2.2]paracyclophanes have been observed previously by *Cram*; they provide



[*] R. Gray and Prof. Dr. V. Boekelheide[**]
Department of Chemistry, University of Oregon
Eugene, Oregon 97403 (USA)

[**] V. B. thanks the Alexander von Humboldt Stiftung for the award of a Senior Fellowship held in residence at the Institut für Organische Chemie der Universität Karlsruhe, 1974—75.

[***] This work was supported by the National Science Foundation.

an excellent method for the introduction of bridges consisting of two carbon atoms[8]. When *(7)* was converted into the corresponding bis(tosylhydrazone) *(8)* and this was treated with sodium methoxide in THF followed by irradiation with a sun lamp, conversion to the desired hydrocarbon *(9)* occurred in 49% yield.

[2.2.2.2](1,2,4,5)Cyclophane *(9)* sublimes readily at 250°C to give tiny, colorless plates [m. p. 350°C; ^{1}H-NMR ($CDCl_3$): a singlet at $\tau = 4.04$ (4H) and an A_2B_2 pattern at 6.50—7.40 (16H); λ_{max}(cyclohexane) = 248 ($\varepsilon = 3610$), 294 (sh, 660), and 303 nm (1050). The NMR chemical shifts of the aromatic hydrogens of *(9)* are at lower field than those of the symmetrical [2.2.2](1,3,5)cyclophane ($\tau = 4.27$); this would suggest that the aromatic rings of *(9)* are boat-shaped with the —CH groups at the bowsprit positions allowing them to be further apart.

Received: November 26, 1974 [Z 131 IE]
German version: Angew. Chem. 87, 138 (1975)

[1] *A. J. Hubert*, J. Chem. Soc. *1965*, 3160; J. Chem. Soc. *C 1967*, 6, 11, 13; *R. D. Stephens*, J. Org. Chem. *38*, 2260 (1973).

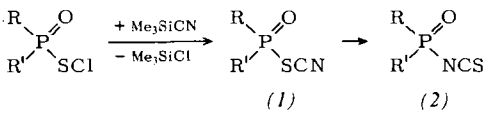
[2] *V. Boekelheide* and *R. A. Hollins*, J. Amer. Chem. Soc. *95*, 3201 (1973); *E. A. Truesdale* and *D. J. Cram*, *ibid. 95*, 5825 (1973).

[3] *M. Cachia* and *H. Wahl*, Bull. Soc. Chim. Fr. *1958*, 1418.

at room temperature to the corresponding isothiocyanatidate[3].

We tried to overcome the difficulties presented by the silver cyanide method by using trimethylsilyl cyanide as reaction partner. This reagent was recently employed in the synthesis of inorganic and organic cyanides[4].

The appropriate sulfenyl chlorides[**] were allowed to react with trimethylsilyl cyanide at −10°C in dichloromethane. Exothermic reaction took place and trimethylsilyl chloride was removed under vacuum at 0°C. The spectroscopic properties of the thiocyanatidates *(1a)*—*(1d)* (Table 1) are identical with those described in our previous papers[3, 5].



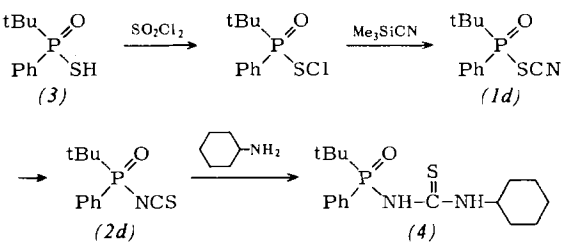
(1) *(2)* (1)

Thiocyanatidates synthesized by the trimethylsilyl cyanide method are distinctly more stable than those obtained by the silver cyanide method. It was possible to isolate *tert*-butyl(phenyl)phosphinothiocyanatidate *(1d)* as a crystalline solid (m.p. in sealed tube: 38—42°C; rearrangement). *(1d)* is stable at room temperature under strictly anhydrous conditions for several days. Starting from the optically active *tert*-butyl(phenyl)phosphinothioic acid we succeeded in preparing optically active *(1d)* which isomerized in the reaction mixture to *(2d)*[1] and could be trapped as the optically active *N*-[*tert*-butyl(phenyl)phosphinoyl]-*N'*-cyclohexylthiourea *(4)*[***].

Table 1. Physical data of the phosphorothiocyanatidates *(1a)*—*(1c)* and phosphinothiocyanatidate *(1d)* and their isomerization products, the isothiocyanatidates *(2a)*—*(2c)* and *(2d)*.

Cpd.	R	R'	^{31}P-NMR [ppm] [a]	IR [cm^{-1}] vP=O	vSCN	B.p. [°C/Torr]	n_D^{20}
(1a)	$(CH_3)_3CCH_2O$	$(CH_3)_3CCH_2O$	−10.8	1270	2170	—	—
(2a)			+18.0	1275	2010	68/0.01	1.4651
(1b)	$(CH_3)_2CHO$	$(CH_3)_2CHO$	− 7.8	1270	2173, 2185	—	—
(2b)			+21.0	1290	2008	65/0.2	1.4692
(1c) [b]	—O—CH_2—CH_2—$CH(CH_3)$—O—		− 2.0		2150	—	—
cis-(2c)			+27.0			—	—
trans-(2c)			+25.5	1225	2005	—	—
(1d)	$(CH_3)_3C$	C_6H_5	−73.0	1208, 1235	2185	—	—
(2d)			−39.0	1210, 1240	2000	97/0.01	1.5750

[a] δ-values, H_3PO_4 as standard.
[b] *(1c)* isomerized to *cis-(2c)* (64%) and *trans-(2c)* (36%) [5].



(3) *(1d)* *(2d)* *(4)* (2)

The reason for the relatively high stability of *(1d)* is, in the light of our earlier findings on the rearrangement of cyclic phosphorothiocyanatidates, due to steric hindrance, which affects the rate of the SCN^--catalyzed $S_N2(P)$ isomerization.

[4] Satisfactory elemental analyses were obtained for all the new compounds reported. Further, the UV, IR, NMR, and Mass spectra of all the new compounds are also in agreement with the given structures.

[5] *V. Boekelheide*, *I. D. Reingold*, and *M. Tuttle*, J. C. S. Chem. Commun. *1973*, 406; *J. Bruhin* and *W. Jenny*, Tetrahedron Lett. *1973*, 1215.

[6] *H. J. Reich* and *D. J. Cram*, J. Amer. Chem. Soc. *91*, 3505, 3517, 3527 (1969).

[7] *J. Attenburrow*, *A. F. B. Cameron*, *J. H. Chapman*, *R. M. Evans*, *B. A. Hems*, *A. B. A. Jansen*, and *T. Walker*, J. Chem. Soc. *1952*, 1094.

[8] *D. J. Cram*, *R. B. Hornsby*, *E. A. Truesdale*, *H. J. Reich*, *M. H. Delton*, and *J. M. Cram*, Tetrahedron *30*, 1757 (1974).

A New Route to Phosphoro- and Phosphinothiocyanatidates

By *Andrzej Łopusiński*, *Jan Michalski*, and *Wojciech J. Stec*[*]

Although intermediate formation of phosphoro- and phosphinothiocyanatidates *(1)* would appear indispensable to describe many reactions leading to the isomeric isothiocyanatidates *(2)*[1, 2], it was only recently that we were able to report evidence for the formation of a phosphorothiocyanatidate in the reaction of bis(neopentyloxy)phosphorylsulfenyl chloride with silver cyanide. The thiocyanatidate isomerizes rapidly

[*] Dr. Andrzej Łopusiński, Prof. Dr. Jan Michalski, and Doz. Dr. Wojciech J. Stec
Polska Akademia Nauk,
Centrum Badań Molekularnych i Makromolekularnych
90-362 Łódź, Boczna 5 (Poland)

[**] Prepared from the corresponding monothioacids [6] or their triethylammonium salts [7] by action of sulfuryl chloride in dichloromethane (see also eq. (2)).

[***] Starting from *(3)* [8], $[\alpha]_D^0 = +18.5°$, *(4)* was obtained according to eq. (2). [*(4)*: m.p. 162—164°C (ethanol), $[\alpha]_D^0 = +53.0°$ (benzene)].

The existence of the relatively stable, optically active compound *(1d)* contraindicates the dissociative mechanism.

Received: November 29, 1974 [Z 133 IE]
German version: Angew. Chem. *87*, 134 (1975)

CAS Registry numbers:
(1a), 54100-38-8; *(1b)*, 54100-39-9; *(1c)*, 54100-40-2; *(1d)*, 54100-41-3; *(2a)*, 54100-42-4, *(2b)*, 54100-43-5; *cis-(2a)*, 54100-44-6; *trans-(2c)*, 54100-45-7; *(2d)*, 54100-46-8; *(3)*, 54100-47-9; *(4)*, 54100-48-0; RR'P(O)SCl (R=R'=$(CH_3)_3CCH_2$), 54100-49-1; RR'P(O)SCl (R=R'=$(CH_3)_2CH$), 54100-50-4; RR'P(O)SCl (R,R'= $-OCH_2CH_2(CH_3)CHO-$), 54100-51-5 RR'P(O)SCl (R=$(CH_3)_3C$,R'=C_6H_5), 54100-52-6; trimethylsilyl cyanide, 7677-24-9; sulfuryl chloride, 7791-25-5; cyclohexylamine, 108-91-8.

[1] *J. Michalski* and *J. Wieczorkowski*, Rocz. Chem. *31*, 585 (1957).

[2] *G. Schrader*, DBP 124085, Chem. Abstr. *67*, 53729 (1967).

[3] *A. Łopusiński* and *J. Michalski*, Angew. Chem. *84*, 896 (1972); Angew. Chem. internat. Edit. *11*, 838 (1972).

[4] *W. Lidy* and *W. Sundermeyer*, Tetrahedron Lett. *1973*, 1449.

[5] *A. Łopusiński*, *J. Michalski*, and *W. J. Stec*, Bull. Acad. Pol. Sci. (in press).

[6] *B. Lenard* and *J. Michalski*, Rocz. Chem. *30*, 655 (1956).

[7] *S. Bluj*, *B. Borecka*, *A. Łopusiński*, and *J. Michalski*, Rocz. Chem. *48*, 329 (1974).

[8] *N. J. Death*, *K. Ellis*, *D. J. H. Smith*, and *S. Trippett*, Chem. Commun. *1971*, 714.

Determination of the Absolute Configuration of Amines[***]

By *Francisc Kerek* and *Günther Snatzke*[*]

Neutral complexes such as the Cu^{II} complexes $[Cu(im)_2(am)_2]$ *(1)* (im: succinimidato, phthalimidato; am: sterically non-hindered primary or secondary amine)[1] offer a new and particularly simple method for determining the absolute configuration of amines. Contrary to the former assumption[2] that chiral amines as monodentate ligands in copper complexes are incapable of inducing circular dichroism (CD) within the d-d bands, we have observed two Cotton effects of opposite signs for each of the complexes *(1)* between 400 and 800 nm. In addition, further Cotton effects are found at shorter wavelengths. The longer wavelength CD bands (Table 1) are far better suited for stereochemical correlations than those at shorter wavelengths. Only the signs of the Cotton effects are required for determining absolute configurations (see Fig. 1).

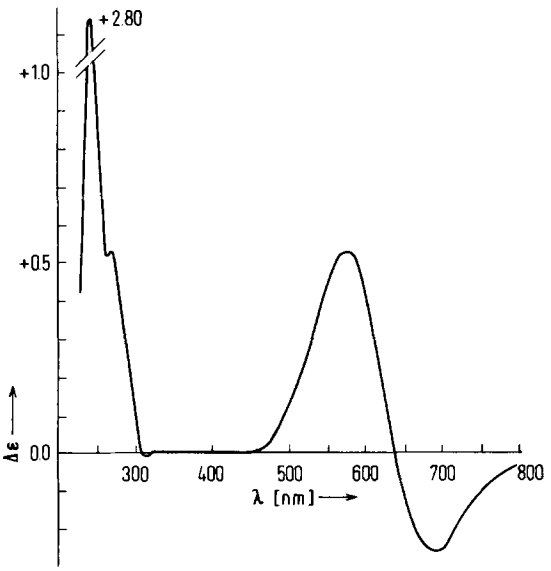


Fig. 1. CD spectrum of $[Cu(su)_2((+)\text{-}sec\text{-}BuNH_2)_2]$, $c = 5 \times 10^{-3}$ mol/l, in CH_2Cl_2.

Table 1. Δε values for several $[Cu(su)_2(am^*)_2]$ complexes *(1)* prepared *in situ* from $[Cu(su)_2(ip)_2]$ or $[Cu(su)_2(py)_2]$ (su = succinimidato; ip = isopropylamine; py = pyridine) in CH_2Cl_2. [Cu] ≈ 0.001–0.01 mol/l, [am*]:[Cu] ≈ 2:1 to 40:1.

Complex	am*	Band II λ_{max} [nm]	Δε [a]	Band I λ_{max} [nm]	Δε [a]
(1a)	L-Alanine methyl ester	610	−0.68	705	+0.49
(1b)	L-Leucine methyl ester	605	−0.62	705	+0.40
(1c)	L-Isoleucine methyl ester	610	−1.56	715	+0.96
(1d)	L-Phenylalanine methyl ester	625	−0.38	725	+0.20
(1e)	L-Lysine methyl ester	620	−0.42	700	+0.42
(1f)	L-Proline methyl ester	620	−1.02	715	+0.60
(1g)	Dimethyl L-aspartate	620	−0.30	720	+0.18
(1h)	L-Tryptophan methyl ester	610	−0.50	710	+0.30
(1i)	L-Serine methyl ester	615	−0.68	710	+0.45
(1j)	L-Histidine methyl ester	540 [b]	−0.18	720	+0.05
(1k)	L-Glutamine methyl ester	610	−0.56	706	+0.31
(1l)	D-Valine methyl ester	610	+1.42	715	−0.82
(1m)	D-Methionine methyl ester	610	+0.46	706	−0.25
(1n)	(*S*)-(+)-Phenylethylamine	620	−0.40	725	+0.20
(1o)	(*S*)-(−)-Dehydroabietylamine	590	−0.12	700	+0.05
(1p)	6β-Amino-5α-cholestane-3β,7α-diol 3-acetate	580	−0.15	705	+0.11
(1q)	6β-Amino-5α-cholestane-3β,5α-diol 3-acetate	580	−0.17	703	+0.12
(1r)	16α-Amino-3-methoxy-1,3,5(10)-estratrien-17β-ol	606	+0.55	705	−0.16
(1s)	16α-Amino-3-methoxy-1,3,5(10)-estratrien-17α-ol	595	+0.45	690	−0.21
(1t)	16β-Amino-3-methoxy-1,3,5(10)-estratrien-17β-ol	605	−0.54	710	+0.40

[a] Converted to [Cu] = 1 mol/l.
[b] Concerning position of bands, see text.

[*] Dr. F. Kerek [**] and Prof. Dr. G. Snatzke
Lehrstuhl für Strukturchemie der Universität
463 Bochum, Postfach 2148 (Germany)

[**] Alexander-von-Humboldt Fellow, permanent address: Laboratory of Organic Chemistry, Polytechnic Institute, Timişoara (Romania)

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

The somewhat involved preparation of the complexes *(1)* according to *Tschugaeff*[1] can be avoided owing to their kinetic lability: thus it suffices to add the optically active amine (am*) to a solution of a "parent complex" (*e.g.* with am = isopropylamine) in dichloromethane, chloroform, or benzene and then to record the CD immediately. Above a molar ratio of about 8 : 1 ([am*] : [Cu]) the CD end values are reached which are also obtained starting from the isolated complexes *(1)*. The signs of the Cotton effects can already be established at much lower am* concentrations. In this way it becomes possible, *e.g.* with as little as 1–2 mg of an amino acid ester, to ascertain whether it belongs to the D or the L series. Rigorous exclusion of moisture is not necessary.

The chiroptical data of bidentate amino acid complexes have been investigated previously (*e.g.* refs.[3–6]). In all cases the proline complexes exhibited the opposite sign to that of all the other amino acid complexes of the same optical series. The CD of the proline complex *(1f)*, however, is in no way exceptional.

Since the complexing constant of amines in *(1)* is far greater than that of other possible ligands, other functional groups do not generally exert interfering effects. Possible chelating with a sterically favorable second amino or hydroxy group can easily be recognized from the appearance of an additional CD band in the region of 530 nm; however, the 700-nm band generally remains informative. Readily oxidizable groups such as —SH (cysteine) destroy the complex.

The above method is much simpler and more reliable than the comparable procedure of reacting amines[7] or amino alcohols[7, 8] with lanthanoid reagents or with pentanedionatonickel complex[8], for which measurements have to be performed in the short-wave range (≈ 300 nm) near the transmission limit of the solutions and the sign of the CD frequently varies with the substrate : complex concentration ratio.

Received: November 14, 1974 [Z 129 IE]
German version: Angew. Chem. 87, 133 (1975)

[1] *L. Tschugaeff*, Ber. Deut. Chem. Ges. *38*, 2899 (1906).
[2] *E. Larsen* and *I. Olsen*, Acta Chem. Scand. *18*, 1025 (1964).
[3] *P. Pfeiffer*, Angew. Chem. *53*, 93 (1945), and references cited therein.
[4] *T. Yasui, J. Hidaka*, and *Y. Shimura*, J. Amer. Chem. Soc. *87*, 2762 (1965).
[5] *K. M. Wellman, S. Bogdansky, C. Pontek, C. R. Have*, and *M. Mathieson*, Inorg. Chem. *8*, 1025 (1968).
[6] *R. D. Gillard* and *S. H. Laurie*, Chem. Commun. *1969*, 488.
[7] *G. N. Mitchell* and *F. I. Caroll*, J. Amer. Chem. Soc. *95*, 7912 (1973).
[8] *J. Dillon* and *K. Nakanishi*, J. Amer. Chem. Soc. *96*, 4057, 4059 (1974).

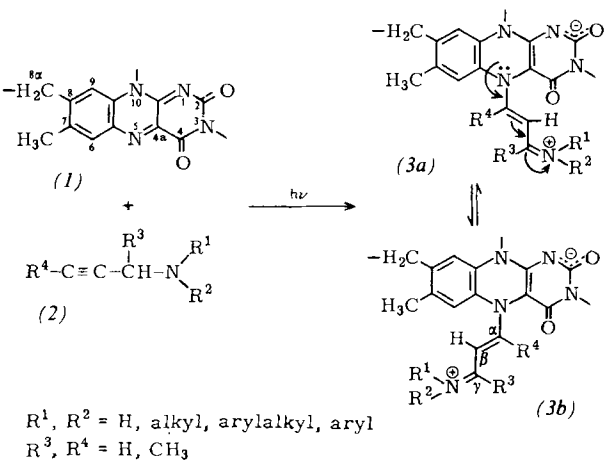
Inhibition of Monoamine Oxidase by Propargylamine: Structure of the Inhibitor Complex[1]

By *Bernd Gärtner* and *Peter Hemmerich*[*]

Mitochondrial monoamine oxidase (MAO) is a key enzyme in the metabolism of biogenic amines[2]. It contains flavin adenine dinucleotide (FAD) as coenzyme and differs characteristically from most common flavoenzymes by the fact that the FAD coenzyme is *covalently* bound to the protein. The structure of this linkage (*via* C-8α of the flavin to a cysteine sulfur of the protein) has been ascertained by *Singer et al.* through enzymatic degradation[3] of the protein and by *Ghisla* and *Hemmerich*[4] who synthesized the modified coenzyme. MAO is irreversibly inhibited[5] by propargylamines *(2)* e.g. pargyline® [*(2)*, $R^1=CH_3$, $R^2=CH_2C_6H_5$, $R^3=R^4=H$].

[*] Prof. Dr. P. Hemmerich and Dr. B. Gärtner
Fachbereich Biologie der Universität
775 Konstanz, Postfach 7733 (Germany)

Chuang et al.[6] first isolated a spectrally pure, soluble preparation of this membrane-fixed flavoprotein with which they also obtained the highly characteristic electronic spectrum of pargyline-enzyme complex. This spectrum has been shown[7] to coincide with the spectrum of a product resulting from photoreduction of flavin with pargyline®. We have elucidated the structure[1] of the product and found it to arise by a novel photo*addition* to N-5 of the flavin nucleus[1] leading to the trimethinecyanine chromophore *(3)*. The terminal groups of this cyanine consist of the now reduced flavin group and the amino group of the photosubstrate.



The "flavocyanines" *(3)* exist in neutral solution in a mesoionic state, where the positive charge is localized in the cyanine part of the molecule and the negative charge in the pyrimidine subnucleus of the flavin. Protonation occurs with p*K* 4—5 at N-1, without essential alteration of the absorption spectrum (approx. 15 nm hypsochromic shift). The cations thus formed are stable towards hydrolysis while reaction of *(3)* with bases results in the characteristic solvolysis of the cyanine system, yielding an aldehyde of type HFl—CH=CH—CH=O as the first intermediate which can be isolated. Further action of base, which proceeds most rapidly with secondary amines, liberates flavin quantitatively as unmodified flavoquinone *(1)*. This chemical reversibility of adduct formation has not yet been verified in the enzymatic system.

According to expectation[8], the trimethine chains possess *trans* configuration throughout (^{1}H-NMR, $J_{CH-CH\,trans}=11.5$—12.0 Hz). Hence, when $R^1=R^2$, *two* and only two *(5)* N÷÷C (α) rotamers *(3a, b)* can be demonstrated directly by ^{1}H-NMR (for each rotameric species *(3a)*, *(3b)* separate signals of α,β,γ 6,9-protons, cf. Experimental). The rotamer population depends on the solvent; equilibration *(3a)*⇌*(3b)* occurs within less than 5 minutes upon dissolution of the crystals at room temperature. The cyanine chromophore is not entirely coplanar with the terminal flavin group, as suggested by molecular models and as supported by the relatively large half width[9] of the longwave band. An additional molecular asymmetry results, leading, in the case of increased steric hindrance by a substituent $R^4=CH_3$, to the ^{1}H-NMR-spectroscopic non-equivalence of prochiral methylene protons ($R^1=CH_2—C\equiv C—CH_3$, ABX_3). We assign the 400 nm band to the lowest energy π-π*-transition of the cyanine chromophore (oscillator strength[10] $f=0.4$—0.6). This transition shows a strong negative solvatochromy (approx. −25 nm upon change from $CHCl_3$ to methanol). This supports the assumption that the 4a,5-azomethine function of the flavocoenzyme is the dehydrogenating enzyme site. One may further conclude that covalent flavin-substrate interactions are relevant in molecular pharma-

cology and, presumably, even in pure enzymology of flavoproteins.

The new synthetic principle can be generally extended to π-electron deficient azaheterocycles.

Experimental:

A well stirred solution of 3-methyllumiflavin[11] (1.50 g, 5.5 mmol) and *N*,*N*-dimethylpropargylamine (4.6 g, 55.0 mmol) in 0.1 M phosphate buffer (600 ml, pH 7.7) was illuminated under argon for 30 hours with a 170 W mercury high-pressure lamp (HERAEUS, Hanau; pyrex cooling jacket). The brown precipitate was filtered off by suction, washed with water (50 ml), dried, and extracted with hot benzene (3 × 50 ml). The residue was reprecipitated from hot chloroform (25 ml) by addition of hot benzene (60 ml), and then from hot methanol (30 ml) by addition of ether (120 ml).

Yield: 600 mg (28%) 5-(γ-dimethyliminiopropenyl)-3-methyl-1,5-dihydrolumiflavin betaine; yellow needles, m.p. 226—227 °C (dec.). UV: λ_{max} (ε) in benzene 430 nm (29650); in chloroform 427 nm (22700); in methanol 402 nm (25500); in H_2O, pH 7.0, 391 nm (25500). ^{1}H-NMR (90 MHz; TMS as internal standard), δ [ppm] in D_6-DMSO: rotamer *(3a)* (82%) α-H 7.85, β-H 5.10, γ-H 7.77; *(3b)* (18%) 8.10, 5.80, 8.01; $J_{\alpha\beta} = J_{\beta\gamma} = 12.0$ Hz; in CF_3COOH: rotamer *(3a)* (73%) 7.68, 5.34, 7.77; *(3b)* (27%) 8.00, 6.12, 7.90; $J_{\alpha\beta} = J_{\beta\gamma} = 12.0$ Hz.

Received: December 23, 1974 [Z 135 IE]
German version: Angew. Chem. 87, 137 (1975)

[1] Part of the Dissertation by *B. Gärtner*, Universität Konstanz 1974.

[2] *R. Kapeller-Adler*: Amine Oxidases and Methods for Their Study, Wiley-Interscience, New York 1970, p. 28.

[3] *E. B. Kearney, J. I. Salach, W. H. Walker, R. Seng*, and *T. P. Singer*, Biochem. Biophys. Res. Commun. *42*, 490 (1971).

[4] *S. Ghisla* and *P. Hemmerich*, FEBS Lett. *16*, 229 (1971).

[5] *E. A. Zeller*, Ann. N. Y. Acad. Sci. *107*, 811 (1963); *L. R. Swett, W. B. Martin, J. D. Taylor, G. M. Everett, A. A. Wykes*, and *Y. C. Gladish*, *ibid. 107*, 891 (1963).

[6] *H. Y. K. Chuang, D. R. Patek*, and *L. Hellerman*, J. Biol. Chem. *249*, 2381 (1974); cf. also: *L. Oreland, H. Kinemuchi*, and *B. Y. Yoo*, Life Sci. *13*, 1533 (1973).

[7] *E. A. Zeller, B. Gärtner*, and *P. Hemmerich*, Z. Naturforsch. *27b*, 1050 (1972). The formerly suggested cyclic adduct structure must be corrected in favor of the isomeric cyanine structure *(3)*. After completion of this investigation [1] (Dissertation accepted on November 18, 1974) we were informed on November 26, 1974 by Dr. *Maycock*, Brandeis University, that he has been able to independently verify the present cyanine structure with a sample [*(3)*, $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$] which we had sent him for comparison with enzymatic material.

[8] *G. Scheibe, W. Seiffert, G. Hohlneicher, C. Jutz*, and *H. J. Springer*, Tetrahedron Lett. *1966*, 5053.

[9] *E. Daltrozzo*, personal communication.

[10] *G. Schaibe, H. J. Friedrich*, and *G. Hohlneicher*, Angew. Chem. *73*, 383 (1961).

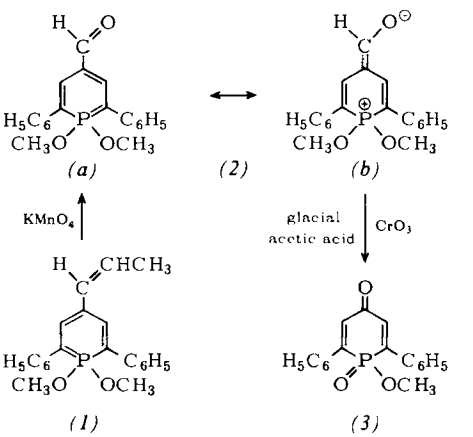
[11] *P. Hemmerich*, Helv. Chim. Acta *47*, 464 (1964).

1,1-Dimethoxy-2,6-diphenyl-λ⁵-phosphorin-4-carbaldehyde and -4-carbonitrile[1]

By *Hans Henning Pohl* and *Karl Dimroth*[*]

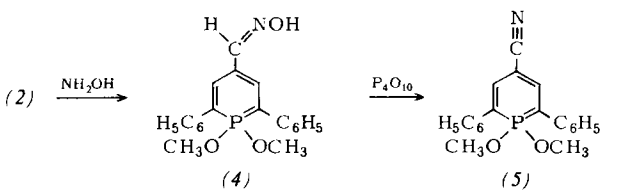
1,1-Heterosubstituted λ⁵-phosphorins *(1)* are characterized by exceptional stability of the λ⁵-phosphorin ring, so that they can be considered as a new type of heteroaromatic compound[2]. In order to study their chemistry we are seeking methods for synthesizing derivatives containing functional groups attached to the phosphorin ring. The starting material for the carbaldehyde *(2)* described in this communication and other compounds accessible therefrom is 1,1-dimethoxy-2,6-diphenyl-4-propenyl-λ⁵-phosphorin *(1)*[3].

On oxidation of *(1)* with potassium permanganate by a phase transfer process[5] in benzene/water containing tetra-*n*-butylammonium bromide[4], the double bond of the side chain is cleaved without destruction of the λ⁵-phosphorin ring. Thin layer chromatography on silica gel permits isolation in more than 60% yield of the carbaldehyde *(2)* which crystallizes in yellowish needles (m.p. 96 °C). It is stable in air, and its solutions have a strong bluish fluorescence.



In the ^{1}H-NMR spectrum ([D_6]-acetone) at room temperature a doublet at δ = 8.63 ppm ($^3J_{P-H} = 38$ Hz) is found for the protons at C-3 and C-5 of the phosphorin ring. At low temperatures this A_2X system passes into an ABX system, which appears well resolved at −60 °C. From the non-equivalence of the protons on C-3 and C-5 it can be concluded that rotation around the axis C(4)—CHO is restricted by delocalization in the sense of the formulas *(2a)* and *(2b)*.

Although the aldehyde is not further oxidized by an excess of potassium permanganate, 1,4-dihydro-1-methoxy-2,6-diphenyl-λ⁵-phosphorin-1,4-dione *(3)* is obtained in about 50% yield on use of chromic acid in glacial acetic acid.



The oxime *(4)*, melting at 141—142 °C (dec.), and the *p*-toluenesulfonylhydrazone, m.p. 160—161 °C, are formed from the aldehyde *(2)* in smooth reactions. Removal of water from *(4)* is effected by P_4O_{10} in benzene, yielding the 4-cyano-substituted λ⁵-phosphorin *(5)* which crystallizes in pale yellowish needles (m.p. 130 °C), and which can be hydrolyzed affording the carboxamide.

Received: December 13, 1974 [Z 134a IE]
German version: Angew. Chem. 87, 135 (1975)

[1] λ⁵-Phosphorin Derivatives with Functional Groups on the Phosphorin Ring, Part 2.—Part 1: *K. Dimroth, W. Schäfer*, and *H. H. Pohl*, Tetrahedron Lett. *1972*, 839.

[2] *K. Dimroth*, Fortschr. Chem. Forsch. (Top. Curr. Chem.) *38*, 1 (1973).

[3] *H. H. Pohl* and *K. Dimroth*, Chem. Ber., in the press.

[4] *A. W. Herriott* and *D. Picher*, Tetrahedron Lett. *1974*, 1511.

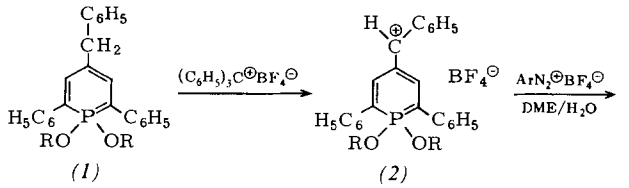
[5] *J. Dockx*, Synthesis *1973*, 441, especially p. 453.

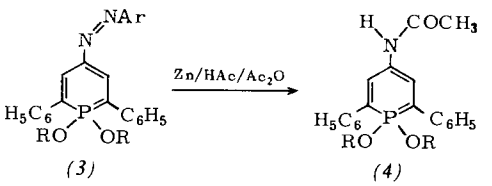
[*] Dr. H. H. Pohl, Stipendiate of the Deutsche Forschungsgemeinschaft (from January 1st 1975 BASF, 67 Ludwigshafen), and Prof. K. Dimroth
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

4-(Acetylamino)-1,1-dialkoxy-2,6-diphenyl-λ⁵-phosphorins[1]

By *Karl Dimroth* and *Manfred Lückoff*[*]

In the course of work aimed at synthesis of λ⁵-phosphorins containing functional groups attached to the phosphorin ring, we succeeded in preparing the 4-(acetylamino)-1,1-dialkoxy-2,6-diphenyl-λ⁵-phosphorins *(4a)* and *(4c)* as key compounds for further reactions. The starting materials are the 4-(arylazo)-λ⁵-phosphorins *(3)*, which in turn can be prepared by means of electrophilic substitution with arenediazonium salts[2] from λ⁵-phosphorin derivatives containing electrofugal leaving groups at C-4. A new reaction is the ready formation of *(3)* to *(3c)* in 70—90% yield of pure compounds from the readily accessible[3] 4-benzyl-λ⁵-phosphorins *(1a)* to *(1c)* by way of the carbenium tetrafluoroborates *(2a)* to *(2c)*[4] and benzene- or *p*-toluene-diazonium tetrafluoroborate in dimethoxyethane containing sodium hydrogen carbonate and a few drops of water. The reactions *(3)*→*(4)* were effected by zinc dust in glacial acetic acid and acetic anhydride. The crystalline, analytically pure *N*-acetyl derivatives *(4a)* and *(4c)* are sensitive to light and give solutions with yellow-green fluorescence; they were separated from the *N*-acetyl-aniline or -toluidine formed simultaneously and isolated in 64 and 69% yield, respectively.





R	(1) M.p.[°C]	(2) M.p.[°C]	(3) M.p.[°C]	(4) M.p.[°C]
(a)	CH_3	101 [5]	148—149	151—152 (Ar = C_6H_5)	209—211
(b)	C_2H_5	72—73	147—148	116—117 (Ar = $C_6H_4CH_3$)	—
(c)	$CH(CH_3)_2$	110—111	115—117	145—147 (Ar = $C_6H_4CH_3$)	206—209

(4a): ^{1}H-NMR (C_6D_6), δ (ppm) = 1.87 (3 H, s); 3.03 (6 H, d, $^3J_{P-H}$ = 14 Hz; 6.8—7.9 (11 H, m); 8.17 (1 H, part of the doublet, $^3J_{P-H}$ = 36.0 Hz).

(4c): ^{1}H-NMR (C_6D_6), δ (ppm) = 0.87 (12 H, d, $^3J_{H-H}$ = 6.5 Hz); 1.95 (3 H, s); 4.10 (2 H, m, $^3J_{H-H}$ = 6.5 Hz, $^3J_{P-H}$ = 10.8 Hz); 6.9—7.9 (11 H, m); 8.17 (1 H, part of the doublet, $^3J_{P-H}$ = 36 Hz).

Received: December 13, 1974 [Z 134b IE]
German version: Angew. Chem. *87*, 135 (1975)

[*] Prof. K. Dimroth and M. Lückoff
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

[1] λ⁵-Phosphorin Derivatives with Functional Groups on the Phosphorin Ring, Part 3.—Part 2: *H. H. Pohl* and *K. Dimroth*, Angew. Chem. *87*, 135 (1975); Angew. Chem. internat. Edit. *14*, 111 (1975).

[2] *W. Schäfer* and *K. Dimroth*, Angew. Chem. *85*, 815 (1973); Angew. Chem. internat. Edit. *12*, 753 (1973).

[3] Review: *K. Dimroth*, Fortschr. Chem. Forsch. (Top. Curr. Chem.) *38*, 1 (1973).

[4] *K. Dimroth*, *W. Schäfer*, and *H. H. Pohl*, Tetrahedron Lett. *1972*, 839.

[5] *H. H. Pohl*, Dissertation, Universität Marburg (Germany) 1974.

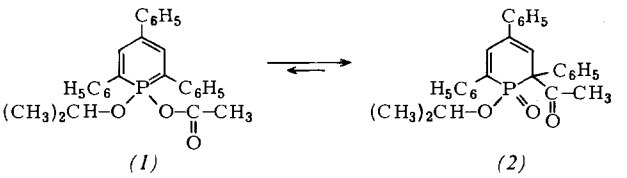
A Rearrangement in the λ⁵-Phosphorin Series Analogous to the Claisen Rearrangement

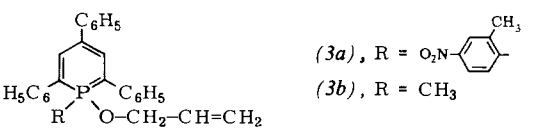
By *Ortwin Schaffer* and *Karl Dimroth*[*]

Dedicated to Professor Eugen Müller

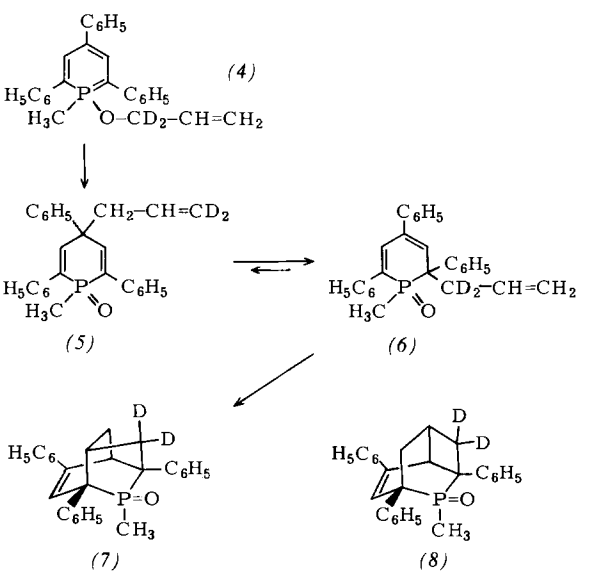
We recently reported[1] a thermal sigmatropic [1,3]-rearrangement analogous to the Fries migration, which leads from 1-acetoxy-1-isopropoxy-2,4,6-triphenyl-λ⁵-phosphorin *(1)* to 2-acetyl-1,2-dihydro-1-isopropoxy-2,4,6-triphenyl-λ⁵-phosphorin-1-one *(2)*. *(1)* exists in reversible equilibrium with *(2)*.

The readily accessible 1-alkoxy-1-aryl-[2] and 1-alkoxy-1-alkyl-2,4,6-triphenyl-λ⁵-phosphorins[3] make it possible to prepare the allyloxy derivatives *(3a)* and *(3b)* and thus to study the thermal rearrangement of the latter compounds.





Both compounds rearrange to isomeric compounds within a few hours when warmed even at *ca.* 110 °C (boiling toluene). Compound *(4)* labeled by means of [1,1-D_2]-allyl alcohol was prepared for a study of the course of the reaction.



Analysis of the ^{1}H-NMR spectra shows that *(4)* first rearranges cleanly to the phosphacyclohexadiene derivative *(5)*

[*] Dr. O. Schaffer and Prof. Dr. Karl Dimroth
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

substituted at C-4. If the rearrangement is prematurely interrupted, *(5)* is obtained analytically pure as a crystalline compound. Heating *(5)* in toluene causes a [3,3]-sigmatropic rearrangement that leads to an equilibrium greatly in favor of *(6)*, this being the reverse reaction of that found in a study of the Claisen rearrangement. However, we found no trace of a reverse rearrangement of *(5)* to *(4)*. On longer heating of *(5)* in toluene, *(6)* is accompanied by a new, stable, excellently crystallizing product which can also be obtained from pure *(6)*. For this compound we propose structure *(7)* [or possibly *(8)*], whose formation is explained by an intramolecular Diels-Alder reaction that is irreversible under the reaction conditions. Proof of the structure is currently being sought by X-ray structure analysis.

As a synchronous thermal $[_3s_5s]$-rearrangement, the reaction *(4)* → *(5)* would be symmetry-forbidden if the orbital symmetry of the λ^5-phosphorin derivative *(4)* is the same as that of a phenyl ether. A synchronous course is not in line with the fact that when *(4)* is warmed in toluene an ESR signal (doublet at 23.5 gauss) appears which can be assigned to the relatively stable phosphacyclohexadienyl radical with five-valent phosphorus[4]. On longer heating, the intensity of this signal decreases. An ESR signal for the allyl radical could not be observed.

The unexpected course of this rearrangement may depend on the geometry of compound *(4)*. The allyl group—unlike that in allyl phenyl ethers—occupies a structural position favorable for attack of the terminal CH_2 group on C-4 of the heterocycle, this being possible due to the tetrahedral structure at the phosphorus atom.

Rearrangement of 1-methyl-1-propargyloxy-2,4,6-triphenylphosphorin, analogous to *(3)*, requires a somewhat higher temperature (*ca.* 140 °C, xylene). Preliminary experiments indicate a course similar to the allyl rearrangement.

Received: December 13, 1974 [Z 134c IE]
German version: Angew. Chem. *87*, 136 (1975)

[1] *M. Constenla* and *K. Dimroth*, Chem. Ber. *107*, 3501 (1974).

[2] *O. Schaffer* and *K. Dimroth*, Angew. Chem. *84*, 1146 (1972); Angew. Chem. internat. Edit. *11*, 1091 (1972).

[3] *P. Kieselack* and *K. Dimroth*, Angew. Chem. *86*, 129 (1974); Angew. Chem. internat. Edit. *13*, 148 (1974).

[4] *K. Dimroth* and *H. Weber*, unpublished work.

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The biochemistry of hypoglycine is reviewed in an article by *K. L. Manchester*. This amino acid (β-(methylenecyclopropyl)-alanine), which occurs in the fruits of some plants, is toxic and leads, in small doses, to vomiting; larger doses lead to hypoglycemia and ultimately to death. The synthesis, purification, and chemical reactions of the amino acid are described. Its effect on the metabolism is to inhibit reactions which involve participation of leucine, an amino acid which is physicochemically very similar to hypoglycine. This leads to interferences with the protein synthesis and with the biological degradation of leucine. Hypoglycine also affects the β-oxidation of fatty acids by inhibition of flavin enzymes. Teratogenic effects on rat embryos have also been observed. [Biochemistry of Hypoglycine. FEBS Lett. *40*, S133—S139 (1974); 56 references]

[Rd 750 IE—R]

The chemical and biological functions of membrane-active complexing agents are reviewed by *Yu. A. Ovchinnikov*. This class of substances, whose prototype is valinomycin, form complexes with alkali and alkaline earth metal ions, which, because of the lipophilic regions of the molecules, are ion carriers. The behavior of valinomycin and its analogs and enniatin, which is also a depsipeptide, in lipid double layers and natural membranes is discussed. Spectral investigations on the dependence of complex formation on the solvent are also described. [Membrane Active Complexons. Chemistry and Biological Function. FEBS Lett. *44*, 1—21; 36 references]

[Rd 752 IE—R]

The active ribosome sites in *Escherichia coli* is the subject of a review by *O. Pongs, K. H. Nierhaus, V. A. Erdmann*, and *H. G. Wittmann*. In the course of the last few years numerous experimental results have been obtained regarding the processes of initiation of protein synthesis, elongation of the peptide chain, and termination, which in turn are subdivided into individual steps. These results and further information obtained on the protein factors necessary for the reactions provide a detailed picture of the regulatory processes on ribosomes during the course of the synthesis. [Active Sites in *Escherichia coli* Ribosomes. FEBS Lett. *40*, S28—S37 (1974); 142 references]

[Rd 756 IE—R]

Structural transformations of ribosomes are discussed in an article by *A. S. Spirin*. Dissociation of the ribosome into two unequal parts proves to be a general building principle and appears to be essential for their functioning. Partial functions of the ribosome have been investigated on both fragments. The unfolding at lower magnesium concentrations, which leads to a lowering of the sedimentation coefficients, and an increase in viscosity, made it possible to study the structure of the ribosomal proteins and their relationship to the ribosomal RNA. The reversible dissociation of ribosomal particles at high alkali metal chloride concentrations permitted the selective elimination of certain proteins. Partial ribosomes could be assembled from the fragments by spontaneous reassociation. [Structural Transformations of Ribosomes (Dissociation, Unfolding and Assembly) FEBS Lett. *40*, S38—S47 (1974); 183 references]

[Rd 757 IE—R]

Vibrational structure in electronic spectra of coordination compounds is the subject of a review by *C. D. Flint*. If such vibrational structure is observed, different selection rules may make it possible to identify vibrational frequencies not observ-

able in the IR and Raman spectrum. Thus, the normal coordinate analysis of the respective complexes is simplified, as the number of approximations made in setting up the force field is reduced. [Vibronic Spectra of Coordination Compounds. Coord. Chem. Rev. *14*, 47—66 (1974); 45 references]

[Rd 760 IE—H]

New results of the photochemistry of complexes of the heavier transition metals are discussed by *P. C. Ford, J. D. Petersen,* and *R. E. Hintze.* Most work in this field is concerned with complexes derived from metal ions with the electron configurations $4d^6$ and $5d^6$. Reactions of coordinated ligands, isomerizations, redox, and substitution reactions were observed. The special feature of these metals compared to the first transition row metals is the higher spin-orbit coupling rendering easier interconversion between excited states of different multiplicities. [Photochemistry of Hexacoordinate Complexes of the Heavier Transition Metals. Coord. Chem. Rev. *14*, 67—105 (1974); 109 references]

[Rd 761 IE—H]

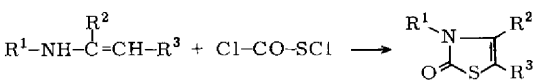
Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

A catalyst for ring-opening polymerization of cyclopentene to form polymers with high *trans*-contents, consists of molybdenum pentachloride (a halide of a metal of Group VIB of the periodic table), triisobutylaluminum (organoaluminum compound) and, as an activator, an aromatic sulfonyl chloride such as benzenesulfonyl chloride. [DOS 2331514; Shell International Research Maatschappij B.V., The Hague (Netherlands)]

[PR 234 IE—W]

2-Oxothiazole-5-carboxylic acid derivatives *(3)* are obtained by treating enamines *(1)* with (chlorocarbonyl)sulfenyl chlor-



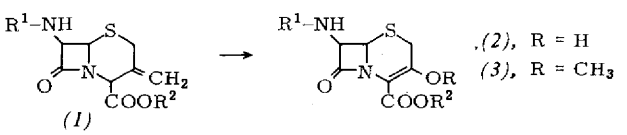
(1) *(2)* *(3)*

R^1=H, alkyl, aryl, or aralkyl; R^2=H, alkyl, or aryl; R^3=carbonitrile or carboxamide

ide *(2)*; these compounds *(3)* have fungitoxic activity. [DOS 2302844; Bayer AG, Leverkusen (Germany)]

[PR 238 IE—K]

Cephalosporin derivatives *(2)* with R=H, which can be used as antibiotics, are obtained by ozonization of 3-methylenece-



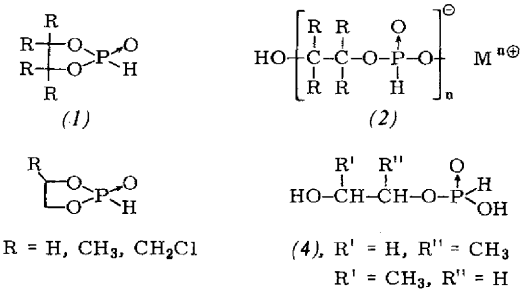
(1) *(2)*, R = H; *(3)*, R = CH_3

R^1=H or acyl; R^2=H or an ester-forming group

pham derivatives *(1)*; derivatives *(3)* with R=methyl are prepared from *(2)* by treatment with diazomethane. [DOS 2359353; Eli Lilly & Co., Indianapolis, Ind. (USA)]

[PR 239 IE—K]

Phosphorous esters of 1,2-glycols having formulas *(1)* and *(2)* (in which R represents a hydrogen atom or an alkyl or, if



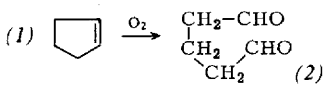
(1) *(2)*

(3), R = H, CH_3, CH_2Cl *(4)*, R' = H, R'' = CH_3; R' = CH_3, R'' = H

appropriate, a haloalkyl group with 1 to 5 carbon atoms, M is a hydrogen atom, metal, ammonium, alkylammonium or mono-, bis-, or tris-(hydroxyalkyl) ammonium, and *n* is a whole number corresponding to the valence of M) are new and in some cases systemic fungicides. They are effective against both soil fungi such as *Pythium* and leaf-parasitizing fungi such as *Phytophora infestans* and *Plasmopara viticola.* Compounds *(3)* and *(4)* are given particular mention. [DOS 2365061; Pepro-Société pour le Développement et la Vente de Spécialités Chimiques, Lyons (France)]

[PR 241 IE—S]

Glutardialdehyde *(2)* is formed on uncatalyzed gas-phase oxidation (1—3 atm, 280—450 °C, 1—30 sec) of cyclopentene *(1)* with a selectivity of 50—70 mol-% and an oxygen consumption

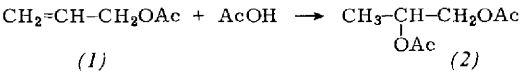


(1) *(2)*

of about 20 %. [DOS 2261657; Bayer AG, Leverkusen (Germany)]

[PR 243 IE—G]

Propylene diacetate ("**propylene glycol diacetate**") *(2)* can be prepared by treating allyl acetate *(1)* with acetic acid on polyphosphoric acid/SiO_2 catalysts (100 atm, 200 °C). Allyl



(1) *(2)*

propionate may be used in place of *(1)*, and propionic or butyric acid in place of acetic acid. [DOS 2219915; Farbwerke Hoechst AG, Frankfurt (Germany)]

[PR 244 IE—G]

Silicate foam materials (water glass foams) are obtained by mixing air into a water glass solution and simultaneously adding a hardening substance such as 1,2-dichloroethyl dichloroisocyanide, benzoyl chloride, *o*-toluenesulfonyl chloride, or dipropyleneglycol bis(chlorofumarate). [DOS 2228359; Bayer AG, Leverkusen (Germany)] [PR 255 IE—W]

Ligandenfeldtheorie (Ligand Field Theory). Chemische Taschenbücher 19. By *P. Schuster*. Verlag Chemie GmbH, Weinheim 1973. 1st Edit., ix, 192 pp., 32 figures, 43 tables, paperback, DM 28.—.

This volume in the "Chemische Taschenbücher" series provides the reader with an introduction to ligand field theory, but it seems doubtful if such relatively short treatment can fulfil the author's intention, stated in the Foreword, *i.e.* to offer an introduction to the beginner or near-beginner and to lead him from there to the stage where he can read and understand original papers "without difficulty".

The book is suited above all—and for this it is suited very well—as a basis for a lecture or seminar on ligand field theory. Without such additional introduction the reader who, as stated in the Foreword, has mastered only the "simplest principles" of quantum mechanics, would hardly be able to follow the necessarily concise expositions. For example, finding the energy levels relating to a many-electron problem would be difficult for such a reader.

Several misprints and blemishes in the setting could certainly be corrected in the next edition: one example is the repeated confusion between v and υ. Superscripts, *e.g.* those characterizing an approximation step, should be placed consistently in parentheses, at least within one and the same formula. The angular momentum quantum number l should not be printed in italics when this is not done with any of the other quantum numbers. The additional problems set are certainly very useful, yet the reviewer doubts whether the reader would be able to solve them after going through this book; they should at least be complemented by provision of the answers.

Karl Hensen [NB 237 IE]

Ionenkristalle, Gitterdefekte und Nichtstöchiometrische Verbindungen (Ionic Crystals, Lattice Defects and Non-stoichiometric Compounds). By *N. N. Greenwood*. Translated by *H.-G. von Schnering* and *B. Kolloch*. Verlag Chemie GmbH, Weinheim 1973. 1st Edit., viii, 185 pp., 60 figures, 26 tables, paperback, DM 28.—.

The declared aim of this book, "to give the first systematic and comprehensive account of modern views on the influence of lattice defects on the properties of ionic solids", is certainly pitched too high, since the first edition of *Kröger*'s "The Chemistry of Imperfect Crystals" appeared as early as 1964, four years before the first edition of the English original of the book reviewed here. The book rather provides an introduction, for the most part intelligibly presented, to the chemistry of imperfect ionic crystals, and its evolution from a lecture manuscript can be recognized, not least by the skilfully selected examples. The first three chapters are devoted to ideal ionic crystals, occupying a relatively large space (about 60 pages), even after taking into account the "chemical" viewpoint that the author intentionally emphasizes. The next three chapters are concerned with lattice defects in "stoichiometric" and "non-stoichiometric" crystals, although in the introduction to Chapter 6 the author himself recognizes this differentiation to be "arbitrary in the narrow sense". The last chapter describes the experimental study of non-stoichiometric phases. Surprisingly, the relation between vacant sites and material transport is handled explicitly in only four pages, and the study of lattice defects by magnetic resonance is merely mentioned (Chapter 4).

Summarizing, it may be stated that this translation, satisfactorily produced and in fluent, almost faultless German, is not exactly good value for money in comparison with the original (DM 16.—), but it is certainly suitable for readers interested in a concise introduction to the chemistry of imperfect ionic crystals.

G. Borchardt [NB 240 IE]

Reaktionsmechanismen der Organischen Chemie. Ein Seminarbuch (Reaction Mechanisms in Organic Chemistry. Seminar Book). By *H. Höver*. Verlag Chemie GmbH, Weinheim and John Wiley & Sons, New York 1973. 1st Edit., 565 pp. 23 figures, 28 tables, paperback, DM 48.—.

Traditional textbooks on reaction mechanisms in organic chemistry generally begin with a section on methods and then treat the various types of reaction. The reader can then test and extend his knowledge by means of the problems set at the end of each section.

The present book turns this arrangement upside down. It begins by setting out the problems on the first pages, and in the 500 pages of the second part accompanies the solution of the specific exercises with a very broad and complete description of the field. The author's intention of presenting a typical seminar book is thus realized.

The 210 problems are presented according to a systematic scheme: Structural formulas are given for the starting materials, but the intermediates and the end products are written as molecular formulas and characterized by IR, UV, and NMR data. Each reaction is studied in detail, so that often more than ten molecular formulas have to be unravelled. Special attention is paid to seeing that the mechanism explains the formation of all the products.

Most of the often very specialized problems are barely soluble by even an advanced student, so that sensible use of this book would be by joint work on the problems within the framework of a seminar. In this way the student would learn in detail all the reaction types in organic chemistry; the greatest emphasis is placed on important research areas such as the Woodward-Hoffmann rules. The chemistry of radicals and photochemistry are treated too sparingly. It is also apparent that the results of kinetic measurements are not sufficiently included in the discussions.

Apart from these criticisms it seems to me that the author has succeeded in producing a comprehensive modern book on reaction mechanism, especially suitable for seminar work with advanced students.

Bernd Giese [NB 241 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Elementarphysik griffbereit. Definitionen, Gesetze, Tabellen. By *N. I. Koschkin* and *M. G. Schirkjewitsch*. Vieweg, Braunschweig 1974. XV, 232 pp., bound, DM 19.80.

Hydrogen Bonding. By *M. D. Joesten* and *L. J. Schaad*. Marcel Dekker, Inc., New York 1974. VI, 622 pp., bound, $ 45.—.

Carbanions: Mechanistic and Isotopic Aspects. By *E. Buncel*. Vol. 9 of the series "Reaction Mechanisms in Organic

Chemistry". Edited by *C. Eaborn* and *N. B. Chapman*. Elsevier Scientific Publishing Company, Amsterdam 1975. X, 270 pp., bound, Dfl. 80.00.

BBA Library 12: Membrane-Active Complexones. By *Yu. A. Ovchinnikov, V. T. Ivanov*, and *A. M. Shkrob*. Elsevier Scientific Publishing Company, Amsterdam 1974. XII, 464 pp., bound, Dfl. 135.00.

Chemical and Biochemical Applications of Lasers, Vol. I. Edited by *C. Bradley Moore*. Academic Press, New York 1974. XI, 398 pp., bound, $ 29.50.

Advances in Chromatography, Vol. 11. Edited by *J. C. Giddings* and *R. A. Keller*. Marcel Dekker, Inc., New York 1974. XI, 196 pp., bound, $ 19.75.

Creation and Detection of the Excited State, Vol. 3. Edited by *W. R. Ware*. Marcel Dekker, Inc., New York 1974. VIII, 193 pp., bound, $ 23.50.

Die Analyse der Luft und ihrer Verunreinigungen in der freien Atmosphäre und am Arbeitsplatz. By *W. Leithe*. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart 1974. 2nd revised edition, XV, 303 pp., bound, DM 74.—.

Chemistry and the Needs of Society. A Symposium held at Imperial College, London, 2—5 April 1974. The Chemical Society, London 1974. IV, 249 pp., stitched, £ 3.00.

Selenium. Edited by *R. A. Zingaro* and *W. Ch. Cooper*. Van Nostrand Reinhold Company, New York 1974. XVII, 835 pp., bound, £ 25.20.

Integral Equations via Imbedding Methods. By *H. H. Kagiwada* and *R. Kalaba*. Vol. 6 of the series "Applied Mathematics and Computation". Edited by *R. Kalaba*. Addison-Wesley Publishing Company, Reading, Mass. 1974. XVIII, 382 pp., bound, $ 19.50; stitched, $ 12.50.

Gas Chromatography of Coating Materials. By *J. K. Haken*. Marcel Dekker, New York 1974. XV, 334 pp., bound, $ 29.75.

Houben-Weyl: Methoden der organischen Chemie. 4th completely revised edition. Edited by *E. Müller* in collaboration with *O. Bayer, H. Meerwein* (dec.), and *K. Ziegler* (dec.). Vol. 15, Part 1: Synthese von Peptiden. Edited by *E. Wünsch*. Georg Thieme, Stuttgart 1974. XLIII, 1006 pp., bound, DM 540.—.

Grundlagen der chemischen Kinetik. By *H. Kehlen, F. Kuschel*, and *H. Sackmann*. Vol. 148 of "Wissenschaftliche Taschenbücher". Akademie-Verlag, Berlin 1974. 196 pp., stitched, *ca.* DM 9.—

Temperaturbeständige Faserstoffe aus anorganischen Polymeren. By *H. Dawczynski*. Vol. 152 of "Wissenschaftliche Taschenbücher". Akademie-Verlag, Berlin 1974. 178 pp., stitched, *ca.* DM 9.—

Analytical Chemistry of Transplutonium Elements. By *B. F. Myasoedov, L. I. Guseva, I. A. Lebedev, M. S. Milyukova*, and *M. K. Chmutova*. From the series "Analytical Chemistry of the Elements". John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1974. X, 404 pp., bound, £ 12.00.

Recent Analytical Developments in the Petroleum Industry. Edited by *D. R. Hodges*. Applied Science Publishers Ltd., Barking 1974. IX, 337 pp., bound, £ 10.00.

Introductory Eigenphysics. An Approach to the Theory of Fields. By *C. A. Croxton*. John Wiley & Sons, London 1974. X, 275 pp., bound, £ 6.95; stitched, £ 3.95.

Systematic Materials Analysis, Vol. III. Edited by *J. H. Richardson* and *R. V. Peterson*. From the series "Materials Science and Technology". Edited by *A. M. Alper, J. L. Margrave*, and *A. S. Nowick*. Academic Press, New York 1974. XIX, 385 pp., bound, $ 29.00.

La Liaison Chimique. By *P. Laszlo*. Vol. I of the series "Leçons de Chimie". Hermann, Paris 1974. XIII, 188 pp., bound, FF 58.

Biochemische Grundlagen der Humangenetik. By *H. Harris*. Verlag Chemie, Weinheim 1974. 292 pp., bound, DM 38.—.

Ullmanns Encyklopädie der technischen Chemie, Band 4: Verfahrensentwicklung und Planung von Chemieanlagen – Dokumentation. Verlag Chemie, Weinheim 1974. XVI, 728 pp., half-leather DM 385.—(Subscription price DM 345.—).

Using the Chemical Literature. A practical guide. By *H. M. Woodburn*. Marcel Dekker, New York 1974. VIII, 302 pp., stitched, $ 14.50.

Applied Spectroscopic Reviews, Vol. 8, Part B. Edited by *E. G. Brame, Jr.*, Marcel Dekker, New York 1974. XIV, 293 pp., bound, $ 29.50.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 4036, 4037, Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim, Pappelallee 3. P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 4031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 3
March 1975
Pages 117–192

What Do We Know About Nuclear Fission?

By Dieter C. Aumann[*]

Dedicated to Professor H.-J. Born on the occasion of his 65th birthday

Nuclear fission, although a physical phenomenon, is also of interest to the chemist. It was discovered by chemists, and chemists have made a material contribution to our present knowledge in this field. A comprehensive theory of nuclear fission has not, as yet, been developed, despite the volume of experimental data that has amassed in the 35 years since its discovery. In the past few years discoveries have been made which cannot be explained with conventional theoretical models of nuclear fission. The most important discovery was that of shape isomerism, a novel type of nuclear isomerism. It would appear that an accurate calculation of fission barriers is a prerequisite for precise explanation of many experimental findings. Recent results in this connection and an outline of the present state of our knowledge of nuclear fission constitute the main theme of this paper.

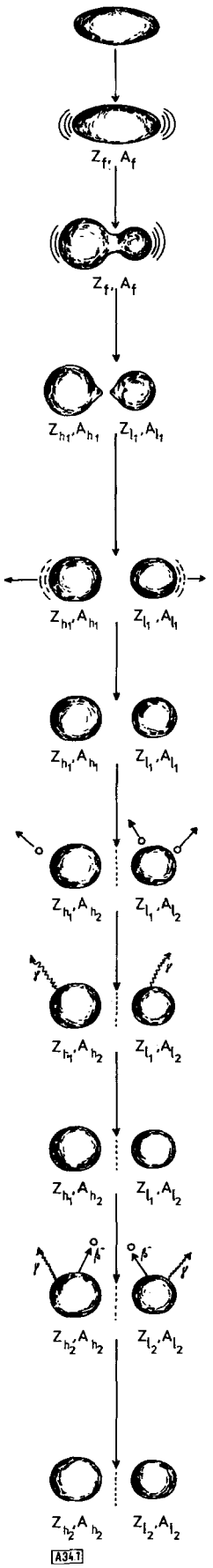
1. Introduction

Only few scientific discoveries have proved so important to the fate of mankind as that of nuclear fission. Its utilization for military purposes, in the form of nuclear weapons, could lead to disaster—as a source of energy it could prove a blessing to the human race. In the Federal Republic of Germany nuclear power accounts for about 3% of the electricity contributed to the national grid. It is to be hoped that this contribution will be increased to about 30% by 1980 and to 40% five years later *i.e.* a contribution of 50000 MW by 1985.

Although 35 years have passed since its discovery, nuclear fission still remains a challenging field for research. A complete theory of nuclear fission has yet to be developed which could suitably describe this complicated nuclear reaction and the phenomena associated with it, such as *e.g.* the probability of fission, energy released in fission, the distribution of neutrons and protons among the fission fragments, the angular distribution of fission fragments, the number and energy of neutrons and gamma quanta emitted by the fission fragments *etc.* Several theoretical models of the fissioning nucleus have been developed, each of which describe some of the aforementioned phenomena, but as yet none is capable of satisfying all experimental findings.

In their two classical publications[1, 2] *Hahn* and *Strassmann* showed that radioactive isotopes of elements from the middle of the periodic system having atomic numbers of about half that of uranium are formed when uranium is irradiated with neutrons. *Meitner* and *Frisch*[3] interpreted this finding, quite correctly, as the splitting or cleaving of the excited uranium nucleus into two roughly equal fragments. They coined the term "nuclear fission" for such a nuclear reaction, and recognized that it was accompanied by the release of a considerable amount of energy. *Frisch*[4] demonstrated that most of this energy is imparted to the fission fragments as kinetic energy and that the fragments are forced apart by the Coulomb repulsion of their nuclear charges. He was able to observe these fission fragments as large pulses in an ionization chamber.

[*] Priv.-Doz. Dr. D. C. Aumann
Institut für Radiochemie der Technischen Universität München
8046 Garching bei München (Germany)



Target nucleus in equilibrium deformation

Nuclear reaction: particle capture or direct reaction, *e.g.* (d,p) or (α,α′)

Excited nucleus with equilibrium deformation of target and E MeV of excitation energy, nuclear charge number Z_f, mass A_f and angular momentum J_f.

Transition state nucleus with saddle point deformation and $(E-E_f)$ MeV of excitation energy (E_f=fission barrier). Lifetime depends on $(E-E_f)$ and is *ca.* 10^{-15} s for thermal neutron capture.

Scission configuration: two nuclear potentials; fragments highly deformed with the degree of deformation depending upon fragment stiffness; kinetic energies of fragments small; occasional small particle emitted. The fragments have nuclear charge numbers Z_{l_1} and Z_{h_1}, masses A_{l_1} and A_{h_1}, spins J_{l_1} and J_{h_1}

$Z_f = Z_{l_1} + Z_{h_1}$; $\quad A_f = A_{l_1} + A_{h_1}$

Accelerating primary fragments under Coulomb interaction; approx. 10^{-20} s for fragments to reach 90% of their final kinetic energy K.E.; they thus travel *ca.* 10^{-11} cm.

Accelerated primary fragments of high excitation energy separated by a relatively large distance.

Neutron emission (ν_l, ν_h) in $10^{-18}-10^{-14}$ s.
Distance of fragments: 10^{-5}—10^{-9} cm.

$A_{l_1} = A_{l_2} + \nu_l$; $\quad A_{h_1} = A_{h_2} + \nu_h$

γ-ray emission in 10^{-12}—10^{-10} s
Distance of fragments: 10^{-1}—10^{-3} cm.

Primary fission products (secondary fission fragments) in their ground state with nuclear charge numbers Z_{l_1} and Z_{h_1}, masses A_{l_2} and A_{h_2}, and spins J_{l_2} and J_{h_2}. These nuclei are neutron rich and β^--unstable.

β-Decay (with $\tau > 10^{-2}$ s, slow process) to secondary fission products. Occasionally β-decay populates a neutron unstable level: emission of delayed neutrons. Radiochemists investigate the long-lived nuclei of this decay process.

$Z_{l_1} = Z_{l_2} - n_l$; $\quad Z_{h_1} = Z_{h_2} - n_h$ (n_l, n_h number of β-decays)

Stable end products

Fig. 1. Schematic representation of the successive steps of nuclear fission (after [13]).

The original works on nuclear fission were reviewed by *Turner*[5] in an article which was able to be published just before the use of nuclear fission for military purposes was recognized, and the outbreak of the second world war hampered further publications in this field. It was as late as 1951 before some of the major works that were carried out on nuclear fission during the war years in the USA were able to be published[6]. Radiochemical investigations carried out in Germany on fission products during the first years after the discovery of nuclear fission were reported by *Seelmann-Eggebert* and *Strassmann*[7]. In the following years several review articles and monographs were published, giving detailed accounts of the latest data on nuclear fission and up-to-date developments on the theory of fission[8-14]. Since 1965, the International Atomic Energy Agency (IAEA) has arranged symposia on the physics and chemistry of fission which are held at intervals of four years[15-17].

Although a physical phenomenon, nuclear fission is of great interest to the chemist for it leads to outstanding and important chemical changes. Isotopes of more than 35 elements having about half the nuclear charge of the original element are formed during the fission of a heavy element. The chemist is responsible for the production of highly pure uranium for use as fuel in reactors, and for the processing of burnt fuel elements which are poisoned with fission products and transuranium elements. Nuclear fission was discovered by chemists, and chemists have made a considerable contribution to the present state of our knowledge in this field. Since the middle sixties, however, refined physical methods of measurement, especially coincidence and multiparameter measurements with semiconductor detectors, faster electronics, larger multichannel analyzers and computers, have pushed radiochemical methods more and more into the background. With radiochemical methods one measures the yields of isotopes of one element or a few elements formed in fission. With physical methods the whole range of fission products can often be recorded in a single experiment. Radiochemical techniques are relatively slow and identify fission products only when all intermediates have already decayed (see Fig. 1). Furthermore, the fission products are detected integrally *i. e.* no distinction is made between otherwise like fission products which have been formed with different kinetic energy, or those arising from the fission of various highly excited nuclei, or those formed directly from the fissioning nucleus or by β-decay of another fission product. Physical coincidence techniques, on the other hand, permit simultaneous measurement and correlation of several quantities; *e.g.* the number of neutrons emitted per fragment can be determined as a function of fragment mass.

Radiochemical methods can, however, be used to great advantage if fission products which are formed in very small yields have to be isolated from the complex mixture of fission products. With chemical methods of separation, the mixture is resolved into components according to the atomic number Z; the mass number A is determined by radioactivity measurements on the isolated fission products, so that very small amounts of an atomic nucleus ${}^{A}_{Z}X$ can be isolated and identified from a large excess of several orders of magnitude ($>10^{12}$) of other fission products. Since the chemical methods integrate over longer times, all the atomic nuclei formed during one experiment are collected so long as their half-life is not too short. Thus extremely less-probable processes can be detected. Hence, for many problems radiochemical methods are irreplaceable. With the aid of such methods it was possible *e.g.* to detect the very low-probability fission of heavy nuclei of average excitation energy into three almost equally sized fragments[18-20] or to measure the population of shielded fission product isomers of very small yield[21]. Radiochemical methods are also superior to physical methods when investigating the fission of nuclei having high specific alpha activity, *e.g.* ^{254}Fm. In the present progress report the most recent results and the present state of our knowledge of nuclear fission will be discussed. In the absence of a comprehensive theory this will be done from the standpoint of the experimenter, especially the radiochemist. The volume of experimental material reported in the literature on this topic is so large, however, that a certain amount of selection has had to be made. An attempt is also made to indicate the gaps in our knowledge of nuclear fission and to outline the problems which can be resolved especially with the aid of radiochemical methods.

2. When and How Does an Atomic Nucleus Fission?

An atomic nucleus can split into two or more fragments if sufficient excitation energy is supplied to it to overcome the fission barrier (fission threshold). This excitation energy is provided by nuclear reactions which are initiated by bombarding the nucleus with neutrons, photons or charged particles. The heaviest elements ($Z>90$) might even split "spontaneously", without being externally excited; in this process, the potential barrier is penetrated similarly as in alpha decay, by quantum mechanical tunnelling. The nature of the fission process (Fig. 1) remains the same in many ways, from very low excitation energies (near the fission threshold) up to moderate excitation energies of fissioning nuclei (about 50 MeV).

Shortly after the discovery of nuclear fission, *Bohr* and *Wheeler*[22] tried to interpret the "splitting process" on the basis of the liquid drop model. The atomic nucleus was regarded as a charged liquid drop whose stability is determined by two opposing forces. The short-range nuclear forces hold the nucleus together, analogous to the surface tension of a liquid drop, while the repulsive Coulomb forces between the protons try to split the nucleus apart. The stability and shape of a nucleus depend upon the balance or imbalance between the electrostatic forces and the nuclear forces. If such a drop is deformed its stability decreases. The surface area of the nuclear drop is at the same time enlarged; work is done against the surface tension, and the potential energy of the nucleus increases, at first much more rapidly than the Coulomb energy decreases. If the electrostatic repulsion is finally greater than the surface tension then deformation of the nucleus increases until the latter finally necks and splits into two parts.

Fig. 2 shows the potential energy of the nucleus as a function of its deformation, calculated according to the liquid drop model. The potential barrier is shown over which the nucleus must pass in "prompt" fission induced by external excitation, or tunnel through in the case of spontaneous fission.

If sufficient activation energy is supplied to a heavy nucleus, it can become deformed to such an extent that its potential

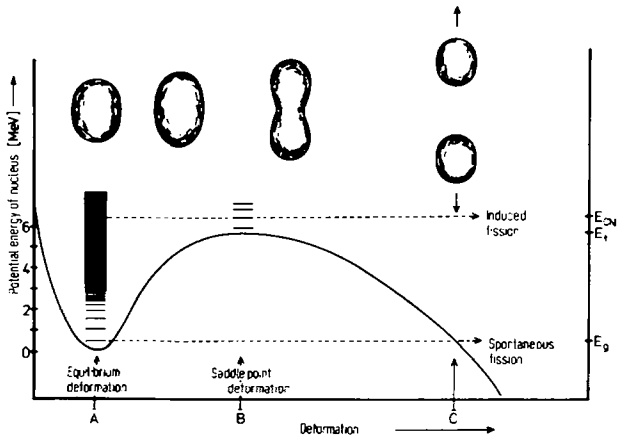


Fig. 2. Schematic representation of the fission barrier according to the traditional liquid drop model. The potential energy of the fissioning nucleus changes with deformation. The energy levels of the nucleus in the ground state and in the saddle point are shown. E_f is the height of the fission barrier; E_{CN} is the excitation energy of the compound nucleus (excited nucleus), which must be higher than E_f for the excited nucleus to fission; and E_g is the ground state of the nucleus from which the spontaneous fission originates. The phases A, B, and C of the fission process are investigated by different experimental methods (see Text).

energy reaches a maximum. This labile equilibrium state between the repulsive Coulomb forces and attractive nuclear forces is referred to as the "saddle point" configuration or "transition" nucleus. The least amount of energy which must be supplied to the nucleus to reach the saddle point is called the critical deformation energy, fission barrier, or fission threshold. The nucleus deformed to the saddle point configuration is expected to have a spectrum of excited states similar to those of a nucleus near its ground state, since the greater part of its excitation energy is present as deformation energy.

The states of the nucleus in the saddle point deformation are called "transition states" or "fission channels". Each fission channel is characterized by a set of quantum numbers and by its saddle point energy.

If the nucleus is deformed beyond the saddle point configuration it is cleaved into two fragments by the Coulomb forces, the nuclear potential of the fissioning nucleus being divided into the nuclear potentials of the two separating fragments. This stage of the deformation is called the "scission configuration". It is at this stage that the distribution of protons and neutrons, excitation energy and angular momentum to the two fission fragments is finally decided. These fission fragments are formed with mass and charge numbers which vary over a wide range, and they contain different amounts of excitation energy. They are accelerated to kinetic energies totalling about 160 MeV by the Coulomb forces, which on their part depend on the proton and neutron composition of the fragments. One thus observes mass, charge and energy distributions in the fission fragments.

If the deformed fission fragments convert into their equilibrium form, their deformation energy is transformed into internal excitation energy. The fragments become heated and neutrons are evaporated off. The fission fragments give up the remainder of their excitation energy in the form of gamma quanta. The fragments are now referred to as secondary fission fragments or primary fission products. These processes are illustrated in Fig. 14 (Section 10).

The secondary fission fragments are formed in the ground state, but they are very neutron rich *i.e.* they are unstable toward β-decay and are thus radioactive. Only at this stage of the fissioning process can radiochemical experiments come to our aid. The radiochemist separates the β-unstable fission products and studies the longer-lived atomic nuclei (> 1 s).

Since a complete theory of the fission process is still lacking, information about this process and its individual steps must be sought by experiment. These experiments ought to answer two questions: 1. When does a nucleus fission? and 2. How does a nucleus fission?

The first question can be answered with experiments in which the fission probability of atomic nuclei and its change with excitation energy is measured. The second question can be studied with experiments which show how mass, charge, energy, and angular momentum of the fissioning nucleus are distributed to the fission fragments and how these distributions change when different types of atomic nuclei are fissioned.

In figure 2 the three phases A, B and C of the fission process are indicated. Phase A involves formation of the compound nucleus, its excitation and its path along the potential barrier, *i.e.* the problem of when a nucleus fissions. The experiments which throw light on the nature of phase A are those in which measurements are made on the lifetimes of spontaneously fissioning nuclei, the fission threshold and fission cross section as a function of mass, charge and energy of the excited nucleus, the competition between fission and other forms of decay of the nucleus such as neutron or gamma quanta emission; in short the probability of fission of nuclei under various conditions.

In phase B saddle point deformation and nuclear states at the saddle point are investigated. Information on this phase is obtained mainly by accurate measurements of the fission cross section as a function of angle and energy. Studies on the angular distribution of the fission fragments and its energy dependence allow characterization of the quantum numbers and energies of the transition states.

The question "How does a nucleus fission?" is answered by experiments in region C which study the descent of the fissioning nucleus from the saddle point deformation to the scission configuration and the formation of the fission fragments. The kinetic energy of the fragments and the number of prompt neutrons and gamma quanta are measured as a function of the excitation energies of the nuclei; it is then possible to determine the distribution of the excitation and deformation energy to the two fragments. Measurements of mass and charge distributions of the fission fragments and the energy dependence of these distributions afford information on the partition of the nucleons of the fissioning nucleus to the two fragments. Determination of the angular momentum of the two fission fragments likewise provides interesting insights into the processes taking place in phase C.

Very frequently it is impossible to measure these quantities for the primary fission fragments, since the time in which they emit neutrons and gamma quanta is very short (see Fig. 1). In addition, these processes lead to new distributions of such quantities in the secondary fission fragments. Attempts must then be made to infer these quantities for the fission fragments from measurements of the corresponding quantities in fission products.

3. The Double-Humped Fission Barrier

In the course of the last 10—15 years more and more experimental findings have indicated that it is too crude to treat an atomic nucleus as an electrically charged drop of incompressible liquid. Admittedly, the liquid drop model describes the average properties of atomic nuclei in the ground state and in the fission process quite conveniently, but it fails in detail.

Thus experimentally determined nuclear masses in the neighborhood of nuclei containing the well-known "magic" number of protons and neutrons, 2, 8, 20, 28, 50, 72 and 126, show a small but clearly systematic deviation from the nuclear masses calculated with the liquid drop model. Although the average deviation of the total binding energy, which lies in the order of $8 \times A$ MeV (A = mass of nucleus), is only a few MeV, the magic nuclei prove to have a binding energy up to 13 MeV higher than would be predicted by the liquid drop model.

The liquid drop model predicts a sharp decrease of the fission barriers as a function of the quantity Z^2/A of the fissioning nucleus. The measured fission thresholds of heavy nuclei, however, decrease much more slowly. Fig. 3 compares experimentally determined fission barriers with those calculated on the basis of the liquid drop model. The barrier heights calculated for elements heavier than thorium are too low and decrease too rapidly with increasing Z. (On the basis of this decrease of the fission barriers predicted by the liquid drop model, it was long ago concluded that there was a theoretical limit to the periodic system at $Z \approx 100$ –110.)

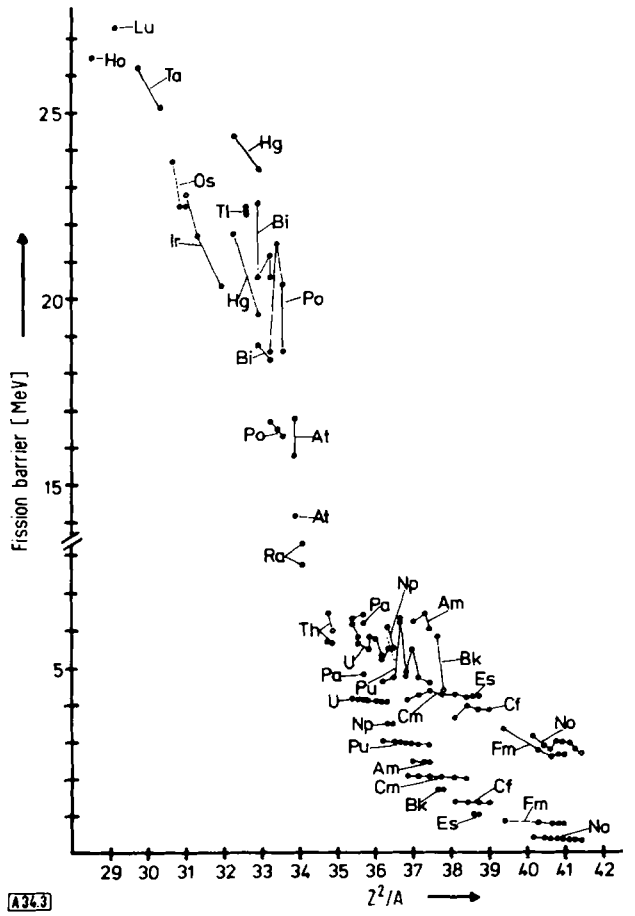


Fig. 3. Fission barriers as a function of Z^2/A of the fissioning nucleus; (○) experimental, (●) calculated with the liquid drop model (values from [23—25]).

The liquid drop model also fails completely when called upon to explain the preferred asymmetric fission of the heavy nuclei into two unequal fragments (see Section 8) and the saw-toothed distribution of the number of neutrons emitted from fission fragments (see Section 13).

These inadequacies of the liquid drop model have always been attributed to "shell effects" originating in the shell structure of the atomic nuclei. The shell model of the atomic nuclei, in which each nucleon is treated as moving independently of the other nucleons in an average potential which is produced by mutual interaction of all nucleons, was able to predict the magic numbers of protons and neutrons which correspond to closed shells. The properties of atomic nuclei in the ground state and in excited states such as spin and parity, magnetic moment, the occurrence of long-lived isomers *etc.* could also be described, firstly for spherical and later also for deformed atomic nuclei after *Nilsson*[26] had extended the shell model to non-spherical nuclei. The experimentally determined deformations of many nuclei in the ground state could be reproduced with the aid of the Nilsson model.

However, the Nilsson model proved unsatisfactory when applied to strongly deformed nuclei, as occur in fission. The binding energy of a nucleus calculated as a function of its deformation did not vary at all in the form of a fission barrier.

Neither of the two nuclear models alone— the liquid drop model nor the shell model—could provide a reliable picture of the strongly deformed fissioning nucleus. It was as late as 1968 before *Strutinsky*[27, 28] was able to amalgamate the liquid drop and the shell model for describing the properties of strongly deformed nuclei quantitatively. The total binding energy of a nucleus is represented as the sum of two quantities: the slowly changing liquid drop energy $E_{LD}(Z,N)$, which is an average value for the uniformly distributed nucleons in the phase-space, and the shell correction $\Delta E_s(Z,N,\beta)$ which oscillates with the deformation β of a nucleus and corresponds to the deviations from this uniform distribution.

$$E(Z,N,\beta) = E_{LD}(Z,N) + \Delta E_s(Z,N,\beta) \qquad (1)$$

The underlying principle is that a macroscopic model, namely the liquid drop model, quantitatively reproduces the smooth trend of the binding energy of the nuclei with respect to their number of nucleons and their deformation, while a microscopic model, namely the single particle or shell model, describes the "local" fluctuations but not the smooth trends. If both models could be united, both the smooth trend and the "local" fluctuations ought to be reproduced[29].

Strutinsky generalized the usual definition of "shells" and regarded them as regions of low density of the single-particle energy levels near the Fermi energy (*i.e.* that energy up to which all single-particle levels in a certain nucleus are occupied). Figure 4 illustrates the effect of a variation of the local level density of single-particle states on the binding energy of a nucleus. In the arrangement shown on the left the binding energy of the nucleus will be greater than in the arrangement shown on the right, since the nucleons occupy the deeper and more bound states because of the lower level density near the Fermi energy.

The variations of the level density not only occur from nucleus to nucleus as a function of the respective number of nucleons, but also in one and the same nucleus, *i.e.* with a constant number of nucleons, as a function of the deformation of the nucleus. It follows, therefore, that shells can occur not only in spherical nuclei but also in deformed nuclei. For a certain

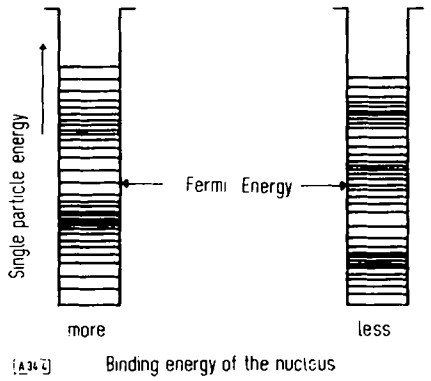


Fig. 4. Effect of local level density of single-particle states on the binding energy of the nucleus (after [30]).

number of nucleons there are quite distinct deformations in which the nucleus is stable. The ^{235}U nucleus is already deformed in the ground state because the most stable arrangement for the number of nucleons of this nucleus results not in a spherical but in a deformed nucleus. Figure 5 gives a qualitative illustration of the distribution of the single-particle states in a nucleus as a function of the deformation.

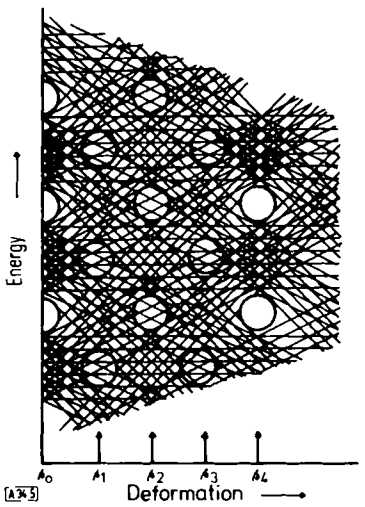


Fig. 5. Schematic representation of the distribution of single-particle states in a deformed nucleus. The low density regions (shells) are shown by circles (after [30]).

The regions of low level density are indicated by circles. They appear at the deformations β_1, β_2, β_3, β_4 *etc.* and correspond to magic numbers of nucleons at specific shapes of the nucleus. If the single-particle levels of a nucleus in a certain deformation are occupied just up to one of these regions then a shell is closed. Such nuclei with this deformation will be exceptionally stable. In Fig. 5, in addition to the well-known shells in spherical nuclei ($\beta=0$), other shells appear at the same energy for deformations β_2 and β_4. Shells likewise appear at deformations β_1 and β_3, while in spherical nuclei regions of high level density are present at the same energy.

The potential energy of a nucleus as a function of its deformation can be calculated in the following five steps[29]:

1. Specification of the shape of the nucleus,
2. Calculation of the "macroscopic" part of the potential energy by means of the liquid drop model,
3. Definition of the single-particle potential "felt" by the nucleons,
4. Solution of the Schrödinger equation to obtain the energies of the single-particle levels, and
5. Calculation of the "microscopic" part of the potential energy, the shell correction, from the single-particle energies.

The total potential energy of a nucleus is then given by the sum of the "macroscopic" energy calculated in Step 2 and the "microscopic" shell correction calculated in Step 5. The magnitude of the shell correction is only a few MeV; the binding energy calculated for heavy nuclei by the liquid drop model is of the order of 1600–2000 MeV. These small corrections, however, are important, since the fission threshold of heavy nuclei is only about 5—6 MeV (see Figures 2 and 7).

Several groups, who have performed such theoretical calculations arrive at qualitatively similar results. They are summarized in review articles by *Nix*[29], *Brack et al.*[31], and *Pauli*[32].

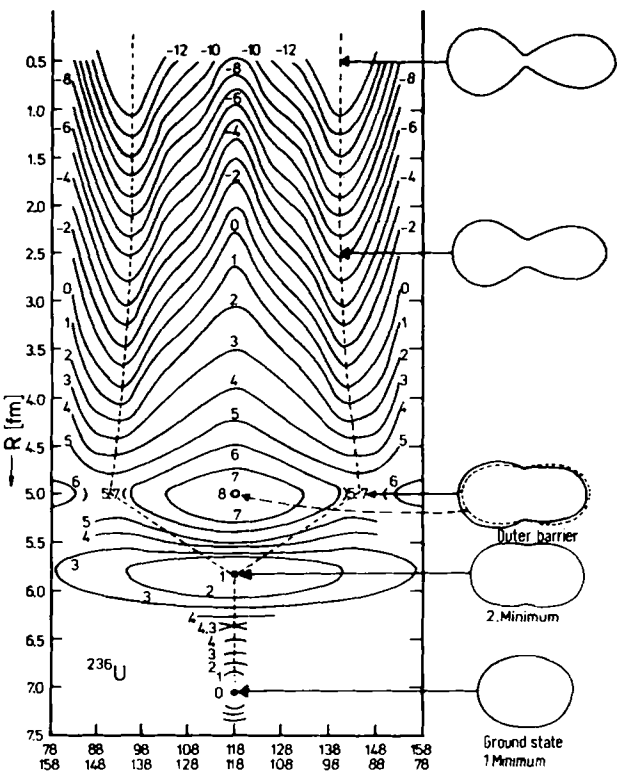


Fig. 6. Potential energy surface for ^{236}U. The sites of equal energy are shown as a function of the shape of the fissioning nucleus. The shape of the nucleus is described by the radius R of the neck and the mass ratio of the portions of the nucleus on either side of the neck plane. The path of minimum potential energy from the ground state, over the inner barrier into the second minimum, over the outer barrier and along a valley to scission is indicated by dotted lines (modified after [33]).

To illustrate the results of such calculations Fig. 6 shows the potential energy surface of the ^{236}U nucleus, *i.e.* its potential energy as a function of its deformation[33]. A vertical cut through such potential energy surfaces along the symmetry axis, *i.e.* along the mass ratio 118/118 yields a trend of the nuclear potential energy which is shown schematically in Fig. 7. The surprising result of these calculations is that the fission barrier in the actinoid nuclei has a double humped shape. The two potential maxima are separated by a second potential minimum, which is located about 2—3 MeV higher than the minimum which represents the ground state of the nucleus. If a nucleus deforms, then its potential energy at first increases with the deformation, reaches a maximum over the first (inner) barrier, then decreases again until the second minimum is reached. In this second minimum the nucleus is two to three times more strongly deformed than in the ground state. Since a nucleus in this second minimum is hindered by the inner and outer potential barriers A and B to decay, it is metastable and relatively long-lived. If the nucleus is deformed further its potential energy increases again. The nucleus then passes over the second barrier, approaches the scission configuration and finally decays into two fragments. The deformations of the nucleus along this path are illustrated in Fig. 7.

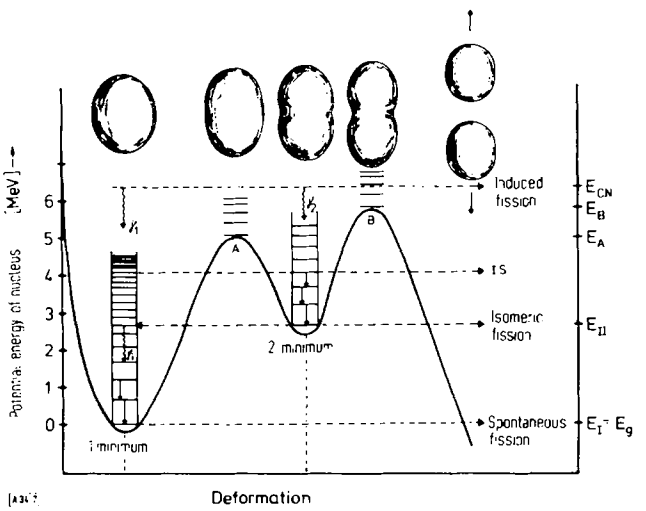


Fig. 7. Schematic representation of the double humped fission barrier as given by amalgamation of liquid drop and shell models. The nuclear states in the first and second minimum are shown together with the excitation states of the nucleus at the barriers A and B. Energy E_I is the ground state of the first minimum, E_{II} is the ground state of the second minimum; E_A and E_B are the heights of the inner and outer barriers, and E_{CN} the excitation energy of the compound nucleus. Spontaneous fission from the ground state and from the isomeric state ensue from the lowest energy level in the first and second minimum, respectively. A nucleus in the second minimum with energy E_{II} is in a metastable state since it lies between two potential barriers. It can tunnel through the potential barrier B and spontaneously fission, or through the potential barrier A and de-excite by gamma emission (γ_i). A compound nucleus formed with an excitation energy E_{CN}, which lies above the potential barrier, can either undergo prompt fission or give up its excitation energy in the form of gamma rays (γ_1 or γ_2) and decay to levels in the first or second minimum. I.S. signifies intermediate structure in sub-barrier fission cross section.

Which experimentally observable events can we expect if the fission barrier has a double humped shape? During the past few years a few phenomena have in fact been discovered which could only be explained with difficulty without the existence of a double humped fission barrier, namely the spontaneously fissionable isomers and the intermediate structures in subthreshold fission cross sections.

4. Spontaneously Fissionable Isomers

The first isomer, which decays by spontaneous fission, was discovered by *Polikanov et al.*[34] in the Joint Institute for Nuclear Research in Dubna (USSR). It was a chance discovery during attempts to synthesize nuclei of the transcurium elements by bombarding isotopes of the actinoids such as ^{235}U, ^{238}U, ^{232}Th with heavy ions such as ^{11}B, ^{16}O, ^{20}Ne, ^{22}Ne. In these experiments a nucleus was formed which decayed by fission with a half-life of 14 ms. This fission activity could subsequently be attributed to the nucleus ^{242}Am. The half-life of 14 ms was shorter by a factor of 10^{19} than that predicted for ^{242}Am on the basis of systematics for ground-state spontaneous fission.

This enormous increase in the probability of fission was difficult to understand. The probability to tunnel through the potential wall, by which the lifetime of the spontaneously fissioning nucleus is determined (see Fig 2), would increase by a factor of 10^{19} if the nucleus had an excitation energy of 2—3 MeV, *i.e.* if it was excited into an excited state in the ground-state minimum of the potential energy curve as shown in Fig. 2. Such an excited state should of course decay in times much shorter than milliseconds to the ground state by emission of gamma quanta.

The transition into the ground state must accordingly be delayed for some reason. Such a delay could be effected by a very high spin of the excited isomeric state, which, however, would have to be 20 ħ and more. And then when it was discovered that the spontaneously fissionable isomer of ^{242}Am is also formed[35] on irradiation of plutonium and americium nuclei with alpha particles, deuterons and neutrons *via* the nuclear reactions $^{239}Pu(\alpha,p)\,^{242mf}Am$, $^{242}Pu(d,2n)\,^{242mf}Am$, $^{243}Am(n,2n)\,^{242mf}Am$, and $^{241}Am(n,\gamma)\,^{242mf}Am$, the puzzle deepened, for the "light" deuterons and neutrons introduce substantially less than 20 ħ of angular momentum into the reaction product. The generation of the high spin *via* gamma cascades, which could occur in the formation of the isomer, also appeared unlikely.

An experiment by *Flerov et al.*[36] also contraindicated a high spin. These authors determined the ratio of the production of the spontaneously fissionable isomer $^{242mf}Am$ to the production of the ground state ^{242}Am, the isomer ratio, as a function of the average angular momentum of the compound nucleus, whose decay leads to formation of the spontaneously fissionable isomer $^{242mf}Am$. The isomeric ratio for a high-spin isomer should increase monotonically with the mean spin of the compound nucleus, a phenomenon which has been confirmed by experiment on other isomeric nuclei. In the production of $^{242mf}Am$ *via* compound nuclei with differing angular momentum, however, it was shown that the isomeric ratio $^{242mf}Am/^{242}Am$ is almost independent of the angular momentum of the compound nuclei. Hence another cause must be responsible for the simultaneous increase in probability of fission and decrease in probability of gamma decay.

Investigations on other heavy nuclei soon showed that the fissionable isomer of ^{242}Am is no exceptional case, but that "fission isomers" occur in many nuclei between Th and Bk. The spontaneously fissionable isomers known to date are shown in Fig. 8[37] together with their half-lives, which lie between 10^{-11} and 10^{2} s.

The first fission isomer to be discovered, ^{242m}Am, is still that with the longest half-life known to-date. Spontaneously fissionable isomers with half-lives in the millisecond range are sought for by an experimental technique which utilizes the momentum which is transferred from the projectile nucleus to the compound nucleus. As target material foils are used which are so thin (*ca.* 20 –50 μg/cm^2) that the reaction products escape from the target because of their momentum. These recoil atoms are allowed to strike a rapidly rotating wheel and the nuclei thus collected out of the accelerator beam are carried past a series of fission-sensitive detectors. Expecially suitable are fission track detectors[38] which are dielectric materials such as mica, glass, plastics (polycarbonates). The structure of these materials is more strongly radiation-damaged along the trail of a charged particle on slowing down heavy ions than on slowing down lighter particles. These "latent" tracks of the heavy ions, *e.g.* of fission products of spontaneously fissionable isomers can be enlarged under certain conditions, by chemical etching in HF or NaOH solutions, so that they become visible under a microscope.

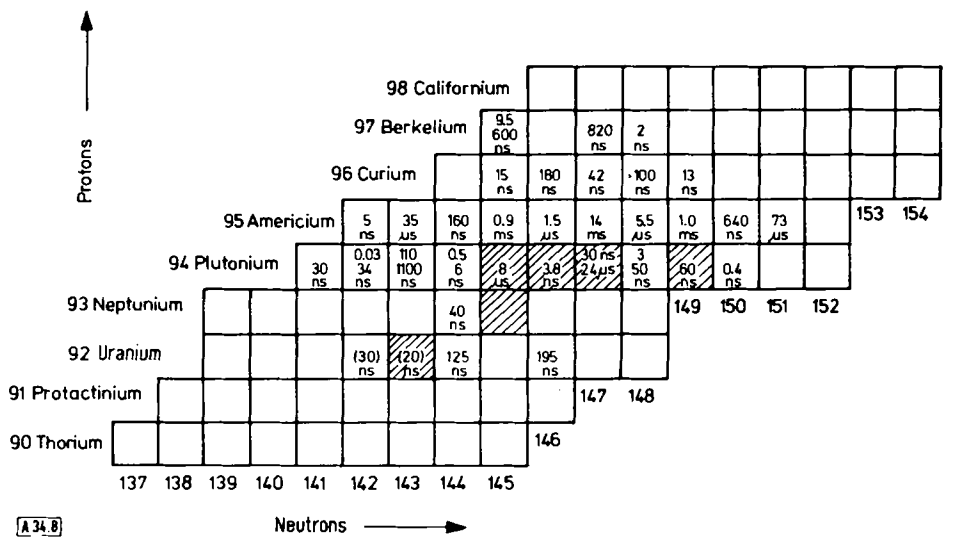


Fig. 8. Section from the chart of nuclides in the region of the actinoids showing the half-lives of all fission isomers known to date. Two numbers in the same field indicates the existence of spin isomers within shape isomers. Shaded fields indicate nuclides for which intermediate structures in the sub-barrier fission cross section have been observed.

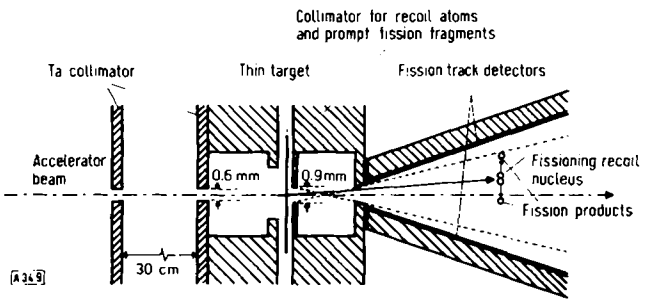


Fig. 9. Experimental arrangement for the measurement of fission isomers with half-lives between 1 microsecond and 5 nanoseconds. The polycarbonate foils used as fission track detectors are arranged to record only delayed fissions from the recoil nuclei flying from the target, not the prompt fissions in the target itself (after [97]).

Such fission track detectors are also used in the method in which the fission isomers with half-lives in the region of microseconds down to about 5 nanoseconds can be measured. Most of the fission isomers discovered to-date have half-lives that lie in this range. The experimental arrangement is illustrated in Fig. 9: A finely collimated beam of protons, deuterons or alpha particles strikes the target from the left. Targets whose thickness lies within the same order of magnitude as the range of the compound nuclei are also used in these experiments; the compound nuclei are driven from the target by transfer of momentum in the direction of the beam. If these nuclei undergo fission during flight between the fission track detectors the fission products will be recorded. The geometrical arrangement hinders direct flight of fission fragments originating from prompt fission from target to fission track detectors. Hence the detectors register only delayed fissions of the fission isomers during the flight of the nuclei. The half-lives are calculated from the velocity of these recoil nuclei and the density of the fission track in the polycarbonate foil as a function of the distance from the target.

The existence of spontaneously fissioning isomers can now be readily explained with the aid of the double-humped fission barrier. If a highly deformed nucleus having an excitation energy which is above the fission barrier (*e.g.* with E_{CN} in Fig. 7) is formed and its excess excitation energy is dissipated in the form of gamma quanta before it fissions, while at the same time the strong deformation of the nucleus is retained, then it can be caught in the ground state of the second minimum of the fission barrier. Since only about 10^{-3}—10^{-2}% of the nuclei reach the second minmum -- the remainder suffer prompt fission—the experimental investigation of these isomeric states is very difficult. They have an excitation energy of 2—3 MeV with respect to the ground state in the first minimum. They are, however, relatively long-lived since the decay is hindered by the inner and outer potential barriers. The nucleus is metastable toward decay by direct radiative transitions to the ground state of the first minimum, *i.e.* the real ground state of the nucleus, for a change in nuclear shape is required prior to gamma decay into the ground state of the first minimum. To do this, the nucleus must

penetrate the potential wall A (see Fig. 7). The enhanced probability of spontaneous fission from the ground state in the second minimum, that is the marked decrease in the half-life of spontaneous fission relative to that from the ground state in the first minimum, is accounted for by the smaller potential barrier B through which the nucleus must tunnel. A nucleus in the ground state of the first minimum, on the other hand, must penetrate the total potential barrier A + B in order to fission spontaneously. The fact that fission isomers have been found only in the case of nuclei between uranium and berkelium is connected with the relative heights of the inner and outer potential barriers. In the case of nuclei above berkelium the outer potential barrier B is so low that the resulting extremely short half-lives have still not been able to be measured. Conversely nuclei below uranium have such a low inner potential barrier that they decay into the first minimum by gamma emission before they can spontaneously fission.

This new type of nuclear isomerism is called shape isomerism so as to emphasize the difference from spin isomerism. Spin isomers are states of one and the same nucleus between which transitions are hindered by gamma emission because their spins differ by several units of ħ. One can compare the shape isomers of atomic nuclei with rotation isomers of molecules, *e.g.* dichloroethane, in which transitions from one configuration to the other are likewise hindered by a potential barrier.

5. Intermediate Structures in the Subthreshold Fission Cross Section

A few years ago the presence of sharp resonances was observed in high resolution measurements of the cross section for induced sub-barrier fission of a few heavy nuclei. These regions of relatively high fission-probability occur in groups separated by wide energy intervals in which no fission takes place. Figure 8 shows those nuclei (shaded) in which intermediate structures have been found in the subthreshold fission cross section[39]. A typical example is shown in Fig. 10[40].

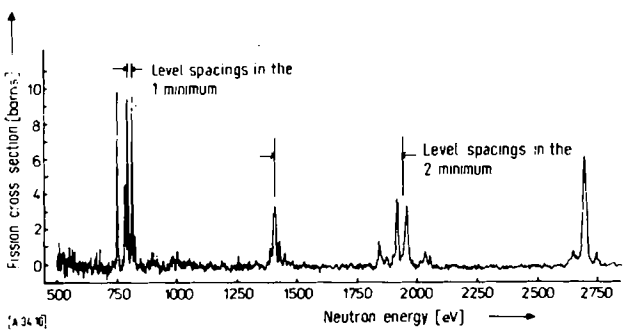


Fig. 10. Subthreshold neutron fission cross section of ^{240}Pu as a function of neutron energy between 500 and *ca.* 3000 eV (after [40]).

In these experiments the compound nucleus formed by penetration of low-energy neutrons into the target nucleus has an excitation energy that lies somewhat below the two potential maxima. In Fig. 7, E_{CN} would lie below E_A. Initially the compound nucleus will have a deformation similar to that of the target nucleus and will be excited to one of the states in the first minimum. The compound nucleus thus formed can only fission by tunneling through the potential barrier. The probability for this at low excitation energies is very small and ought to increase monotonically with neutron energy. The occurrence of some resonance groups is difficult to explain if the fission barrier has only one hump, but is quite understandable if there is a second minimum in the potential energy surface. Then, for a nucleus of the same total excitation energy the average level density in the second minimum must be smaller than in the first minimum because a part of the total excitation energy of a nucleus in the second minimum is bound as deformation energy, so that only a smaller amount is available for other modes of excitation. If the energy of the compound nucleus at a level in the first minimum happens to be approximately equal to the energy of a nuclear state in the second minimum then a coupling of the two states takes place. The nucleus can pass over from the level and deformation of the first minimum into the level and deformation of the second minimum. From this excited state of the shape isomer the probability of fission is increased because of the greater penetrability of the outer barrier B, similarly to the greater probability of fission of the shape isomer compared to that of the nucleus in the ground state. The fine structure in Fig. 10 corresponds, therefore, to the level density of the compound nucleus in the first minimum at an excitation energy of about 5 MeV which originates from the binding energy of the captured neutron. Each group of resonances corresponds to a level in the second minimum.

6. Spectroscopy of Shape Isomers

If the inner potential barrier is not significantly higher than the outer one, a shape isomer can also tunnel through the inner barrier and de-excite by gamma emission to the ground state of the first minimum (γ_i in Fig. 7) instead of spontaneously fissioning. So far such a γ-decay of the shape-isomeric state into the first minimum has been detected only in the case of the 200 ns isomer of ^{238}U[41]. A gamma peak was measured at 2.514 MeV, which is ascribed to a transition from the 0^+ ground state in the second minimum to the lowest 2^+ rotational level at 0.045 MeV in the first minimum. The half-life of this gamma decay agrees with that measured for the spontaneous fission of the shape isomer ^{238mf}U. The branching ratio between gamma decay and spontaneous fission, which has been determined as being about 40, shows that in this case the first barrier is easier to penetrate than the second. This is the first exact measurement to be made of the excitation energy of a shape isomer – which, in this case, amounts to 2.56 MeV.

A group in Munich[42] has recently proved experimentally that fission isomers are indeed strongly deformed nuclei, more strongly deformed than nuclei in the ground state minimum. This being the case, rotational states ought to occur in the excitation spectrum in the second minimum (since a deformed nucleus can rotate and its rotational energy is quantized) built on the shape isomeric state. Since deformation of the nucleus in the second minimum ought to be much greater than that in the ground state it follows that the rotational states must lie closer together than in the rotational band built on the ground state in the first minimum.

By bombarding ^{238}U with 25 MeV alpha particles the Munich team produced the shape isomer $^{240mf}Pu$, whose half-life is 3.8 ns. The compound nucleus ^{240}Pu formed in this nuclear reaction either fissions promptly or decays by emission of gamma quanta into the first minimum (γ_1 in Fig. 7) or, with much lower probability, into the second minimum (γ_2) and there into the isomeric ground state. In the case of even-even nuclei the last transitions (shown by arrows in Fig. 7) ought to be E2 transitions within the rotational band built on the isomeric ground state. These ought to be strongly converted, however, and have lifetimes much shorter than 0.1 ns, *i.e.* short in comparison with the lifetime of the fission isomer. A measurement of coincidences between the conversion electrons from these last transitions and the fission fragments of the isomeric fission from the ground state of the second minimum did in fact show lines in the spectrum of the conversion electrons which could be interpreted as components of three E2 transitions between the states of a rotational band. The rotational constant of 3.33 keV calculated therefrom is considerably smaller than that of the rotational band of the ground state in the first minimum (7.16 keV). It corresponds to the largest moment of inertia, *i.e.* to the largest deformation of an atomic nucleus that has so far been observed. Hence it presents direct evidence that the shape isomer of the ^{240}Pu nucleus is, in fact, connected with a deformation larger than the ground-state deformation.

Attempts to detect the gamma rays alone which are emitted by the compound nucleus when it decays to the ground state of the second minimum have so far been unsuccessful[43].

7. Mass Distribution

A plot of fission fragment or fission product yield as a function of the number of nucleons, *i.e.* mass number, independent of the number of protons, provides a mass distribution or mass yield curve. Radiochemical methods give only the yields of primary and secondary fission products of mass A_{h_2} and A_{l_2}, respectively (see Fig. 1), after emission of prompt neutrons. One determines the cumulative yield of a long-lived fission product at the end of the β-decay chain for as many mass numbers as possible, *i.e.* the sum of the yields of all fission products of a definite mass *e.g.* A_{h_2}. Figure 12 (Section 9) shows the β-decay chain of mass 141. In this chain the yield of ^{141}Ce is determined a few hours after irradiation, *i.e.* after the precursors with short half-lives have already decayed.

The mass distribution of the primary fission fragments before emission of prompt neutrons can be determined by instrumental methods, in which the kinetic energies and/or velocities of the two fragments formed are measured simultaneously. Naturally, these quantities also are determined on the fragments after evaporation of neutrons. The influence of the neutrons emitted by the accelerated fragments on the energies and velocities of the fragments can, however, be taken into consideration, so that the energies and velocities and, because of conservation of momentum and mass, also the masses of the fragments before neutron emission are obtained[44, 45].

The limited mass resolution and low sensitivity of this method are the main reasons for it not having replaced the time-consuming radiochemical method, which only affords the secondary mass distribution, albeit with unequivocal and complete mass (and atomic number) resolution even for very low yield fission products (10^{-8}% and less). The radiochemical method can also be employed in fission systems where the physical method fails, *e.g.* if the specific rate of fission or the ratio of fission to alpha decay rates is very low.

Figure 15 (Section 10) shows the mass distributions of primary and secondary fission fragments of the thermal neutron induced fission of ^{235}U. In the mass distribution curve of the secondary fragments the yield maxima are centered at a mean value of about two mass units lower than the maxima in the curve of the primary fragments. This shift is caused by prompt neutron emission. In fission systems in which the mass distribution of primary and secondary fragments is known, the number of emitted neutrons as a function of the mass of the fission fragments can be obtained indirectly (see Section 12).

The structure of the mass yield curve changes characteristically with the atomic number and mass of the fissioning nucleus and its excitation energy. An overview of the dependence is given in Fig. 11. In the case of the heavier actinoid nuclei (Fig. 11c) asymmetric fission into two different heavy fragments is preferred. The mass distribution curves have two strongly pronounced peaks and a low minimum in the region of symmetric fission. The heavy maximum remains almost constant at mass number 138—140, independent of the mass and atomic number of the fissioning nucleus, while the light maximum is shifted rather linearly to heavy masses. This almost constant position of the heavy maximum is observed in the fission of ^{229}Th with thermal neutrons and other fission systems through to the spontaneous fission of ^{256}Fm[48] (Fig. 11a and 11c). The stable position of this maximum is obviously connected with the closed-proton ($Z = 50$) and closed-neutron ($N = 82$) shells of nuclei, which are found in the mass region of the left flank of the heavy maximum.

Symmetric fission increases with increasing excitation energy of the fissioning nucleus. The valley between the maxima of asymmetric fission tends to rise and the mass distribution tends to become broader. Nuclei whose atomic number and mass are smaller than that of the thorium isotopes have a high fission barrier (see Fig. 3). Fission of such nuclei requires a higher excitation energy than is possible with thermal neutrons, but takes place on bombardment with fast neutrons or charged particles of sufficiently high energy.

In the fission of nuclei of intermediate atomic number ($88 \leqslant Z \leqslant 91$, Fig. 11e) the two asymmetric maxima are accompanied by a third symmetric maximum, since both symmetric and asymmetric fission can occur with similar probability. Only symmetric fission is observed in the case of the lighter nuclei ($Z \leqslant 88$, Fig. 11f), and here also the width of the yield curve increases with increasing excitation energy.

Only recently was it discovered that ^{258}Fm ($^{257}Fm + n_{th}$) fissions symmetrically (Fig. 11a)[49]. This is all the more surprising since the spontaneous fission of the neighboring nuclei ^{256}Fm and ^{257}Fm is asymmetric[49–51]. However, as is shown in Fig. 11, there is a distinct trend toward symmetric fission with increasing mass number of the fermium nucleus.

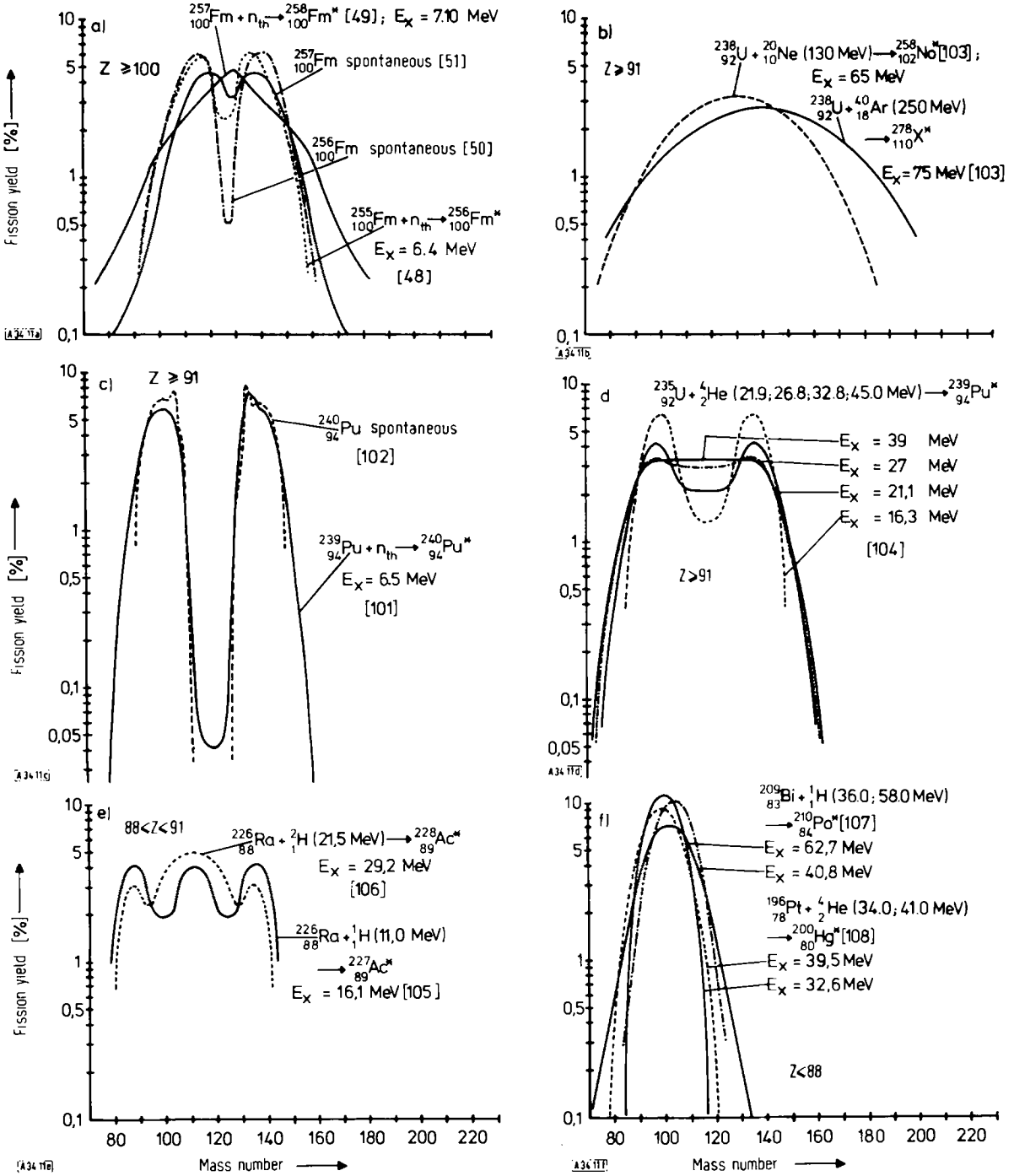


Fig. 11. Mass yield curves as a function of nuclear atomic number Z and mass of the fissioning nucleus, and its excitation energy. The curves, so far as the fission yields were not given in percent, where normalized to a total fission yield of 200%. a) and c) lower excitation energy: $E_x \leq 7$ MeV; spontaneous fission or fission with thermal neutrons. b), d), e) and f): moderate excitation energy: $E_x \leq 75$ MeV; fission with fast neutrons and charged particles (protons, deuterons, alpha particles, heavy ions).

8. Mass Asymmetry of Nuclear Fission

The preferred asymmetric fission of the actinoid nuclei into a smaller and a larger fragment is one of the oldest and still much unsolved puzzles of nuclear fission. The theoretical concepts developed so far have been unable to give a complete and satisfactory qualitative explanation of all the observations made on nuclear fission. True, the liquid drop model describes symmetric fission very well, but it fails in that it predicts symmetric mass distributions for all fissioning nuclei. Asymmetric fission has frequently been explained qualitatively as resulting from shell effects in the fission fragments leading to preferred formation of nuclei with magic or almost magic numbers of nucleons. The mass division in the fissioning nucleus should, according to this concept be determined near to the scission configuration of the nucleus, when the influence of shell effects in the fragments is greatest.

Recently, however, it became clear that the calculations which so successfully describe the double-humped fission barrier (see Sections 3—5) can also explain the asymmetric mass distribution. The calculations show that the ground state in the first minimum, the first fission barrier and the shape

isomeric state in the second minimum have lowest potential energy in deformations which are reflection symmetric with respect to a plane lying in the middle and perpendicular to the longer axis of the fissioning nucleus. The second outer fission barrier, however, is lowered if the nucleus is deformed asymmetrically like a pear[29, 31-33, 53, 54]. This is clearly evident from the potential energy surface of ^{236}U illustrated in Fig. 6 in which the asymmetric and symmetric deformations in various positions are also shown. In the neighborhood of the second fission barrier an asymmetric deformation is accompanied by an energy gain of up to a few MeV. If one assumes that a nucleus prior to fission follows the path of minimum potential energy toward scission, then the route to asymmetric fission passes over the first maximum and through the second minimum along the symmetry axis, but goes around rather than over the symmetric second maximum moving over an asymmetric saddle point left and right of the maximum.

The ground state of a ^{236}U nucleus (Fig. 6) occurs at $R \approx 7.05$ fm. The path of minimum potential energy passes over the first barrier at $R \approx 6.4$ fm, for which the shape of the nucleus is symmetrical. A symmetric deformation is likewise preferred in the second minimum at $R \approx 5.8$ fm. At $R \approx 5.0$ fm, however, the nucleus crosses the second barrier with a strongly asymmetric shape. The deformation corresponds to a mass ratio of 145/91 for the two fragments. This asymmetric saddle point lies *ca.* 2.3 MeV lower than the symmetric maximum. Finally, the asymmetrically deformed, increasingly elongated and necked nucleus moves along a valley to scission. The valley runs out at a mass ratio of *ca.* 140/96, which is in good agreement with that in the fission of ^{236}U at low excitation energy[33].

The transition from asymmetric fission in the light Fm nuclei to symmetric fission in the heavy Fm nuclei (see Fig. 11) is likewise reproduced by these calculations[33]. In the case of the light Fm nuclei the descent to scission follows the path of minimum potential energy over an asymmetric saddle point, and asymmetric deformation is retained up to the point of scission. In the case of heavy Fm nuclei the asymmetric saddle point appears to be only slightly lower or not lower than the symmetric maximum and to occur at low mass asymmetries, so that symmetric shapes are preferred along the whole route to scission. In the heavy Fm isotopes symmetric fission seems to occur when the number of neutrons is $N \approx 158$, *i.e.* when two fragments with approximately double magic numbers of nucleons can be formed, namely nuclei around the double magic nucleus $^{132}_{50}$Sn.

The same single-particle effects responsible for the nuclear deformations in the ground state and a double-humped fission barrier, are also responsible for occurrence of the asymmetric saddle point. As the excitation energy increases, so also increases the probability of symmetric fission, until at high excitation energies a symmetric mass distribution occurs in all nuclei. This transition is probably due to the fact that the influence of single-particle effects at higher energies decreases and the nuclei behave as described by the liquid drop model and fission symmetrically.

If the mass distribution is really determined at the outer barrier then different barriers ought to exist for symmetric and asymmetric fission. Recently, it was in fact found by experiment that in the case of the nuclei ^{227}Ac and ^{228}Ac, the symmetric barrier is higher than the asymmetric barrier by about 1.2 and 2.0 MeV, respectively[55].

In order to test the theoretical concepts on the origin of asymmetric mass distribution, the mass distributions of as great a number of nuclei as possible should be determined as a function of their mass, atomic number, and excitation energy. The "peak-to-valley" ratio, which actually represents the ratio of symmetric to asymmetric fission, must be measured as accurately as possible.

Such investigations are especially necessary on nuclei in the transition region between asymmetric and symmetric fission. The heavy actinoids from Cf to Md have already been the subject of intensive studies in this connection[48, 90]. The other transition region lies between Po and Ra. Unfortunately, there are very few long-lived species of these nuclei which can be prepared in sufficiently large amounts (^{210}Po, ^{226}Ra, ^{228}Ra, ^{227}Ac). Further, the production and handling of these nuclides make special demands on the radiochemist because of their high radioactivity. Nuclei between Po and Ra can also be produced by bombardment of nuclei between Au and Bi with charged particles. However, because of the high Coulomb barrier between target nucleus and projectile, compound nuclei with high excitation energy and high angular momentum are formed. Therefore, phenomena at lower excitation energy cannot be investigated in this way.

A detailed comparison of mass distributions of spontaneous fission from the ground state in the first minimum, of shape isomeric fission from the ground state in the second minimum, and of prompt fission of one and the same nucleus, *e.g.* of ^{240}Pu, can provide information as to whether the route to fission, which starts in the first minimum is exactly the same as that which starts in the second minimum, *i.e.* whether the fragments in the three fission processes are formed in the same region of the potential energy surface.

A number of measurements have been made on mass distributions in the fission of the shape isomers ^{242mf}Am[92], ^{239mf}Am, ^{237mf}Pu, ^{238mf}U, ^{236mf}U[93] and ^{240mf}Pu[94] with semiconductor detectors. According to these measurements the mass distributions in the fission of shape isomers differ little, if at all, from the other two types of fission. However, in these experiments it was impossible to measure the "peak-to-valley" ratios very accurately. This could be accomplished radiochemically if the ratio is not too extreme. But how can fission products of induced prompt fission be distinguished from those of the shape isomers? One makes use of the recoil of either the compound nucleus or the fission product. In the case of long-lived shape isomers (^{240mf}Am, ^{242mf}Am, ^{244mf}Am) a thick target, in which the compound nuclei are stopped, can be transported mechanically from the particle beam after a radiation time of 2–3 half-lives of the shape isomer to a catcher foil. This foil collects the delayed fission products which have a longer range than the compound nuclei of the shape isomer and are able to escape from the target. Alternatively, a thin target is irradiated and the compound nuclei escaping from the target are collected on a wheel (as described in Section 4) and transported in front of a catcher foil on which the fission products of the shape isomers are captured.

The fission products of shape isomers of shorter half-life can be separated from those of induced prompt fission with the experimental setup shown in Fig. 9 if two thin foils are placed in the conical holder instead of the polycarbonate foil. The upper foil must be so thin (*e.g.* 5–6 μm plastic) that it will allow penetration of the fission products formed from the shape isomers during flight with energies of 80–100 MeV. The products of prompt fission flying from the target which do not strike the foils directly because of the collimator but can stray around in the irradiation chamber with thermal energies are, on the other hand, retained by the uppermost foil. The lower foil must be so thick that the fission products of the shape isomer which have penetrated the upper foil are finally retained (15–20 μm aluminum). After irradiation the upper foil is carefully removed and the lower one drawn off and dissolved. The fission products can then be separated from this solution and purified radiochemically[95].

9. Charge Distribution

While the mass distribution indicates the apportioning of the nucleons (neutrons plus protons) of the fissioning nucleus to the two fission fragments, the charge distribution gives a clear indication of how the protons are apportioned. No protons are emitted from the fission fragments. Hence the nuclear charges of the fission fragments and the primary fission products are equal. The nuclear charge does not change until the β-decay of the primary fission products into secondary fission products.

If the yield of fission fragments is plotted as a function of their nuclear charge one obtains a curve that is very similar to the mass distribution curve. Since the protons and neutrons are distributed almost equally within a nucleus, each fission fragment will, to a first approximation, become a share of protons ($Z_{h,l}$ and $Z_{l,l}$) which is proportional to its share of nucleons ($A_{h,l}$ and $A_{l,l}$), *i.e.* $Z_{h,l} \sim A_{h,l}$. The ratio of protons and neutrons in the fission fragments will be about the same as that in the fissioning nucleus. The concept is referred to as the UCD (unchanged charge density) rule ($Z_{h,l}/A_{h,l} = Z_{l,l}/A_{l,l} = Z_f/A_f$).

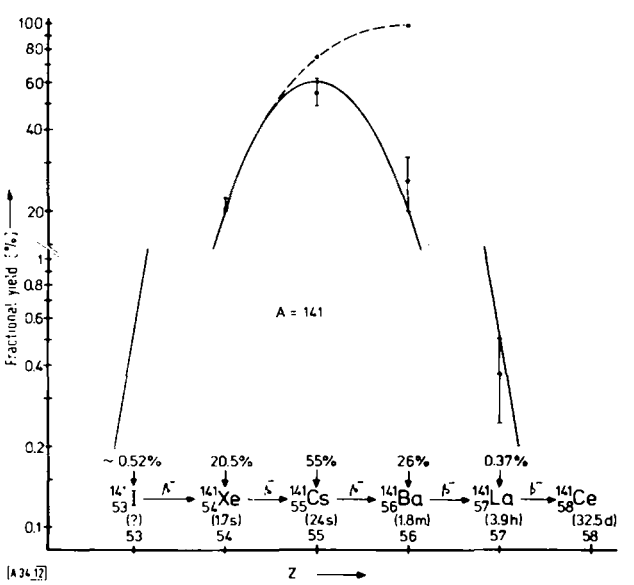


Fig. 12. Charge dispersion for fission products of mass $A = 141$ in the fission of ^{235}U with thermal neutrons. The unbroken curve corresponds to Eq. (2) with $c = 0.80$ and $Z_p = 54.97$. The dashed curve illustrates the cumulative yields (●) (independent yield (○) plus yield from β-decay of precursor). The yield of $^{141}_{53}I$ is estimated from the curve, the yields of the other fission products are measured values [56].

Many experimental investigations have shown, however, that the ratio Z/A is not the same for all fragments, but is greater in the light fragments (index l) than in the heavy fragments (index h) ($Z_{h,l}/A_{h,l} < Z_f/A_f < Z_{l,l}/A_{l,l}$).

To simplify the problem one considers only fission fragments or fission products of the same mass and tries to characterize a most probable nuclear charge Z_p for this mass number, *i.e.* the most probable combination of protons and neutrons for this mass number. The proton-neutron combinations with mass number $A = 141$ (isobaric nuclei) formed in the fission of ^{236}U with thermal neutrons are shown in Fig. 12[56]. A total of 5.70% of the fissions lead to nuclei with mass number 141[91]. Each nucleus of the chain is formed directly as primary fission product from the fissioning nucleus ("independent yield") and by β-decay from its precursor.

If the independent yields of nuclei of the same mass number are plotted against their charge number one obtains the charge dispersion curve, whose maximum represents the most probable charge Z_p (not necessarily an integer) of the mass chain under consideration (Fig. 12). From the Z_p value for fission products of a certain mass number one obtains the Z_p value for the corresponding fission fragments by addition of the number of neutrons evaporated from these fragments to the mass number of the products. Since only the average number of neutrons evaporated from the fragments is known, odd mass numbers are obtained[56].

Charge dispersion curves can be represented by a Gaussian distribution of the nuclear charge within the elements of a mass chain (see Fig. 12). The most probable charge Z_p fixes the position of the dispersion curve within the mass chain, and the parameter c its width.

$$P(Z) = (\pi \cdot c)^{-1/2} \exp[-(Z - Z_p)^2/c] \qquad (2)$$

Up to the present most primary yields of fission products have been measured for the fission of ^{235}U with thermal neutrons[56, 57]. For this fissioning system the most probable charges of those mass chains are shown in Figure 13 for which one or more independent fission yields could be measured. Charge dispersion curves with a width parameter of $c = 0.80$ were fitted to the experimentally determined fractional independent yields.

Most data on charge distribution have until recently been obtained by radiochemically determined independent yields of the individual members of the mass chains. Each determination of an independent fission yield necessitates careful and, in most cases, rapid radiochemical separation of the pertinent fission product, so that the primary distribution is not obscured by the β-decay. Only for a few "shielded" nuclides whose precursors are β-stable can independent yields be determined without being adversely affected by the β-decay (^{86}Rb, ^{96}Nb, ^{126}Sb, ^{128}I, ^{130}I, ^{136}Cs, ^{150}Pm). Very few laboratories are suitably equipped for working with high radioactivities or for carrying out rapid radiochemical separations[58, 59]. The independent yield of many fission products, however, cannot be determined by present day working techniques since their

half-lives or those of their precursors are too short. Hence, primary yields are known for only a few fissioning nuclei and for only a small portion of their fission products.

In the past few years physical methods have been developed for the determination of charge distribution. In one of these methods the fission products are separated in a mass separator; the mean lengths of the β-decay chains of individual masses are determined directly by counting the β-particles with photoemulsions or proportional counters[60-62]. In this method short β-half-lives do not present difficulties since mass separation is achieved within a microsecond; but likewise only the fission products after neutron emission are measured.

A second physical method affords information about charge distribution by simultaneous measurement of the kinetic energy of complementary fission fragments and the characteristic X-rays which they emit and which are associated with the primary charge of the fragments[63]. The nuclear charge of the fragments is determined from the energy of the X-rays. The masses of the fission fragments before neutron emission are obtained from their kinetic energy *via* conservation of mass and momentum (see Section 7).

In this method the charge distribution over the whole mass range, with the exception of low-yield masses in the minimum or on the flanks of the yield curve, is measured in a single experiment. However, owing to limited resolution only the general trend of the most probable charge Z_p can be determined as a function of fragment mass.

In a further method the intensities of the prompt gamma transitions from the 2^+ to the 0^+ level of the ground state rotational band in "even-even" fission product nuclei are measured. From these measurements the independent yields of the fission products, and hence the charge dispersion can be determined in a few mass chains. This method has so far only been used in studies on the spontaneous fission of ^{252}Cf[64].

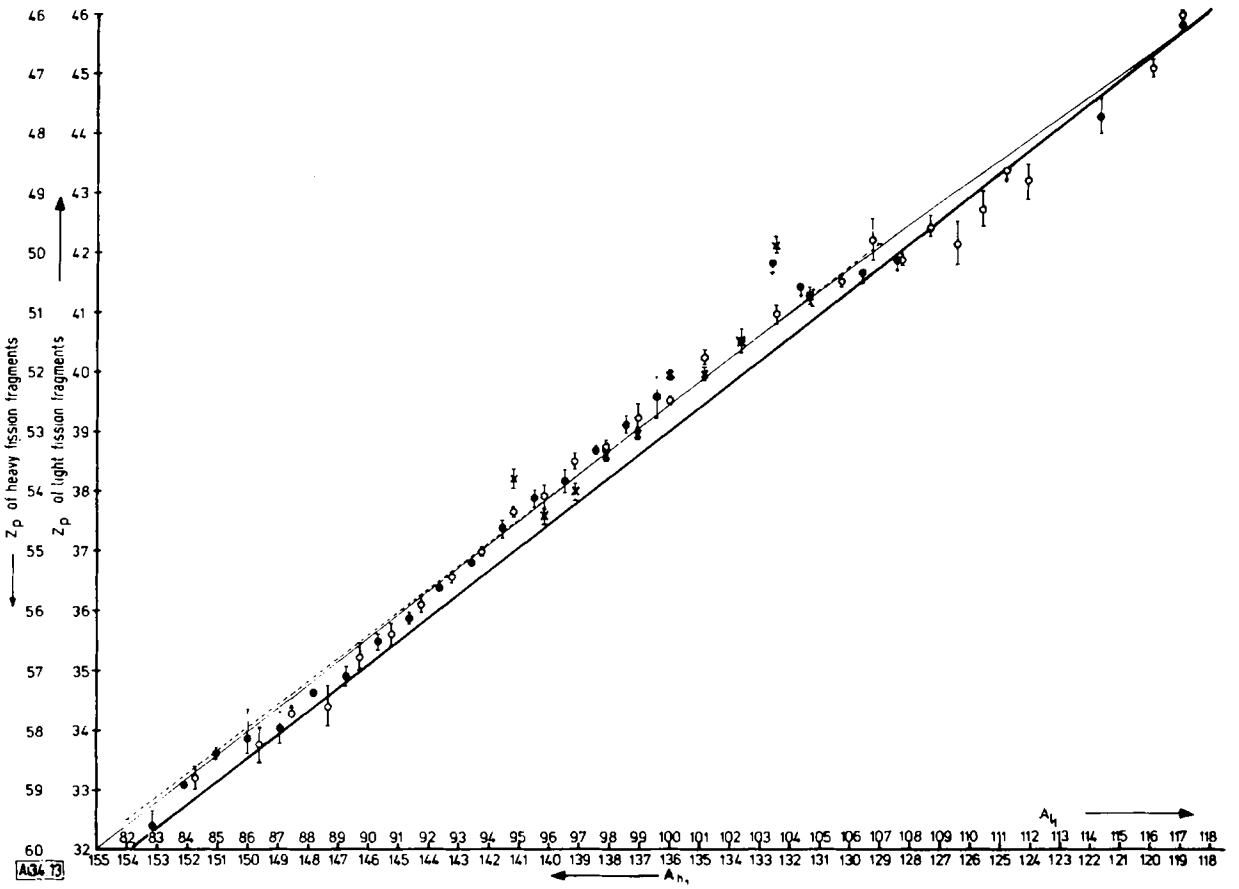


Fig. 13. Most probable nuclear charge Z_p of heavy and light fission fragments as a function of their masses A_h or A_l in the fission of ^{235}U with thermal neutrons. Radiochemical measurements: (●) light fragments, (○) heavy fragments. Physical measurements: a) with mass separator and nuclear emulsion [62]: × heavy fragments, b) measurement of characteristic X-rays [63]: --- line of best fit to the measured values. The thin solid line represents the "normalized" Z_p values of *Wahl* [56]. The charges of the fission fragments would lie on the thick solid line if their charge densities were to correspond to those in the fissioning nucleus. For these lines $Z_{p_h}(UCD) = A_{h_1}(92/236)$ and $Z_{p_l}(UCD) = A_{l_1}(92/236)$.

The most recent Z_p values measured by physical methods have also been plotted in Fig. 13. It can be seen that there is good agreement with the Z_p values determined by radiochemical methods.

From Fig. 13 it is evident that the light fission fragments have a higher and the heavy fission fragments a lower charge density than that of the fissioning nucleus. The average deviation from the UCD rule is about 0.5 charge units. The "normalized" Z_p values by *Wahl*[56], also plotted in Fig. 13, have been calculated for the mass numbers $A_{h_1} > 134$ ($A_{l_1} < 102$) from $Z_p = Z_p(UCD) - (0.45 \pm 0.1)$. This Z_p function was extrapolated to $A_{h_1} = 118$ with the reasonable assumption that the charge division is also symmetric when the mass division is symmetric. These "normalized" Z_p values and $c = 0.80 \pm 0.14$

afford the best reproduction of experimentally determined independent yields.

Considerably fewer measured values are available for the charge distribution in the fission of other nuclei *e.g.* ^{233}U and ^{239}Pu with thermal neutrons or in the spontaneous fission of nuclei such as ^{252}Cf. The values available do, however, confirm the trend found in the case of ^{235}U. The data for charge distribution in the symmetric fission of ^{235}U are also not complete. It can be seen from Fig. 13 that a few Z_p values for masses 120– 130 lie below the Z_p (UCD) straight line. It would be important in this connection to show whether a real effect is involved (influence of the closed-proton shell with 50 protons); in other words, to show that the Z_p curve does not pass smoothly over into the Z_p (UCD) line but first of all crosses it at nuclei around $Z=50$ and then approaches it from the other side. Measurements in this mass region are very difficult owing to the low yield of symmetric fission products. The conception of a new experimental methodology is called for, such as super-rapid chemistry in the gas-phase, rapid chemical separations connected with mass spectrometric measurements, gas-jet recoil-transport method[96].

Much less is known about charge distribution in the fission of nuclei having moderate excitation energy. So far, only radiochemical methods and mass spectrometric methods have been employed in such studies[65–71]. These measurements indicate, that with increasing excitation energy of the fissioning nucleus:

1. the Z_p values are shifted towards those of β-stable nuclei and

2. the width of the charge dispersion curves increases.

Thus in the fission of ^{235}U with thermal neutrons a most probable charge of $Z_p=55$ was measured for the fission products with mass $A=141$ (see Fig. 12 and 13), *i.e.* the yield of $^{141}_{55}Cs$ is the highest of the mass 141 isobars. In this case the excitation energy of the fissioning nucleus ^{235}U is $E_x=6.5$ MeV. In the fission of ^{236}U nuclei with an excitation energy of 39.3 MeV—which are formed on bombardment of ^{232}Th with 44.3 MeV alpha particles—a value of $Z_p=56$ was measured[70]. That is, the most probable charge is shifted about one unit toward that of the β-stable nucleus ($^{141}_{59}Pr$) of mass chain 141; the fission product $^{141}_{56}Ba$ is now formed in highest yield. Radiochemical measurements of independent yields are easier in the case of fission with moderate excitation energy than in fission with low excitation energy. Since the Z_p values shift nearer to those of β-stable nuclei, the independent yields of the fission products which can be measured are higher and consequently easier to determine.

Interpretation of the results of charge distribution measurements in fission of nuclei with moderate excitation energy is difficult since one does not know how many neutrons evaporate before fission and how many are emitted by the fission fragments themselves[72, 73]. In nuclei whose excitation energy is higher than the binding energy of one or more neutrons, neutron emission competes with fission. The nucleus remaining after emission of a neutron can either emit a further neutron, if it still possess sufficient excitation energy, or fission. Hence a mixture of differently fissioning nuclei is formed ("multiple chance fission").

10. Angular Momentum of Fission Fragments

The fissioning compound nucleus formed by a nuclear reaction has an angular momentum $\vec{J}_f$ which is made up of the spin of the bombarding particle $\vec{J}_a$, the spin of the target nucleus $\vec{J}_A$ and their relative orbital angular momentum $\vec{l}_{aA}$. The law of conservation of angular momentum requires that the angular momentum $\vec{J}_f$ in the fission of the compound nucleus remains conserved and be distributed as intrinsic angular momenta $\vec{J}_{h_1}$ and $\vec{J}_{l_1}$ of the two fission fragments and their relative orbital angular momentum $\vec{l}_{h_1}$:

$$\vec{J}_A + \vec{J}_a + \vec{l}_{aA} = \vec{J}_f = \vec{J}_{h_1} + \vec{J}_{l_1} + \vec{l}_{h_1}$$

If the primary fission fragments are formed with a larger angular momentum than that of the fissioning nucleus (*e.g.* spontaneously fissioning ^{252}Cf with spin 0), angular momentum must be "generated" in some way in the fission fragments during the fission process. For example, torques can be generated on each fragment by electrostatic repulsion if the fragment system exhibits a certain asymmetry at the moment of scission[74]. The diagonal component of the Coulomb repulsion between the mutually asymmetrically oriented fission fragments initiates post-scission rotation of the fragments in opposite directions about an axis perpendicular to the fission axis. The spins $\vec{J}_{h_1}$ and $\vec{J}_{l_1}$ of the two complementary fragments can then be greater than the spin of the fissioning nucleus since they are approximately anti-parallel and thus largely cancel each other. Rotational states can also be excited between saddle and scission configuration by interaction of the deformed fragments in their strong Coulomb field; this also results in generation of angular momentum in the separated fragments[75, 52].

Determination of the angular momentum of the primary fission fragments provides us with information about the properties of the fissioning nucleus between the saddle point configuration and the state shortly after the scission configuration. If the fissioning compound nucleus has high angular momentum (*e.g.* the compound nucleus ^{239}Pu, which is formed by bombardment of ^{235}U with 36 MeV ^4_2He particles, has an average angular momentum of 15 h[76]), then part of it will appear as intrinsic angular momentum of the fission fragments. Measurements of the angular distribution of fission fragments in fission with moderate excitation energy show that only a small part of the angular momentum generated in the compound nucleus appears as orbital angular momentum between the fragments[8, 9, 77, 78].

Figure 14 shows a schematic representation of the decay of the primary fission fragment ^{150}Pm. One can imagine the fission fragments rotating with the vectors of the angular momentum lying in a plane that is perpendicular to the symmetry axis of the fissioning nucleus. The spin distribution of the primary fission fragments is modified by the emission of prompt neutrons and gamma rays. The magnitude and orientation of the angular momentum of the fragments have a particular influence on the properties of the gamma emission. Measurement of the number of photons per fission fragment together with a knowledge of the multipolarity of the radiation allow an estimation to be made of the spin of the fragments. Information about the angular momentum of the primary

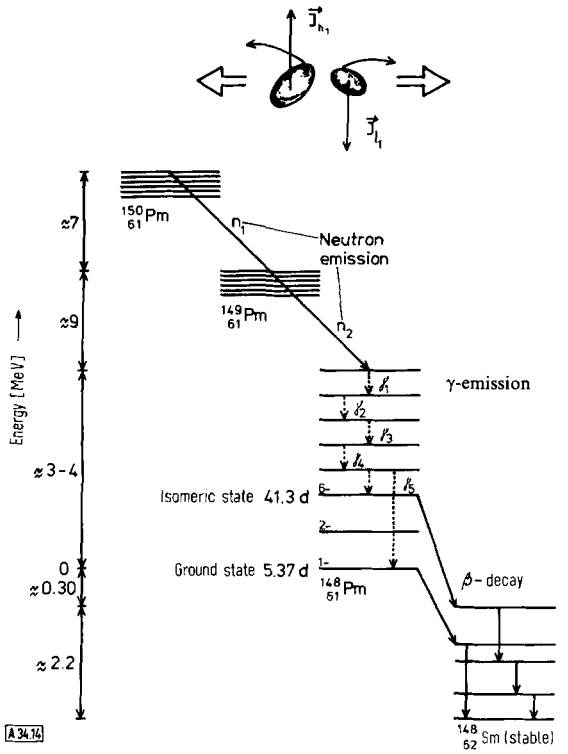


Fig. 14. Schematic representation of the decay of the primary fission fragment $^{150}_{61}$Pm by neutron and gamma emission to the 1^- ground state (half-life: 5.3 d) and isomeric 6^- level (half-life: 41.3 d) of the fission product $^{148}_{61}$Pm and its decay to the stable end product $^{148}_{62}$Sm. One can imagine that after fission, the fission fragments rotate in opposite directions about axes perpendicular to the direction of fission. They have an excitation energy of ca. 20 MeV, which is mainly given up by the emission of neutrons. After evaporation of neutrons the remaining excitation energy is removed by gamma emission. The last gamma transition ends either at the isomer level or at the ground state.

fission fragments can also be obtained by the following measurements on prompt gamma rays[79, 80]:

1. Measurement of the angular distribution of the prompt gamma radiation emitted by the fission fragments.

2. Measurement of the energy and intensity of the prompt gamma transitions of the 2^+, 4^+, 6^+ and 8^+ levels of the ground state rotational band in several "even-even" fission products.

A further method providing information about the angular momentum of primary fission fragments is based on the radiochemical determination of independent isomeric ratios of fission products, *i.e.* of the ratio of the independent yield of a long-lived isomer of a fission product (in Fig. 14 the 6^- state of ^{148}Pm with a half-life of 41.3 d) to the independent fission yield of the ground state of the same fission product (in Fig. 14 the 1^- ground state with a half-life of 5.37 d). The independent portion of fission product yields arises directly from the primary fission fragments by emission of prompt neutrons and gamma rays; hence the relative population of the ground state and isomeric state of a fission product can be related to the initial angular momentum of the fission fragments. The isomeric pair must have a β-stable or long-lived precursor, so that there is either no contribution or, at worst, only a small correctable contribution from β-decay of its precursor[9, 77].

Calculation of the angular momentum of the primary fission fragments from the measured relative yields of isomeric fission products is based on the concepts of the statistical model. The formalism of the calculations was introduced by *Huizenga* and *Vandenbosch*[81] for the calculation of isomeric ratios in

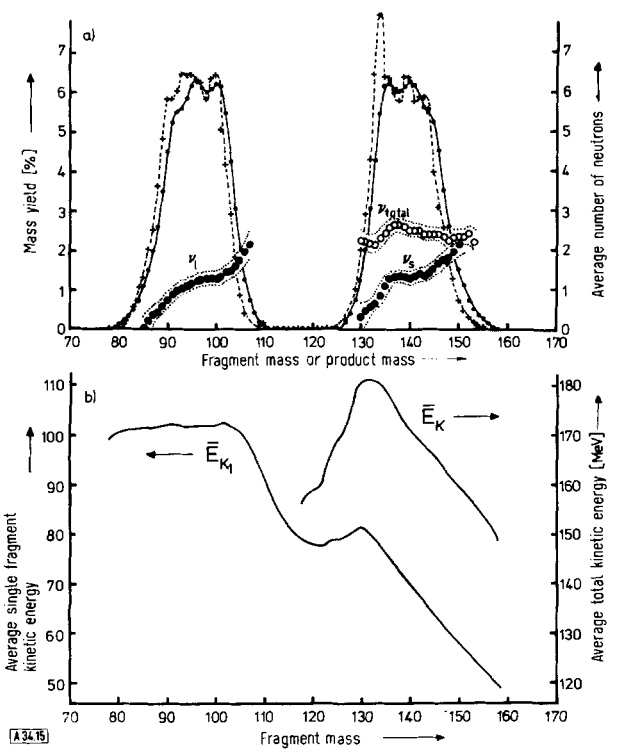


Fig. 15. a) Average number of prompt neutrons emitted from the fission fragments as a function of the fragment mass, obtained by comparison of pre- (●) and post- (+) neutron emission fragment mass distribution for fission of ^{235}U with thermal neutrons. Both mass distributions are shown, ν_l and ν_h represent the number of evaporated prompt neutrons (after [46, 47]). b) Average single fragment kinetic energy and total kinetic energy of the fission fragments as a function of their mass for fission of ^{235}U with thermal neutrons (after [44]).

nuclear reactions such as (n,γ) and (p,n) reactions. In such nuclear reactions the distribution of angular momentum of the compound nuclei can be calculated. The distribution of angular momentum of the compound nucleus in nuclear fission can also be calculated, but then the distribution of the angular momentum to the primary fission fragments cannot be followed accurately. To obtain information about the intrinsic angular momentum of the primary fission fragments from the isomeric ratios of fission products one now asks which distribution of angular momentum must occur in the primary fission fragments in order to explain the observed isomeric ratio. This spin distribution is modified by the neutrons and gamma quanta emitted by the primary fission fragments which remove angular momentum from the system (see Fig. 14). A knowledge of the angular momentum carried away by the neutrons and γ-rays is required.

Table 1 lists the results obtained in some of these studies. A complete compilation of all experimental results obtained so far (apart from those in Refs. [79] and [82]) is given in Ref. [83].

Although still far from being complete, the experimental results obtained todate allow us to draw a few general conclusions[79]:

1. The variation in angular momentum between fission fragments is not large; however,

2. fission fragments in symmetrical fission appear to have a smaller angular momentum than in asymmetrical fission.

3. If the fissioning compound nucleus is formed with higher excitation energy and higher angular momentum *via* nuclear reactions with charged particles (which impart a higher orbital angular momentum than thermal neutrons), a part of this higher angular momentum appears as internal angular momentum of the fission fragments, the remainder as orbital angular momentum between the parting fragments.

11. Kinetic Energy of Fission Fragments

When an excited compound nucleus of mass $M^*(A_f, Z_f)$ fissions into the two fragments $M_h(A_{h_1}, Z_{h_1})$ and $M_l(A_{l_1}, Z_{l_1})$ the total energy E_f released is given by

$$E_f = M^*(A_f,Z_f) - M_h(A_{h_1},Z_{h_1}) - M_l(A_{l_1},Z_{l_1})$$

At the moment of scission of the nucleus the total potential energy of the fission fragments consists of the mutual Coulomb energy E_c and the deformation energy $E_d = E_{d_h} + E_{d_l}$ of the two fragments. The difference between E_f and the potential energy appears in the form of internal energy E'_x and rotational energy E'_{rot}:

$$E_f - (E_c + E_d) = E'_x + E_{rot}$$

As soon as the fragments have separated the Coulomb energy becomes the kinetic energy of the fragments, and the deformation energy of each fragment is transformed into internal excitation energy. When the two fragments are separated by a large distance their total kinetic energy is $E_K = E_c + E'_{rot}$ and the total internal excitation energy $E_x = E_d + E'_x$ *i.e.*,

$$E_f = E_K + E_x$$

The total kinetic energy of all known fissionable nuclei is proportional to $Z_f^2/A_f^{1/3}$. This is to be expected if the kinetic energy of the fission fragments stems mainly from the Coulomb repulsion of the fragments after fission. In symmetric fission ($A_{h_1} = A_{l_1} = A_f/2$, $Z_{h_1} = Z_{l_1} = Z_f/2$) the two fragments, whose charge centers at the moment of scission are separated by a distance D, have a Coulomb energy of

$$E_K = \frac{Z_{h_1} \cdot Z_{l_1} \cdot e^2}{D} = \frac{Z_{h_1} \cdot Z_{l_1} \cdot e^2}{r_0(A_{h_1}^{1/3} + A_{l_1}^{1/3})} = const. \frac{Z_f^2}{A_f^{1/3}}$$

where r_0 is the nuclear radius parameter.

Table 1. Average angular momentum of fission fragments from radiochemical measurements of isomeric ratios and physical studies of the γ-deexcitation of the fission fragments.

Fissioning compound nucleus	Target	Projectile; energy [MeV]	Method [a]	Average angular momentum of fragments	Ref.
^{236}U	^{235}U	n_{th}	RC: ^{131}Te, ^{133}Te	6	[84]
^{236}U	^{232}Th	α; 33	RC: ^{131}Te	7	[84]
^{236}U	^{235}U	n_{th}	RC: ^{111}Pd	3—4	[85]
^{236}U	^{235}U	n_{th}	RC: ^{148}Pm	9	[21]
^{234}U	^{233}U	n_{th}	RC: ^{148}Pm	9	[21]
^{236}Np	^{235}U	p; 10	RC: ^{95}Nb	12	[86]
^{236}Np	^{235}U	p; 20—85	RC: ^{133}Xe	4—8	[87]
^{236}Np	^{235}U	p; 20—65	RC: ^{134}Cs	16	[88]
^{239}Pu	^{235}U	α; 27—44	RC: ^{111}Pd	4—6	[76]
^{239}Pu	^{235}U	α; 27—44	RC: ^{134}Cs	12—16	[76]
^{239}Pu	^{237}Np	d; 15—21	RC: ^{134}Cs	12—16	[76]
^{242}Pu	^{238}U	α; 35	RC: ^{134}Cs	11	[82]
^{236}U	^{235}U	n_{th}	P1: fragments in the mass range		
			91.5—93.5	5.3	[80]
			97.5—99.5	8.6	[80]
			136—138	5.7	[80]
			140—142	10.0	[80]
^{252}Cf		spontaneous fission	P2: $^{100,102}Zr$	6.4	[79]
			$^{112,114,116}Pd$	4.8	[79]
			$^{138,140}Xe$	8.4	[79]
			$^{146,148,150}Ce$	8.9	[79]

[a] RC: Radiochemical determination of the isomeric ratio on the fission products listed; P1 and P2: results of measurements 1 and 2, resp., (see text) of prompt gamma rays.

The average distance D between the charge centers (which almost coincide with the mass centers) of the fission fragments at the moment of scission can be determined by measuring the kinetic energy E_K.

At low and moderate excitation energies of one and the same fissioning nucleus the total kinetic energy is almost independent of the excitation energy; the average distance between the fragments at the point of scission remains nearly constant, even if the excitation energy increases. The increased excitation energy of the fissioning compound nucleus is transformed into excitation energy of the fragments.

If the total kinetic energy of the fission fragments is plotted as a function of the mass of the fragments, then a decrease in kinetic energy is observed in the case of symmetric fission (Fig. 15b). It can be concluded, therefore, that the distance at the scission point for symmetric fission is greater than that for asymmetric fission.

12. Excitation Energy of Fission Products

The excitation energy $E_x = E_{x_h} + E_{x_l}$ is obtained by calculating the total energy released in fission E_f and measuring the total kinetic energy E_K. Thus, fragments formed on symmetric fission have a higher excitation energy than those arising from asymmetric fission. The fission fragments lose their excitation energy by emission of prompt neutrons and gamma rays. A fragment with an excitation energy E_{x_h} can emit an average number ν of neutrons having binding energy E_{Bn} and kinetic energy E_{Kn} and release the energy E_γ in the form of gamma rays.

The total excitation energy of the two fragments formed in a fission process is distributed according to the following equation:

$$E_x = E_{x_h} + E_{x_l} = \nu_h(E_{Bn_h} + E_{Kn_h}) + E_{\gamma_h} + \nu_l(E_{Bn_l} + E_{Kn_l}) + E_{\gamma_l}$$

13. Prompt Neutrons

The number of prompt neutrons as a function of fragment mass can be determined in two ways, either

1. indirectly, from the difference between the initial and final fragment mass distributions (Figure 15a shows the neutron yield determined in this way as a function of fission fragment mass in the fission of ^{235}U with thermal neutrons), or

2. directly; the results of a number of such measurements are shown in Fig. 16 for the fission of ^{235}U with thermal neutrons.

Saw-tooth shaped distribution curves have also been obtained for other fissioning nuclei. It is evident from such curves that light fragments emit more neutrons than heavier fragments in nearly symmetric fission. The reason for this seems to be closely connected with the stiffness or deformability of the fissioning fragments. Fragments with completely or almost completely closed shells ($Z=50$, $N=50$ or 82) are spherical and especially rigid, whereas fragments with only partially filled shells, such as those having masses around 110 or 160, are more readily deformed. If fission leads to formation of two fragments, one of which has a fully closed shell and the other a partially filled shell, the greater portion of the deformation energy on scission will be imparted to the "soft"

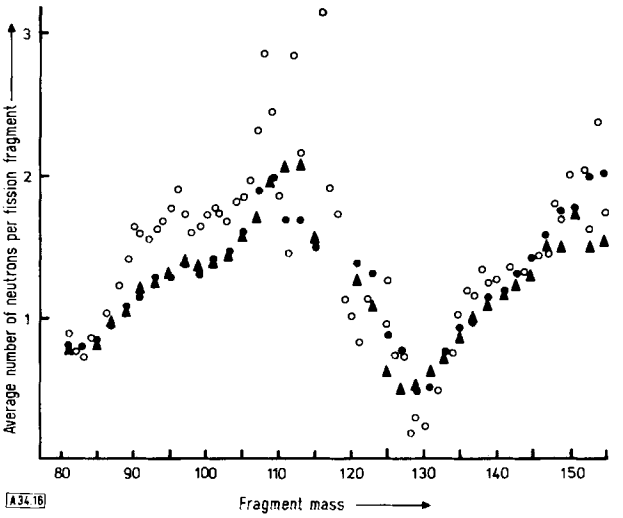


Fig. 16. Average number of prompt neutrons emitted from the fission fragments as a function of the fragment mass, obtained by direct counting of the neutrons in the fission of ^{235}U with thermal neutrons. ○, ▲, and ● represent the results of *Milton* and *Fraser* [109], *Maslin et al.* [110], and *Boldeman et al.* [98], respectively.

fragment and a lesser amount to the "hard" fragment with a completely closed shell. Hence, after fission a higher excitation energy will be contained in the soft fragment, which will then emit more neutrons than the stiff spherical fragment. If both fragments have only partially filled shells, and they readily deform, then a greater amount of deformation energy will be stored in each of them after fission. Moreover, since the distance between the charge centers of highly deformed fragments is greater, their kinetic energy will be smaller (see Section 11). This is the case, for example, in the symmetric fission of ^{235}U with thermal neutrons. Symmetric fragments emit more neutrons (see Fig. 16) and have a smaller average total kinetic energy (see Fig. 15) than asymmetric fragments.

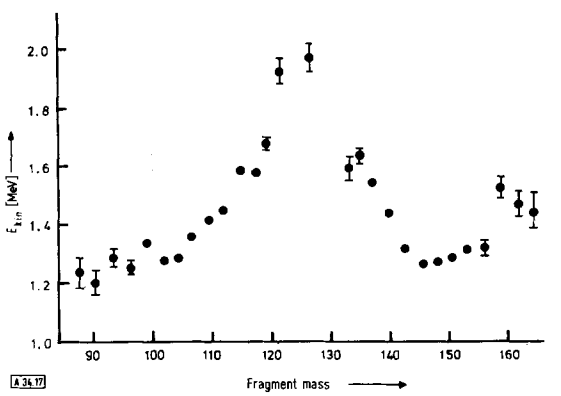


Fig. 17. Average center-of-mass kinetic energy of the prompt neutrons as a function of fragment mass for spontaneous fission of ^{252}Cf (after [99]).

The average energy which prompt neutrons carry away from the fragments, and which consists of binding energy and kinetic energy, does not vary very much from fragment to fragment and lies between 7 and 9 MeV. The average kinetic energy of the prompt neutrons emitted by fission fragments in the spontaneous fission of ^{252}Cf is shown in Fig. 17 as a function of fragment mass.

The amount of excitation energy carried away from the fragments by the neutrons can be calculated from the kinetic

energy of the neutrons, their binding energy—which can be calculated with the aid of a nuclear mass formula, *e.g.* that of *Myers* and *Swiatecki*[24]—and from the neutron yield as a function of fission fragment.

14. Prompt Gamma Rays

After evaporation of prompt neutrons, the remaining excitation energy of the fission fragments is removed by emission of gamma rays (see Fig. 14). Since the time in which the gamma rays are emitted (10^{-10}—10^{-12} s) is considerably longer than the time in which the neutrons are evaporated off ($< 10^{-14}$ s), it can be assumed that emission of gamma quanta takes place after evaporation of neutrons.

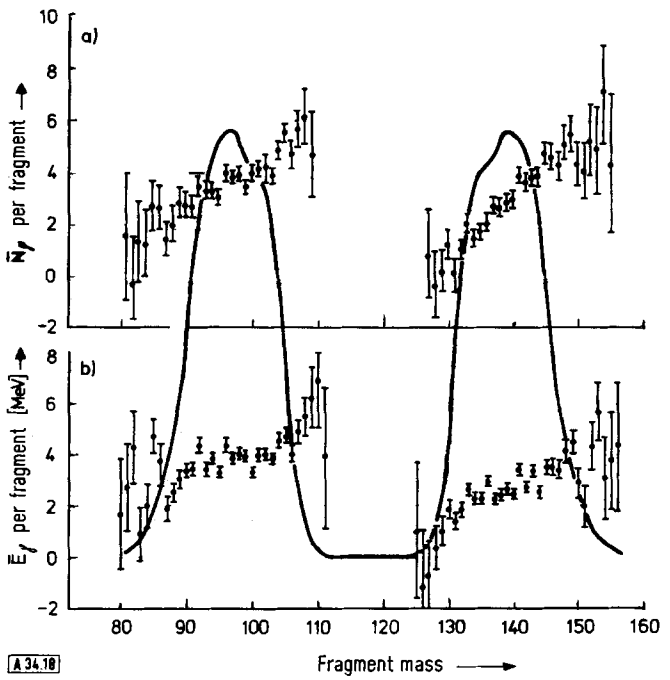


Fig. 18. Average total energy ($\bar{E}_\gamma$) and average number ($\bar{N}_\gamma$) of the gamma quanta emitted from the fission fragments as a function of fragment mass in the fission of ^{235}U with thermal neutrons (after [100]).

Figure 18 shows the average total energy $\bar{E}$ and average number $\bar{N}$ of gamma rays emitted by fission fragments as a function of fragment mass. Both curves are saw-toothed and can be compared with the curve of the average number of neutrons emitted by individual fragments as a function of fragment mass (Fig. 15a and 16).

Fission fragments near those with closed shells $Z = 50$ and $N = 82$, *i.e.* with a mass of about $A_{h_1} = 132$, emit on average only about half as many gamma rays as the complimentary fragments with masses of about $A_{l_1} = 104$. Such a phenomenon would be scarcely expected if the competition between neutron and gamma ray emission is determined merely by the excitation energy. Higher excitation energies would result in increased neutron emission. However, the angular momentum of the fission fragment has a strong influence on the number of gamma quanta emitted by a fragment. The angular momentum is reduced by only a few units by emission of prompt neutrons. If the fragment still possesses a high spin after neutron emission this will be removed by a cascade of gamma quanta, and the emission of gamma quanta will increase relative to that of neutrons. It must be remembered, however, that the gamma cascade is also dependent on the nuclear structure of the fragments. If these have a lower level density, fewer gamma quanta with higher energy will be emitted than by nuclei with larger level densities. Experimental results for the emission of prompt neutrons and gamma quanta have been collected and discussed in detail by *Nifenecker*[89].

15. Conclusion

In this paper only a very limited and concise review of the results and problems of nuclear fission is presented. Many important experimental results have had to be omitted. Thus, important themes such as the probability of fission under the most varied conditions, the spontaneous fission of heavy nuclei from the ground state, the angular distribution of fission fragments, ternary fission, delayed neutrons, and the radioactive decay of fission products, have either not been dealt with at all or have been treated in only a cursory fashion. These themes also include numerous interesting problems for the radiochemist, whose investigations can lead to important conclusions regarding the phenomenon of "nuclear fission".

Received: April 9, 1974 [A 34 IE]
revised: July 2, 1974
German version: Angew. Chem. *87*, 77 (1975)

[1] *O. Hahn* and *F. Strassmann*, Naturwissenschaften *27*, 11 (1939).
[2] *O. Hahn* and *F. Strassmann*, Naturwissenschaften *27*, 89 (1939).
[3] *L. Meitner* and *O. R. Frisch*, Nature *143*, 239 (1939).
[4] *O. R. Frisch*, Nature *143*, 276 (1939).
[5] *L. A. Turner*, Rev. Mod. Phys. *12*, 1 (1940).
[6] *C. D. Coryell* and *N. Sugarman* in National Nuclear Energy Series: Radiochemical Studies: The Fission Products. McGraw-Hill, New York 1951.
[7] *W. Seelmann-Eggebert* and *F. Strassmann*, Z. Naturforsch. *2a*, 80 (1947).
[8] *J. Halpern*, Annu. Rev. Nucl. Sci. *9*, 245 (1959).
[9] *J. R. Huizenga* and *R. Vandenbosch* in *P. M. Endt* and *P. B. Smith*: "Nuclear Reactions". North Holland, Amsterdam 1962, Vol. 2, p. 42.
[10] *E. K. Hyde*: The Nuclear Properties of the Heavy Elements. Prentice Hall, Englewood Cliffs, N. J. 1964, Vol. 3.
[11] *A. J. Obukhov* and *N. A. Perfilov*, Sov. Phys. Usp. *10*, 559 (1968).
[12] *J. S. Fraser* and *J. C. D. Milton*, Annu. Rev. Nucl. Sci. *16*, 379 (1966).
[13] *J. E. Gindler* and *J. R. Huizenga*, in *L. Yaffe*: Nuclear Chemistry. Academic Press, New York 1968, Vol. 2, p. 1.
[14] *J. R. Huizenga*, Science *168*, 1405 (1970).
[15] Proceedings of the IAEA Symposium on Physics and Chemistry of Fission, Salzburg 1965. IAEA, Vienna 1965.
[16] Proceedings of the Second IAEA Symposium on Physics and Chemistry of Fission, Vienna 1969. IAEA, Vienna 1969.
[17] Proceedings of the Third IAEA Symposium on Physics and Chemistry of Fission, Rochester, N. Y. 1973. IAEA, Vienna 1974.
[18] *R. H. Jyer* and *J. W. Cobble*, Phys. Rev. Lett. *17*, 541 (1966).
[19] *R. H. Jyer* and *H. W. Cobble*, Phys. Rev. *172*, 1186 (1968).
[20] *K. W. MacMurdo* and *J. W. Cobble*, Phys. Rev. *182*, 1301 (1969).
[21] *D. C. Aumann*, *W. Gückel*, and *H. Zeising*, unpublished.
[22] *N. Bohr* and *J. A. Wheeler*, Phys. Rev. *56*, 426 (1939).
[23] *R. W. Hasse*, Ann. Phys. *68*, 377 (1971).
[24] *W. D. Myers* and *W. J. Swiatecki*, Nucl. Phys. *81*, 1 (1966).
[25] *V. S. Barashenkov*, *A. S. Illjinov*, and *V. D. Toneev*, Nucl. Phys. *A 206*, 131 (1973).
[26] *S. G. Nilsson*, Kgl. Dan. Vidensk. Selsk. Mat. Fys. Medd. *29*, No. 16 (1955).
[27] *V. M. Strutinsky*, Nucl. Phys. *A 95*, 420 (1967).
[28] *V. M. Strutinsky*, Nucl. Phys. *A 122*, 1 (1968).
[29] *J. R. Nix*, Annu. Rev. Nucl. Sci. *22*, 65 (1972).
[30] *V. M. Strutinsky* and *H. C. Pauli*, see [16], p. 155.

[31] *M. Brack, J. Damgaard, H. C. Pauli, A. Stenholm-Jensen, V. M. Strutinsky,* and *C. Y. Wong,* Rev. Mod. Phys. *44,* 320 (1970).

[32] *H. C. Pauli,* Phys. Rep. (Section C of Phys. Lett.) *7,* 35 (1973).

[33] *M. G. Mustafa, U. Mosel,* and *H. W. Schmitt,* Phys. Rev. *C 7,* 1519 (1973).

[34] *S. N. Polikanov, V. A. Druin, V. A. Karnaukhov, V. L. Mikheev, A. A. Pleve, N. K. Skobolev, V. G. Subbotin, G. M. Ter-Akop'yan,* and *V. A. Fomichev,* Sov. Phys. JETP *15,* 1016 (1962).

[35] *S. M. Polikanov,* Sov. Phys. Usp. *11,* 22 (1968).

[36] *G. N. Flerov, Yu. P. Gangrsky, B. N. Markov, A. A. Pleve, S. M. Polikanov,* and *H. Jungclausen,* Sov. J. Nucl. Phys. *6,* 12 (1968).

[37] *H. C. Britt,* At. Data Nucl. Data Tables *12,* 407 (1973).

[38] *R. L. Fleischer, P. H. Price,* and *R. M. Walker,* Annu. Rev. Nucl. Sci. *15,* 1 (1965).

[39] *A. Michaudon,* Advan. Nucl. Phys. *6,* 1 (1973).

[40] *E. Migneco* and *J. P. Theobald,* Nucl. Phys. *A 112,* 603 (1968).

[41] *P. A. Russo, J. Pedersen,* and *R. Vandenbosch,* see [17], Vol. 1, p. 271.

[42] *H. J. Specht, J. Weber, E. Konecny,* and *D. Heunemann,* Phys. Lett. *41 B,* 43 (1972).

[43] *D. Benson, Jr., C. M. Lederer,* and *E. Cheifetz,* Nucl. Phys. *A 201,* 445 (1973).

[44] *H. W. Schmitt, J. H. Neiler,* and *F. J. Walter,* Phys. Rev. *141,* 1146 (1966).

[45] *H. W. Schmitt, R. W. Lide,* and *F. Pleasonton,* Nucl. Instrum. Methods *63,* 237 (1968).

[46] *J. Terrell,* see [15], Vol. 2, p. 3.

[47] *J. Terrell,* Phys. Rev. *127,* 880 (1962).

[48] *J. P. Unik, J. E. Gindler, L. E. Glendenin, K. F. Flynn, A. Gorski,* and *R. K. Sjoblom,* see [17], Paper Vol. 2, p. 19.

[49] *W. John, E. K. Hulet, R. W. Lougheed,* and *J. J. Weselowski,* Phys. Rev. Lett. *27,* 45 (1971).

[50] *K. F. Flynn, F. P. Horwitz, C. A. A. Bloomquist, R. F. Barnes, R. K. Sjoblom, P. R. Fields,* and *L. E. Glendenin,* Phys. Rev. *C 5,* 1725 (1972).

[51] *J. P. Balagna, G. P. Ford, D. C. Hoffman,* and *J. D. Knight,* Phys. Rev. Lett. *26,* 145 (1971).

[52] *J. R. Nix* and *W. J. Swiatecki,* Nucl. Phys. *71,* 1 (1965).

[53] *H. C. Pauli* and *T. Ledergerber,* Nucl. Phys. *A 207,* 1 (1973); see also [17], Vol. 1, p. 463.

[54] *P. Möller* and *J. R. Nix,* see [17], Vol. 1, p. 103.

[55] *E. Konecny, H. J. Specht,* and *J. Weber,* Phys. Lett. *45 B,* 329 (1973); see also [17], Vol. 2, p. 3.

[56] *A. C. Wahl, A. E. Norris, R. A. Rouse,* and *J. C. Williams,* see [16], p. 813.

[57] *H. O. Denschlag,* Habilitationsschrift, Universität Mainz 1971.

[58] *G. Herrmann* and *H. O. Denschlag,* Annu. Rev. Nucl. Sci. *19,* 1 (1969).

[59] *S. Amiel* in *L. Yaffe:* Nuclear Chemistry. Academic Press, New York 1968, Vol. 2, p. 251.

[60] *E. Konecny, H. Gunther, H. Rösler, G. Siegert,* and *H. Ewald,* Z. Phys. *231,* 59 (1970).

[61] *K. Sistemich, P. Armbruster, J. Eidens,* and *E. Roeckl,* Nucl. Phys. *A 139,* 289 (1969).

[62] *H. Gunther, G. Siegert, R. L. Ferguson, H. Ewald,* and *E. Konecny,* Nucl. Phys. *A 196,* 401 (1972).

[63] *W. Reisdorf, J. P. Unik, H. C. Griffin,* and *L. E. Glendenin,* Nucl. Phys. *A 177,* 337 (1971).

[64] *E. Chefietz, J. B. Wilhelmy, R. C. Jared,* and *S. G. Thompson,* Phys. Rev. *C 4,* 1913 (1971).

[65] *A. C. Pappas, J. Alstad,* and *E. Hagebø,* see [16], p. 669.

[66] *H. Umezawa, S. Baba,* and *H. Baba,* Nucl. Phys. *A 160,* 65 (1971).

[67] *H. Umezawa,* J. Inorg. Nucl. Chem. *33,* 2731 (1971).

[68] *H. Marshall* u. *L. Yaffe,* J. Inorg. Nucl. Chem. *35,* 1797 (1973).

[69] *L. D. Miller* and *L. Yaffe,* J. Inorg. Nucl. Chem. *35,* 1805 (1973).

[70] *J. A. McHugh* and *M. C. Michel,* Phys. Rev. *172,* 1160 (1968).

[71] *B. L. Tracy, J. Chaumont, R. Klapisch, J. M. Nitschke, A. M. Poskanzer, E. Roeckl,* and *C. Thibault,* Phys. Rev. *C 5,* 222 (1972).

[72] *E. Cheifetz, Z. Fraenkel, J. Gabin, M. Lefort, J. Péter,* and *X. Tarrago,* Phys. Rev. *C 2,* 256 (1970).

[73] *E. Cheifetz* and *Z. Fraenkel,* Phys. Rev. Lett. *21,* 36 (1968).

[74] *M. Hoffman,* Phys. Rev. *B 133,* 714 (1964).

[75] *O. Rasmussen, W. Nörenberg,* and *H. J. Mang,* Nucl. Phys. *A 136,* 456 (1969).

[76] *D. C. Aumann* and *J. E. Gindler,* Argonne Nat. Lab. Rep. ANL-7930, p. 25 (1972).

[77] *H. Warhanek* and *R. Vandenbosch,* J. Inorg. Nucl. Chem. *26,* 669 (1964).

[78] *R. Vandenbosch, H. Warhanek,* and *J. R. Huizenga,* Phys. Rev. *124,* 846 (1961).

[79] *J. B. Wilhelmy, E. Cheifetz, R. C. Jared, S. G. Thompson,* and *H. R. Bowman,* Phys. Rev. *C 5,* 2041 (1972).

[80] *P. Armbruster, H. Labus,* and *K. Reichelt,* Z. Naturforsch. *26a,* 512 (1971).

[81] *J. R. Huizenga* and *R. Vandenbosch,* Phys. Rev. *120,* 1305 (1960); *R. Vandenbosch* and *J. R. Huizenga, ibid. 120,* 1313 (1960).

[82] *V. D. Loveland* and *Y. S. Shim,* Phys. Rev. *C 4,* 2282 (1971).

[83] *D. C. Aumann,* Habilitationsschrift, Technische Universität München 1971.

[84] *D. G. Sarantites, G. E. Gordon,* and *C. D. Coryell,* Phys. Rev. *138 B,* 353 (1965).

[85] *D. C. Aumann, K. F. Flynn, J. E. Gindler,* and *L. E. Glendenin,* J. Inorg. Nucl. Chem. *31,* 1935 (1969).

[86] *C. Rudy, R. Vandenbosch,* and *C. T. Ratcliffe,* J. Inorg. Nucl. Chem. *30,* 365 (1968).

[87] *J. H. Forster* and *L. Yaffe,* Can. J. Chem. *46,* 1763 (1968).

[88] *G. B. Saha, J. Tomita,* and *L. Yaffe,* Can. J. Chem. *46,* 1763 (1968).

[89] *H. Nifenecker, C. Signarbieux, R. Babinet,* and *J. Poitan,* see [17], Vol. 2, p. 117.

[90] *R. C. Ragaini, E. K. Hulet, R. W. Lougheed,* and *J. Wild,* Phys. Rev. *C 9,* 399 (1974).

[91] *E. A. C. Crouch,* At. Energy Res. Estab., Harwell (Great Britain), Rep. AERE-R 7209 (1973).

[92] *C. A. Fontenla, G. L. Griffith, R. B. Leachman,* and *A. M. Friedman,* Proc. Int. Conf. Nuclear Physics, München 1973. North Holland, Amsterdam 1973, Vol. 1, p. 608.

[93] *R. L. Ferguson, F. Plasil, G. D. Alam,* and *H. W. Schmitt,* Nucl. Phys. *A 172,* 33 (1971).

[94] *J. Weber, H. J. Specht, E. Konecny,* and *D. Heunemann,* Nucl. Phys. *A 221,* 414 (1974).

[95] *D. C. Aumann* and *E. Kowarschik,* personal communication; *E. Kowarschik,* Diplomarbeit, Technische Universität München 1974.

[96] *D. C. Aumann* and *D. Weismann,* Nucl. Instrum. Methods *117,* 459 (1974).

[97] *N. L. Lark, G. Sletten, J. Pedersen,* and *S. Bjørnholm,* Nucl. Phys. *A 139,* 481 (1969).

[98] *J. W. Boldeman, A. R. De L. Musgrove,* and *R. L. Walsh,* Aust. J. Phys. *24,* 821 (1971).

[99] *H. R. Bowman, J. C. D. Milton, S. G. Thompson,* and *W. J. Swiatecki,* Phys. Rev. *129,* 2139 (1963).

[100] *F. Pleasanton, R. L. Ferguson,* and *H. W. Schmitt,* Phys. Rev. *C 6,* 1023 (1972).

[101] *K. F. Flynn* and *L. E. Glendenin,* Argonne Nat. Lab. Rep. ANL-7749 (1970).

[102] *B. Laidler* and *F. Brown,* J. Inorg. Nucl. Chem. *24,* 1485 (1962).

[103] *S. A. Karamyan, F. Nurmuratov, Yu. Ts. Oganesyan, Yu. E. Penianzhkevich, B. J. Pustyl'nik,* and *G. N. Flerov,* Sov. J. Nucl. Phys. *8,* 401 (1969).

[104] *R. Vandenbosch, T. D. Thomas, S. E. Vandenbosch, R. A. Glass,* and *G. T. Seaborg,* Phys. Rev. *111,* 1358 (1958).

[105] *R. C. Jensen* and *A. W. Fairhall,* Phys. Rev. *109,* 942 (1958).

[106] *R. C. Jensen* and *A. W. Fairhall,* Phys. Rev. *118,* 771 (1960).

[107] *T. T. Sugihara, J. Roesmer,* and *J. W. Meadows, Jr.,* Phys. Rev. *121,* 1179 (1961).

[108] *E. F. Neuzil, M. E. Phelps,* and *F. Ross,* J. Inorg. Nucl. Chem. *27,* 1463 (1969).

[109] *J. C. D. Milton* and *J. S. Fraser,* see [15], Vol. 2, p. 39.

[110] *E. E. Maslin, A. L. Rodgers,* and *W. G. F. Core,* Phys. Rev. *164,* 1520 (1967).

High Pressure Kinetic Investigations in Organic and Macromolecular Chemistry[**]

By Gérard Jenner[*]

High pressure kinetics appears to be a valuable tool in investigating the mechanism of specific organic reactions. For instance, in pericyclic, Mentshutkin, cage, and polymerization reactions, such studies reveal various features of the transition state, in particular its localization along the reaction coordinate and its nature. However, precise conclusions require separation of the different effects (electrostatic, steric, orbital, *etc.*) which may contribute to the structure of the transition state.

1. Introduction

The rate of chemical reactions in gaseous and condensed phases is influenced by pressure:

1) Compressing the reaction medium increases the concentration of the reacting molecules.

2) Pressure changes the rate of intermolecular diffusion.

3) Pressure compresses the molecules themselves, deforming the "electron clouds" and affecting the collision rate.

In dense liquid phase, the free space required for the formation of the transition state is restricted and the influence of pressure upon the reaction rate overshadows all other effects.

The high pressure thermodynamics of solutions is well known and it is unnecessary to give details in this paper. The fundamental relationships governing the condensed phase equilibria may be written as functions of the activation volume $\Delta V^{\neq}$:

$$\left[\frac{\partial \ln k}{\partial p}\right]_T = -\left[\frac{\partial \Delta G^{\neq}}{RT\partial p}\right]_T = -\frac{\Delta V^{\neq}}{RT} \tag{1}$$

$$\left[\frac{\partial \Delta S^{\neq}}{\partial p}\right]_T = \left[\frac{\partial \Delta V^{\neq}}{\partial T}\right]_p \tag{2}$$

$$\left[\frac{\partial \Delta H^{\neq}}{\partial p}\right]_T = \Delta V^{\neq} - T\left[\frac{\partial \Delta V^{\neq}}{\partial T}\right]_p \tag{3}$$

In these expressions the activation parameters (free energy $\Delta G^{\neq}$, enthalpy $\Delta H^{\neq}$, entropy $\Delta S^{\neq}$) characterizing the transition state have their usual meaning.

Since the activation quantity $\Delta V^{\neq}$ will assume an important place in our investigations of reaction mechanisms, a short outline will be presented here, although the concept has been thoroughly analyzed and discussed elsewhere[1-3].

Rigorously speaking the activation volume is the difference in partial molal volume between the transition state and the initial state. $\Delta V^{\neq}$ often has to be considered as a composite quantity made up essentially of two contributing volumes, the first being related to the structural change during the crossing from the initial to transition state and the second representing the volume change due directly to the modified interaction between the surrounding molecules of solvent and the reacting molecules when they form the transition state (these changes are not only localized in the solvent, but also within the molecules). In principle $\Delta V^{\neq}$ can be calculated exactly by the methods of quantum and statistical mechanics, but in practice the computations for a liquid phase reaction are too involved to be worthwhile.

Expressed on the molar scale (rate constant k_c) and molal scale (rate constant k_x), the Evans-Polanyi relationship is written:

$$\Delta V^{\neq} = -RT\left(\frac{\partial \ln k}{\partial p}c - \beta \Sigma \gamma_i\right) \tag{4}$$

$$\Delta V^{\neq} = -RT\left(\frac{\partial \ln k}{\partial p}x\right) \tag{5}$$

$\Sigma \gamma_i$: stoichiometric change between the transition state and the initial state
β: isothermal compressibility of the solution

As shown by these expressions, to obtain the value of $\Delta V^{\neq}$ at zero pressure it is necessary to write k_c or k_x as a function of p. Unfortunately, no exact function is known for this purpose, and many analytical expressions must be considered according to the magnitude of $\Delta V^{\neq}$ and the pressure range. Simple power series[4] and other empirical relations[5-8] have been proposed:

$$\ln k = a_0 + a_1 p + a_2 p^2 \tag{6}$$

$$\ln k = \frac{a+bp}{1+cp} \tag{7}$$

$$\frac{\ln (k/k_0)}{p} = A + Bp^{0.523} \quad (\textit{Benson-Berson}[8]) \tag{8}$$

$$\frac{\ln(k_{n+1}/k_n)}{p_{n+1}-p_n} = A' + B'\frac{(p_{n+1}+p_n)}{2} \quad (\text{incremental}[7]) \tag{9}$$

These relations obviously imply different pressure dependencies of $\Delta V^{\neq}$ (*e.g.* the quadratic polynomial (6) which is widely used imposes a linear relationship between $\Delta V^{\neq}$ and p). Analytical expressions should be regarded simply as mathematical tools allowing a fitting of experimental results but not as physical models. Caution is required when using several of these methods simultaneously. In any case the best solution is to collect as many experimental kinetic points as possible in the low pressure region and to compare the mathematical values of $\Delta V^{\neq}$ with the value obtained experimentally from the slope of the curve $\ln k = f(p)$.

The various procedures for an accurate determination of $\Delta V^{\neq}$ have been reviewed and commented upon recently[9], particularly the semi-empirical approach of *Benson* and *Berson*[8]

[*] Dr. G. Jenner
Laboratoire de Chimie Organique Appliquée
Institut de Chimie de l'Université
BP 296/R8, 67008 Strasbourg-Cedex (France)

[**] Based upon a lecture delivered at the 12th Meeting of the European High Pressure Research Group, Marburg/Lahn (Germany), March 1974.

which has given rise to some criticism; despite its very poor theoretical basis, however, the method seems to give reasonable approximate values of the activation volume (Table 1).

Table 1. Comparison of several methods for determining $\Delta V^{\neq}$ in Diels-Alder reactions involving isoprene ($\Delta V^{\neq}$ in cm^3/mol).

Method / Dienophile	Graphic	Power series (quadratic)	*Benson-Berson* [8]	Incremental
acrylonitrile [10] (21 °C)	−35.4	−33.1	−34.7	−33.7
methyl acrylate [10] (21 °C)	−31.5	−30.8	−32.8	—
methyl vinyl ketone [10] (20 °C)	−38.1	−36.9	—	—
isoprene [11] (70 °C)	−42.0	−41.3	−43.6	−41.8
maleic anhydride [12] (35 °C)	−37.4	−39.0	−36.5	—

The calculation of the activation volume of an organic reaction permits choice of optimal experimental conditions for a proposed synthesis. Moreover, a knowledge of $\Delta V^{\neq}$ leads to a better understanding of the transition state in relation to the initial and final states, and provides useful information about its structure and properties which is essential for establishing the mechanism of organic reactions. An interpretation usually requires that the activation volume can be resolved into components whose values are known at least approximately. For apolar reactions (such as Diels-Alder reactions), the electrostatic contribution is negligibly small, so that the measured activation volume is related directly to the geometric changes incurred on going from the initial to the transition state.

Reactions in the liquid phase can be crudely classified into three groups:

1) Decompositions and neutralization of ionic charges, which are hardly affected by pressure or show a negative pressure effect ($\Delta V^{\neq} > 0$);

2) Reactions with weak pressure effect ($\Delta V^{\neq}$ close to zero) represented by nonpolar reactions consuming and regenerating a radical or a molecule;

3) Ionization and bimolecular reactions which are generally subject to a strong pressure acceleration ($\Delta V^{\neq} < 0$)[13].

Depending upon the sign and the magnitude of $\Delta V^{\neq}$, the volume balances of organic reactions show different profiles. As is apparent from Figure 1, four kinds of behavior may be distinguished, two displaying a monotonous volume change along the reaction coordinate and two others with volume extrema for the transition state (the case with $\Delta V^{\neq} > 0$ and a volume maximum is very rare[14]).

Table 2. Activation volumes for some classes of reactions.

Reaction type	$\Delta V^{\neq}$ [cm^3/mol]
radical decompositions [15]	0 to +15
rearrangement reactions (Cope, Claisen)	− 8 to −15
radical polymerizations	−10 to −25
Mentshutkin reactions	−20 to −40
ionization reactions	−15 to −45
Diels-Alder reactions	−25 to −50

This report considers the particular pressure effect upon the kinetics of four reaction groups: thermal pericyclic reactions;

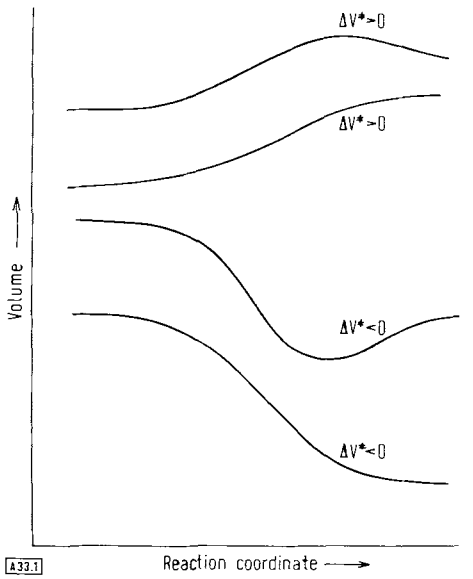


Fig. 1. Various volume profiles of organic reactions.

Mentshutkin reactions; cage reactions; and polymerization reactions.

2. Pericyclic Reactions

According to the terminology of *Woodward* and *Hoffmann*[16, 17] pericyclic reactions are concerted reactions characterized by a quasi-cyclic transition state; moreover the stereochemistry depends solely upon the number of electrons and not the number of participating carbon atoms (or centers). These reactions exhibit large negative activation volumes and provide an example of transition states with few localized charges. Among these reactions, the most thoroughly investigated are the Diels-Alder and the Cope reactions.

2.1. Diels-Alder Reactions

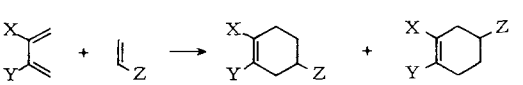
It is obvious that the Diels-Alder reaction is strongly pressure accelerated since the adduct always constitutes the most condensed phase. Besides, the use of pressure avoids the retrodienic reaction whose activation volume is positive (about $+10\,cm^3/mol$). On the other hand, pressure favors not only the Diels-Alder reaction but also the polymerization reactions, and sometimes also decomposition of the dienophile[18, 19].

Use of a very efficient radical polymerization inhibitor and observation of optimal pressure and temperature conditions ensure that the reaction proceeds solely in the direction of diene-dienophile addition[18].

Two aspects of the Diels-Alder reaction may be considered separately with regard to their pressure effect: stereospecificity on the one hand and the kinetics on the other.

2.1.1. Regioselectivity in High Pressure Diels-Alder Reactions

The thermal condensation of a diene and a dienophile generally leads only to cyclohexene derivatives, especially at low temperatures[20].



If the diene is asymmetric, both isomers are obtained (*e.g.* in reactions involving isoprene).

With the aid of NMR spectroscopy, *Brun*[18, 21] was able to determine the percentage of both isomers in the mixture of adducts formed by reaction of isoprene with crotonaldehyde.

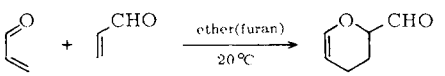
Table 3. Bulk condensation of isoprene and crotonaldehyde (5.5 mol/l each). Reaction time 20 h, temperature 22 °C.

Pressure [bar]	Yield of adduct [%]	Isomer "*para*"	Isomer "*meta*"
1	0	—	—
6000	3.1	60	40
8000	16.8	64	36
10000	31.7	72	28

These results can be explained to a first approximation by electrostatic arguments. The "*para*" isomer is the most polar compound, and it is known that the compression of a reaction mixture induces a volume contraction favoring the formation of polar substances[22, 23]. In fact, pressure increases the polarity of the medium and hence also the electrostatic interactions between the solvent and the polar reaction products. However, as the stereochemistry of the Diels-Alder reactions is little affected by changing the solvent[24], electrostatic effects should play a minor role[25, 26]. A more plausible explanation involves a perturbational view of orbital effects[27].

Gonikberg, Elyanov, et al.[28, 29] have studied the reaction between 1-vinylcyclopentene and methyl acrylate at 80 °C under 1 and 6000 bar, as well as the addition of *trans*-piperylene to methyl acrylate at somewhat higher temperatures and pressures. The variation of the composition of the adduct mixture is explained by steric considerations since models of cyclic transition states for the 1-*cis* isomer have the most compact structure.

Thermal dimerization of acrolein is a limiting case of the Diels-Alder reaction in which the dienophile also behaves as a diene. Surprisingly only the "*meta*" isomer is ever obtained[18] regardless of pressure.



This reaction is highly selective and at room temperature seems to proceed only under high pressure. Once again the stereochemistry can be predicted by a perturbation method[27].

Table 4. Dimerization of acrolein (2.30 mol/l) at 20 °C in furan. Reaction time 8 h.

Pressure [bar]	Adduct [%]
1	0
2000	0.7
3000	1.0
6000	1.3
> 6000	[a]

[a] Explosive decomposition of acrolein.

2.1.2. Pressure Effect upon the Kinetics of Diels-Alder Reactions

As shown by Table 5, pressure strongly affects the kinetics of diene cycloadditions.

Table 5. Values of the ratio k_p/k_o for some isoprene cycloadditions [10]. Diene/dienophile = 1/1; room temperature; solvent 1-bromobutane.

Pressure [bar]	Dienophile acrylonitrile (21 °C)	Dienophile methyl acrylate (21 °C)	Dienophile methyl vinyl ketone (20 °C)
1	1	1	1
1000	3.4	3.0	4.1
1500	7.0	4.6	—
2000	10.5	8.3	12.3
3000	24.4	17.5	19.5
5000	74.4	57.3	—
8000	561	438	—
10000	1650	1530	—

The activation volumes of some recently studied Diels-Alder reactions are given in Table 6.

Table 6. Activation volumes for some Diels-Alder reactions involving isoprene as diene carried out in 1-bromobutane.

Dienophile	T (°C)	$\Delta V^{\neq}$ [cm³/mol]	ΔV [cm³/mol] [a]
acrylonitrile [10]	21	−35.0	−37.0
methyl acrylate [10]	21	−31.5	−36.9
methyl vinyl ketone [10]	20	−38.0	−37.1
isoprene [11]	40	−35.0	−41.9
	50	−40.0	−44.1
	60	−41.0	−45.9
	70	−42.0	−47.8
DMB [b] [30]	70	−37.0	−45.3

[a] Overall volume change between the final state and the initial state.
[b] 2,3-Dimethyl-1,3-butadiene (also the diene in this reaction).

Two mechanisms are conceivable for Diels-Alder reactions: either a concerted (4 + 2) center electrocyclic reaction involving synchronous formation of two σ bonds in the transition state, or a two-step process involving formation of a delocalized bond and crossing through an intermediate diradical. The reported values for $\Delta V^{\neq}$ (Table 6) strongly suggests the simultaneous formation of two bonds in the activation process, *i. e.* the concerted one-step mechanism. Moreover, the highly ordered transition state is confirmed by the high negative activation entropies[11].

The results of *Grieger* and *Eckert et al.*[12, 31–36] are also in very good agreement with this conclusion. In some cases the activation volume was more negative than the volume change on reaction, giving a minimum in the volume profile along the reaction coordinate. This was attributed by *Eckert* to additional contraction as a result of secondary interactions between non-bonding atoms in the transition state which do not occur in the cyclohexene compound.

Nevertheless, caution should be exercised before generalizing these conclusions to include all thermal Diels-Alder reactions because a two-step mechanism cannot always be formally excluded if a compound readily forms a relatively stable diradical. For example, *Stewart*[37] has measured the pressure effect on the cyclodimerization of chloroprene and has observed competing mechanisms. Even though the values of the cited activation volumes are probably not exact owing to the excessive pressure interval employed, he could show that the reaction yields not only vinylcyclohexenes, but also an appreciable amount of divinylcyclobutanes, so that the transition state corresponding to the intermediate diradical is about 10 cm³/mol less compact than the transition state of the one-step case.

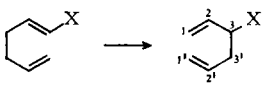
Table 7. Activation volumes for some Diels-Alder reactions studied by *Grieger* and *Eckert* [12,31—36].

Diene	Dienophile [a]	T [°C]	Solvent	$\Delta V^{\neq}$ [cm³/mol]	$\overline{\Delta V}$[b] [cm³/mol]
isoprene	MA	35	acetone	−39.0	−35.9
1-methoxy-butadiene	MA	35	1-chloro-butane	−43.9	−30.4
cyclohexa-diene	MA	35	dichloro-methane	−39.6	−30.3
cyclopenta-diene	DMAC	10	ethyl acetate	−30.2	−33.6
DMB [a]	BA	10	none	−28.6	−32.4

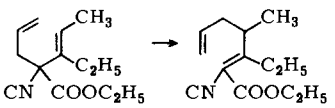
[a] MA, maleic anhydride; DMAC, dimethyl acetylenedicarboxylate; BA, *n*-butyl acrylate; DMB, 2,3-dimethyl-1,3-butadiene.
[b] Overall volume change calculated from partial molar volumes.

2.2. Cope Reactions

The Cope reaction is another pericyclic reaction. If we consider a σ bond adjacent to one or more π systems, then the migration of this σ bond to a new position in a noncatalyzed intramolecular reaction is termed a sigmatropic transposition of order [*n*, *m*] by *Woodward* and *Hoffmann*[16, 17]. For instance the Cope rearrangement is a sigmatropic [3,3]-shift.



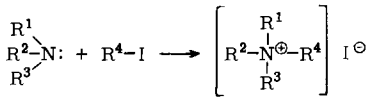
Walling and *Naiman*[38] studied the following Cope reaction at 119 °C at pressures up to 6000 bar



Their results show that the nature of the solvent has very little influence on the reaction rate and that the activation volume is close to $-10\,cm^3/mol$, indicating a cyclic transition state with marked bonding between fragments of the rearranging molecules.

3. Mentshutkin Reactions

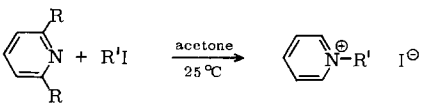
These reactions consist in the addition of an organyl iodide to a tertiary amine.



The process may serve as a model reaction because it is a typical simple bimolecular polar reaction and is sufficiently sensitive to the size and disposition of the substituents attached to nitrogen.

Such reactions are of course pressure accelerated. However, the major source of interest in these investigations is the effect of pressure on sterically hindered Mentshutkin reactions. Since highly substituted compounds are usually more compact than their less hindered counterparts, hindered transition states would seem to have smaller volume requirements than unhindered ones. As a consequence hindered reactions should be accelerated more by pressure than their unhindered analogs. This implies that $\Delta V^{\neq}$ generally becomes more negative when the reactional centers are more sterically crowded. Hence it becomes plausible that the expression suggested for $\Delta V^{\neq}$ in eq. (1) contains a negative term $\Delta V^{\neq}_{steric}$ arising from the overlap of interacting orbitals of the two reacting molecules; the pathway to the transition state entails an interpenetration of the steric groups with a consequent diminution in volume which is roughly proportional to the size of the overlapping groups.

This question has been widely investigated[39–45]. An interesting study by *Le Noble* and *Ogo*[46] on the Mentshutkin reactions



afforded the values for the activation volume given in Table 8.

Table 8. Activation volumes for some hindered Mentshutkin reactions at 25 °C in acetone.

Iodide R′	Amine R	$\Delta V^{\neq}$ [cm³/mol]
CH_3	H	−21.9
	CH_3	−24.4
	C_2H_5	−27.3
	$CH(CH_3)_2$	−30.2
C_2H_5	H	−23.3
	CH_3	−23.9
	C_2H_5	−28.9
	$CH(CH_3)_2$	−35.0 [a]
$CH(CH_3)_2$	H	−26.5
	CH_3	−28.2

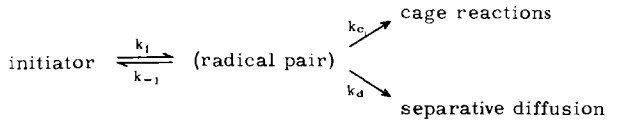
[a] Estimated.

The results show that the activation volume becomes more negative with increasing substitution, either of the amine or of the iodide.

Two explanations have been proposed for the effect of pressure on steric hindrance. *Gonikberg*[40, 41] regards the transition state as rigid and the substituents as compressible spheres; in calculating the magnitude of $\Delta V^{\neq}$ he arrives at values very close to those observed, although he neglects electrostriction arising from strong interaction of the polar transition state with neighboring molecules. This procedure of estimating $\Delta V^{\neq}$ has been criticized[3, 42], and *Weale*[42] proposes another method of calculation based both on covalent and ionic radii of the N and I atoms. The results of *Le Noble et al.* (Table 8) help to clarify these explanations: there really does exist a correlation between steric hindrance and rate accelerations at high pressures. However, although it is permissible to neglect solvation in comparative studies on pressure effects on the rate constants at various pressures ($\Delta\Delta V^{\neq}/\Delta p$), it must be taken into account in estimating the absolute value of $\Delta V^{\neq}$.

4. Cage Reactions

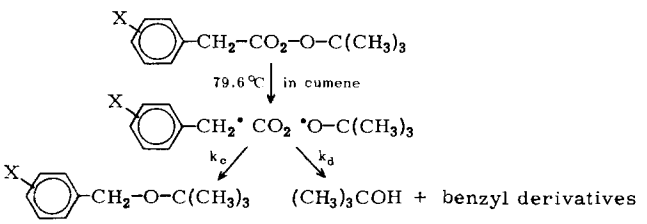
Radical reactions which occur only over short distances and in which geminate radical pairs recombine are regarded as cage reactions. The general scheme is indicated as:



The pressure dependence of the decomposition of two-bond initiators has been investigated by *Neumann et al.*[47-54], who pointed out that the $\Delta V^{\neq}$ values determined for these decompositions do not necessarily reflect the volume change during homolytic scission. The observed rate constant is in fact written as a composite quantity:

$$k_{obs} = k_1\left[\frac{k_d+k_c}{k_{-1}+k_d+k_c}\right] \qquad (10)$$

In the following reaction, only combination and diffusion compete[51].



Partitioning of the initial cages from ring-substituted *tert*-butyl phenylperacetate decomposition gives ethers *via* combination and benzyl radical products and *tert*-butyl alcohol subsequent to diffusion. In this reaction the ratio $k_c/(k_c+k_d)$ increases while separative diffusion is retarded with increasing pressure; the overall activation volume has an apparently low positive value (about $+4\,cm^3/mol$). In other cage reactions, anomalous pressure dependences may be found for geminate radicals, for example in the decomposition of azocumene[53].

These reactions provide an example of the difficulties which often arise in the interpretation of mechanisms on the basis of activation volume values.

5. Addition Polymerization Reactions

Almost the entire quantitative work on high pressure polymerizations has centered on reactions proceeding by a free radical mechanism, and very little attention has been devoted to ionic polymerizations at high pressures. Although radical polymerization reactions are sometimes complex, many of them are well understood under pressure[3, 55-63]. This section will deal with a few aspects of high pressure polymerizations which have hitherto received little attention or none at all.

5.1. Radical Copolymerizations

In radical copolymerization processes, pressure affects the competitive kinetics of homopropagation and crosspropagation. Pressure can modify the reactivity of each monomer and its corresponding radical according to the Evans-Polanyi equation:

$$\frac{\partial(\ln r_A)}{\partial p} = \frac{\Delta V_{AA}^{\neq} - \Delta V_{AB}^{\neq}}{RT} \qquad (11)$$

r_A is the reactivity ratio of the comonomer A at pressures 0 and p.

The quantity $\Delta V_{AA}^{\neq} - \Delta V_{AB}^{\neq}$ measures the influence of pressure on the competitivity between homopropagation ($\sim\!\sim A^{\bullet} + A$) and crosspropagation ($\sim\!\sim A^{\bullet} + B$).

Reference to the literature reveals that in high pressure copolymerizations the reactivity ratios are generally little affected by pressure. However, it must be pointed out that these ratios are often rather imprecise and in some cases the pressure range is so small that no generally valid conclusion can yet be drawn. The most useful results have been obtained for systems in which one of the monomers is acrylonitrile or vinyl acetate. The activation volumes calculated from the pressure dependence of the reactivity ratios are listed in Table 9.

Table 9. Activation volumes for some radical copolymerizations.

System	Ref.	Solvent	T [°C]	$\Delta V_{AA}^{\neq} - \Delta V_{AB}^{\neq}$ [cm³/mol]	$\Delta V_{BB}^{\neq} - \Delta V_{BA}^{\neq}$ [cm³/mol]
acrylonitrile (A) ethyl cinnamate (B)	[64]	bulk	60	−4.7	−7.5
acrylonitrile (A) styrene (B)	[65]	toluene	70	[a]	−9.8
acrylonitrile (A) methyl methacrylate (B)	[65]	toluene	70	[a]	−9.5
acrylonitrile (A) indene (B)	[19]	heptane	50	−4.0	0.0
vinyl acetate (A) indene (B)	[19]	heptane	50	+2.5	0.0

[a] Not calculated.

The transition state in the propagation reaction is mainly affected by the last unit of the macroradical. *Asai* and *Imoto*[66] noted that the pressure dependence of monomer reactivity is also related to the resonance stabilization of the activated complex and the resultant radical. The more pronounced pressure effect is observed for that monomer whose radical exhibits the greater resonance stabilization energy, although steric effects also play an important role. *Yala-Lutokanu*[19] found an interpretation based on the "*Q-e* scheme" to give satisfactory agreement between calculated and observed reactivity ratios.

5.2. Pseudocationic Polymerization

Abdi-Oskoui[67, 68] investigated the high pressure polymerizations of isoprene initiated by iodine or hydrogen iodide.

Iodine participates in many polymerizations as the cation I^+ and thus initiates a cationic mechanism. The iodine-initiated polymerization of isoprene at high pressures is characterized by the complex character of the iodine molecule[67]. In this case, proof has been obtained for a radical mechanism; but even if a cationic mechanism must be excluded, it is still possible to imagine a pseudocationic one involving an organic iodide as propagation agent.

This seems to be the case in the polymerization of isoprene in presence of hydrogen iodide[68]. When a solution of isoprene in dichloromethane is subjected to very high pressures (above

10 kbar) at room temperature a fast reaction takes place in the presence of catalytic amounts of HI which simultaneously gives a cyclic dimer of isoprene (limonene) and a polymer with mainly 1,4 *trans* structure. In the absence of water only cyclodimerization occurs.

Progressive addition of water to the reaction medium increases the polymer yield, but not so much as expected. Moreover, the water concentration has very little effect on the yield of dimer (Table 10).

Table 10. Polymerization of isoprene (5.35 mol/l) with aqueous HI (2.79×10^{-2} mol/l) in CH_2Cl_2 at room temperature. Pressure 12500 bar; reaction time 15 h.

Added water [mol/l]	Total yield [%]	Cyclic dimer [%]
0	16.2	14.6
0.67	19.4	12.1
1.34	20.0	12.2
1.68	28.3	14.1
6.70	34.7	15.3

The activation volume is about $-10\,cm^3$/mol, for any solvent. The radical polymerization of isoprene exhibits a more negative ΔV^* value (about $-20\,cm^3$/mol). The absence of a radical mechanism is confirmed by experiments with a radical inhibitor (no change in kinetics). That water is necessary to initiate the polymerization supports a cationic mechanism; however, the water concentration is so high that carbonium ions will hardly be able to exist in such a medium. Moreover, once the polymerization has been initiated, the further reaction is little affected by an increase in water concentration. These observations lead us to consider a pseudocationic mechanism in which a small amount of HI reacts with isoprene to give an organic iodide through which the propagation would take place.

Another characteristic of this reaction consists in the structural change of the polymer induced by pressure. With increasing pressure the 1,4 *cis* addition (17 % at 1 bar) diminishes, then vanishes above 12 kbar, whereas the amount of 1,4 *trans* units varies from 65 to 78 % in the same pressure interval.

5.3. Anionic Polymerization at High Pressures

Anionic polymerization is a reaction in which the growing end of the macromolecule carries a negative charge or is negatively polarized.

It is well known that the circumstances of a reaction exert a profound effect upon the structure of the anionic polymer, especially for polydienes. For instance the nature of the solvent plays a very important role, but other parameters may also influence the microstructure, *e.g.* pressure. In our laboratory we have spent several years on investigating[69-71] the influence of pressure on the butyllithium-initiated anionic polymerization of isoprene. We noted that the structure of the polymer obtained in a hydrocarbon solvent is very sensitive to pressure changes.

Analysis of the ionic factors shows that the mechanism is chiefly determined by the degree of interaction between the initiating anionic species and the growing chain, leading to three possible propagation forms[72]: contact ion pairs, solvent-separated contact ion pairs (loose ion pairs), and free ions[73,74]. In hydrocarbons, organic lithium compounds readily associate so that the polymer structure would result from associates of the growing chain in which the C—Li bond is strongly polarized[75]. The addition of a polar solvent destroys the associates to produce selectively solvated species and leading to intermediary structures with progressive enrichment in 3,4 units. The presence of the methyl group in the molecule of isoprene can also play an important role in changing the configuration of either the anion or the attacking monomer.

The pressure effect on the concentration of 1,4 *cis* and 3,4 units according to the polymerization solvent is shown in Table 11.

Table 11. Pressure effect upon the ratio (in %) of the 1,4 *cis* and 3,4 structures in the anionic polymerization of isoprene at room temperature in various solvents [*n*-butyllithium] = 0.02 to 0.10 mol/l.

Solvent / Pressure [bar]	*n*-Heptane		Anisole		1,4-Dioxane	
	1,4 *cis*	3,4	1,4 *cis*	3,4	1,4 *cis*	3,4
1	78	5	48	20	0	65
1000	62	8	—	—	0	65
6000	54	12	40	28	0	65
9000	50	13	38	27	0	65
14000	44	14	—	—	—	—

In weakly solvating solvents such as heptane, pressure induces far-reaching transformations by significantly reducing the percentage of the 1,4 *cis* units. In an "intermediary" solvent (anisole), the decrease is less pronounced. In the case of dioxane, the 1,4 *cis* units are absent in the whole pressure range. The pressure effect thus appears to resemble that of a solvent such as dioxane in which contact ion pairs are produced[74], probably by intervention in the association equilibria of the growing chain. Obviously, in the presence of ionic species such as occur in anionic polymerizations, the major contribution to ΔV^* comes from electrostatic effects. Pressure seems to intensify the electric field and its role would ultimately resemble that of a solvent favoring the appearance of an electric dipole between the gegenion and the end of the growing chain[76]. Nevertheless, a steric effect must also be taken into account such as was illustrated in Section 5.2 for the pseudocationic polymerization of isoprene. In that case the electrostatic contribution is not very important and so the structure change is determined mainly by steric effects.

6. Conclusion

This article does not aim at providing an exhaustive review. Instead, selected examples are presented to illustrate the role of high-pressure kinetic studies in elucidating the mechanism of organic reactions. In order to obtain valuable information from high pressure studies it is necessary to resolve the overall activation volume into its component effects and to investigate them separately.

Received: June 28, 1974 [A 33 IE]
German version: Angew. Chem. 87, 186 (1975)

[1] *M. Gonikberg*: Chemical Equilibria and Reaction Rates at High Pressures. Israël Program for Scientific Translations, Jerusalem 1963.

[2] *R. Bradley*: High Pressure Physics and Chemistry, Vol. 2. Academic Press, New York 1963.

[3] *K. E. Weale:* Chemical Reactions at High Pressures. Spon, London 1967.

[4] *C. Walling* and *D. Tanner*, J. Amer. Chem. Soc. *85*, 612 (1963).

[5] *H. Heydtmann* and *H. Stieger*, Ber. Bunsenges. Phys. Chem. *70*, 1095 (1966); *73*, 640 (1969).

[6] *B. Baliga* and *E. Whalley*, Can. J. Chem. *48*, 528 (1970).

[7] *S. Dickson* and *J. Hyne*, Can. J. Chem. *49*, 2394 (1971).

[8] *J. Benson* and *J. Berson*, J. Amer. Chem. Soc. *84*, 152 (1962).

[9] *C. Eckert*, Ann. Rev. Phys. Chem. *23*, 239 (1972).

[10] *C. Brun* and *G. Jenner*, Tetrahedron *28*, 3113 (1972).

[11] *J. Rimmelin* and *G. Jenner*, Tetrahedron *30*, 3081 (1974).

[12] *R. Grieger* and *C. Eckert*, Amer. Inst. Chem. Eng. J. *16*, 766 (1970).

[13] It may be noted that in some cases, bimolecular diffusion-controlled reactions are retarded by very high pressures. See *S. Hamann* in ref. [2], p. 203.

[14] *C. McCune*, *F. Cagle*, and *S. Kistler*, J. Phys. Chem. *64*, 1773 (1960).

[15] A very high positive activation volume ($+29.2\,cm^3/mol$) has recently been reported by *Y. Ogo* (personal communication) for the initiation reaction in the radical polymerization of methyl methacrylate.

[16] *R. Woodward* and *R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).

[17] *Nguyen Trong Anh:* Les règles de Woodward-Hoffmann, Ediscience, Paris 1970; Die Woodward-Hoffmann-Regeln und ihre Anwendung. Verlag Chemie, Weinheim 1972.

[18] *C. Brun*, *G. Jenner*, and *A. Deluzarche*, Bull. Soc. Chim. Fr. *1972*, 2332.

[19] *T. Yala-Lutokanu*, *G. Jenner*, and *A. Deluzarche*, Bull. Soc. Chim. Fr. *1974*, 609.

[20] *A. Onishenko:* Diene Synthesis. Israël Program for Scientific Translations, Jerusalem 1964.

[21] *C. Brun*, Dissertation, Université Louis-Pasteur, Strasbourg 1971.

[22] *T. Asano*, *A. Sera*, and *R. Goto*, Tetrahedron Lett. *1968*, 4777.

[23] *D. Gay*, Can. J. Chem. *49*, 3231 (1971).

[24] *J. Sauer*, Angew. Chem. *79*, 76 (1967); Angew. Chem. internat. Edit. *6*, 16 (1967).

[25] *M. Sommer* and *G. Rasch*, Wiss. Z. Tech. Hochsch. Chem. Leuna-Merseburg. *14*, 300 (1972).

[26] *Nguyen Trong Anh*, Bull. Soc. Chim. Fr. *1973*, 2721.

[27] *R. F. Hudson*, Angew. Chem. *85*, 63 (1973); Angew. Chem. internat. Edit. *12*, 36 (1973).

[28] *B. Elyanov*, *B. Rudenko*, *M. Gonikberg*, and *V. Kucherov*, Izv. Akad. Nauk SSSR, Ser. Khim. *1964*, 1082.

[29] *S. Shakova* and *B. Elyanov*, Izv. Akad. Nauk SSSR, Ser. Khim. *1973*, 1504.

[30] *J. Rimmelin* and *G. Jenner*, work in progress.

[31] *R. Grieger* and *C. Eckert*, J. Amer. Chem. Soc. *92*, 2918, 7149 (1970).

[32] *R. Grieger* and *C. Eckert*, Trans. Faraday Soc. *66*, 2579 (1970).

[33] *R. Grieger* and *C. Eckert*, Ind. Eng. Chem. Fundam. *10*, 369 (1971).

[34] *B. Poling* and *C. Eckert*, Ind. Eng. Chem. Fundam. *11*, 451 (1972).

[35] *J. McCabe* and *C. Eckert*, Accounts Chem. Res. *7*, 251 (1974).

[36] *J. McCabe* and *C. Eckert*, Ind. Eng. Chem. Fundam. *13*, 168 (1974).

[37] *C. Stewart*, J. Amer. Chem. Soc. *94*, 635 (1972).

[38] *C. Walling* and *M. Naiman*, J. Amer. Chem. Soc. *84*, 2628 (1962).

[39] *A. Harris* and *K. E. Weale*, J. Chem. Soc. *1961*, 146.

[40] *M. Gonikberg*, *V. Zhulin*, and *B. Elyanov:* The Physics and Chemistry of High Pressures. Soc. Chem. Ind., London 1961, p. 146.

[41] *M. Gonikberg*, Russ. J. Phys. Chem. *37*, 248 (1963).

[42] *J. Stewart* and *K. E. Weale*, J. Chem. Soc. *1965*, 2849, 2854.

[43] *H. Heydtmann*, *A. Schmidt*, and *H. Hartmann*, Ber. Bunsenges. Phys. Chem. *70*, 444 (1966).

[44] *Y. Okamoto* and *H. Shimizu*, J. Amer. Chem. Soc. *90*, 6145 (1968).

[45] *C. Swain* and *N. Hershey*, J. Amer. Chem. Soc. *94*, 1901 (1972).

[46] *W. Le Noble* and *Y. Ogo*, Tetrahedron *26*, 4119 (1970).

[47] *R. Neuman* and *J. Behar*, J. Amer. Chem. Soc. *89*, 4549 (1967); *91*, 6024 (1969).

[48] *R. Neuman* and *J. Behar*, Tetrahedron Lett. *1968*, 3281.

[49] *R. Neuman* and *R. Bussey*, Tetrahedron Lett. *1968*, 5859.

[50] *R. Neuman* and *R. Bussey*, J. Amer. Chem. Soc. *92*, 2440 (1970).

[51] *R. Neuman* and *J. Behar*, J. Org. Chem. *36*, 654, 657 (1971).

[52] *R. Neuman* and *G. Holmes*, J. Amer. Chem. Soc. *93*, 4242 (1971).

[53] *R. Neuman* and *M. Amrich*, J. Amer. Chem. Soc. *94*, 2730 (1972).

[54] *R. Neuman*, Accounts Chem. Res. *5*, 381 (1972).

[55] For styrene: *G. Guarise*, Polymer *7*, 497 (1966).

[56] For styrene: *Y. Ogo*, *M. Yokawa*, and *T. Imoto*, Makromol. Chem. *171*, 123 (1973).

[57] For α-methylstyrene: *T. Mitani*, *Y. Ogo*, and *T. Imoto*, Rev. Phys. Chem. Japan *42*, 25 (1972).

[58] For ethylene: *P. Ehrlich* and *G. Mortimer*, Advan. Polym. Sci. *7*, 386 (1970).

[59] For ethylene: *V. Gierth*, Angew. Makromol. Chem. *12*, 9 (1970).

[60] For ethylene: *G. Luft* and *R. Steiner*, Chem.-Zt. Chem. App. *95*, 11 (1971).

[61] For vinyl chloride: *A. Gosato-Arnaldi*, *G. Guarise*, and *G. Talamin*, Polymer *10*, 385 (1969).

[62] For fluoroolefins: *L. A. Wall:* Fluoropolymers. Wiley-Interscience, New York 1972, p. 127.

[63] For aldehydes: *C. Walling* and *T. Augurt*, J. Amer. Chem. Soc. *88*, 4163 (1966).

[64] *W. Dellsperger* and *K. E. Weale*, Polym. Prepr. Amer. Chem. Soc. Div. Polym. Chem. *11*, 645 (1970).

[65] *R. Burkhart* and *N. Zutty*, J. Polymer Sci. *57*, 795 (1962).

[66] *H. Asai* and *T. Imoto*, J. Chem. Soc. Japan *85*, 152 (1964).

[67] *H. Abdi-Oskoui*, *G. Jenner*, *A. Deluzarche*, and *A. Maillard*, Makromol. Chem. *146*, 45 (1971).

[68] *H. Abdi-Oskoui*, *G. Jenner*, and *C. Brun*, Makromol. Chem. *164*, 149 (1973).

[69] *G. Jenner*, Bull. Soc. Chim. Fr. *1966*, 3133.

[70] *G. Jenner*, Ber. Bunsenges. Phys. Chem. *70*, 1139 (1966).

[71] *G. Jenner*, *J. Hitzke*, and *M. Millet*, Bull. Soc. Chim. Fr. *1970*, 1183.

[72] For simplification; in fact there exist other more complex propagating species such as triple ions, quadrupoles, and higher aggregates. For more details, see: *H. Hirohara* and *N. Ise*, J. Polym. Sci., Part D *6*, 295 (1972).

[73] *M. Szwarc:* Carbanions, Living Polymers and Electron Transfer Processes, Wiley-Interscience, New York 1968.

[74] *A. Essel* and *Quang Tho Pham*, J. Polym. Sci., Part A-1 *10*, 2793 (1972).

[75] *A. Guyot* and *J. Vialle* [J. Macromol. Sci. Chem. *A4*, 107 (1970)] suggest that the active species in cyclohexane are mainly ion pairs of unassociated polyisoprenyllithium.

[76] *G. Jenner*, J. Macromol. Sci. Chem., in press.

^{13}C Spin-Lattice Relaxation Times and the Mobility of Organic Molecules in Solution

By Eberhard Breitmaier, Karl-Heinz Spohn, and Stefan Berger[*]

While the chemical shifts and coupling constants of ^{13}C NMR belong to the most powerful tools available to the organic chemist for the solution of structural problems, increasing interest is being shown in ^{13}C spin-lattice relaxation times T_1 as structural parameters. Together with the nuclear Overhauser effects arising by proton decoupling of ^{13}C NMR spectra, the T_1 values of ^{13}C nuclei in a molecule permit conclusions to be drawn with regard to relaxation mechanisms. They reflect the inter- and intramolecular mobility of a molecule, and thus complement the results of temperature-dependent NMR spectroscopy. The T_1 differences within a molecule show, for instance, whether the molecular motion is anisotropic in solution, whether the internal motion of groups is subject to steric hindrance, the extent to which strong intermolecular or interionic interactions affect the flexibility of the molecule, and which parts of the molecule are rigid and which are flexible. Finally, differences between the T_1 values measured for the ^{13}C nuclei of a molecule frequently provide a reliable aid in the assignment of ^{13}C NMR spectra, particularly in cases of signal crowding and multiplet overlapping.

1. Introduction[1, 2]

1.1. Nuclear Precession

Only nuclei possessing mechanical angular momentum p (nuclear spin) are suitable probes for nuclear magnetic resonance spectroscopy. The angular momentum imparts a magnetic moment $\mu = \gamma p$ to these nuclei. The ratio γ between the magnetic moment and the mechanical angular momentum is designated as the gyromagnetic constant.

If a nucleus possessing a spin is placed in a static magnetic field, then its magnetic vector $\boldsymbol{\mu}$ precesses about the direction of the field vector $\mathbf{H}_0$. Figure 1 depicts the nuclear precession in a perpendicular x,y,z coordinate system in which the z axis is defined as the direction of the field vector $\mathbf{H}_0$. According to the Larmor equation (1) the frequency of precession ν_0 is proportional to the magnetic field strength H_0 and lies in the radiofrequency range.

$$\nu_0 = \frac{\gamma}{2\pi} H_0 \qquad (1)$$

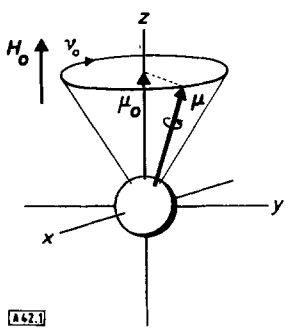


Fig. 1. Nuclear precession.

[*] Prof. Dr. E. Breitmaier and Dr. K.-H. Spohn
Chemisches Institut der Universität
74 Tübingen 1, Auf der Morgenstelle (Germany)
Dr. S. Berger
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

1.2. Equilibrium Magnetization

The magnetic vector $\boldsymbol{\mu}$ cannot precess randomly but only at certain angles to the vector $\mathbf{H}_0$ of an external magnetic field. The number m of such orientations is determined by the spin quantum number I of the nucleus, according to the quantum mechanical relation

$$m = 2I + 1 \qquad (2)$$

Nuclei having $I = 1/2$, *e.g.* ^1H and ^{13}C, can therefore adopt two possible modes of precession, *i.e.* about the direction of the field vector $\mathbf{H}_0$ ("$+1/2$") and in the opposite direction ("$-1/2$"). Precession about $\mathbf{H}_0$ is the energetically more stable alternative (Fig. 2). An assembly of nuclei in a magnetic field

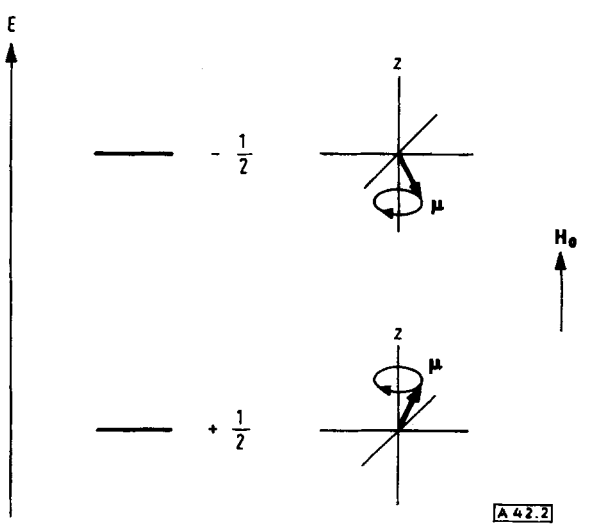


Fig. 2. Nuclear magnetic energy levels (for nuclei with $I = 1/2$).

$\mathbf{H}_0$ will therefore tend towards a Boltzmann equilibrium distribution in which more magnetic vectors precess about the $\mathbf{H}_0$ direction (Fig. 3a) than about the opposite direction. This excess gives rise to the equilibrium magnetization $\mathbf{M}_0$ along the direction of the field vector $\mathbf{H}_0$ (Fig. 3a).

1.3. Nuclear Magnetic Resonance

Continuous or pulsed radiation of radio frequency can induce transitions between nuclear magnetic energy levels (Fig. 2) provided that two conditions are met: the radio frequency ν_1 and the Larmor frequency ν_0 must be equal (resonance), and the vector $\mathbf{H}_1$ of the radio frequency must rotate perpendicular to the field vector $\mathbf{H}_0$. In this way the magnetic vectors are compelled to precess in phase (Fig. 3b), which in turn favors flipping of the magnetic vectors (Figs. 3c and 3d), such that population differences between the nuclear spin levels are balanced. The resultant magnetization $\mathbf{M}_y$ is then not only perpendicular to the standing vector $\mathbf{H}_0$ of the static field but also perpendicular to the rotating vector $\mathbf{H}_1$ of the alternating field (Fig. 3d). This transverse magnetization $\mathbf{M}_y$ thus rotates in the xy plane. In so doing it induces an alternating potential in the receiver coil of an NMR spectrometer (nuclear induction) whose frequency is the difference between the applied radio frequency and the Larmor frequency of the excited nucleus (NMR signal).

The nuclear magnetic resonance process can be represented more simply if the x,y,z coordinate system is allowed to rotate at the Larmor frequency ν_0 about the z axis (x',y',z coordinate system)[2-4]. One thus produces a standing picture in which the magnetization $\mathbf{M}_0$ is directed along the z axis at equilibrium (Fig. 4a). The radio frequency, whose vector $\mathbf{H}_1$ now rotates with the x' axis, deflects the $\mathbf{M}_0$ vector (Fig. 4b) and thus builds up the transverse magnetization $\mathbf{M}_{y'}$. The angle of deflection Θ of $\mathbf{M}_0$ (twist, flip, or pulse angle) depends upon the duration of radio-frequency irradiation in pulsed nuclear magnetic resonance. This radiation time, which lies in the μs range, is called the pulse width. If the radio frequency remains switched on just until $\mathbf{M}_0$ is deflected by 90° or $\pi/2$ (as in Fig. 4c), then the term 90° pulse or $\pi/2$ pulse is employed. Twice that time leads to a 180° or π pulse which inverts the vector $\mathbf{M}_0$ and hence also the Boltzmann distribution of the nuclear spin in Fig. 3a.

1.4. Spin-Spin and Spin-Lattice Relaxation

During nuclear resonance and thereafter, recovery processes regenerate the nuclear spin equilibrium which is characterized by the equilibrium magnetization $\mathbf{M}_0$ and the complete absence of transverse magnetization ($\mathbf{M}_{y'}=0$). These relaxation processes can be readily appreciated in the rotating coordinate system x',y',z (Fig. 5).

Spin-spin relaxation (Fig. 5b—5e) is a decay of the transverse magnetization $M_{y'}$ produced in an NMR experiment. It is assumed to occur continuously as a single exponential. The precessing magnetic vectors lose their phase coherence and once again adopt a regular distribution over the precession cone, regardless of whether their Boltzmann distribution over the nuclear magnetic energy levels (Fig. 3a) has already been reestablished or not. This process can be registered by the receiver of an NMR spectrometer as an exponential decay of the nuclear induction current with time constant T_2 (free induction decay, abbreviated to FID; cf. Figs. 6d and 6e). The spin-spin relaxation time T_2 indicates the time after which the nuclear induction current has dropped to 1/e of its original value.

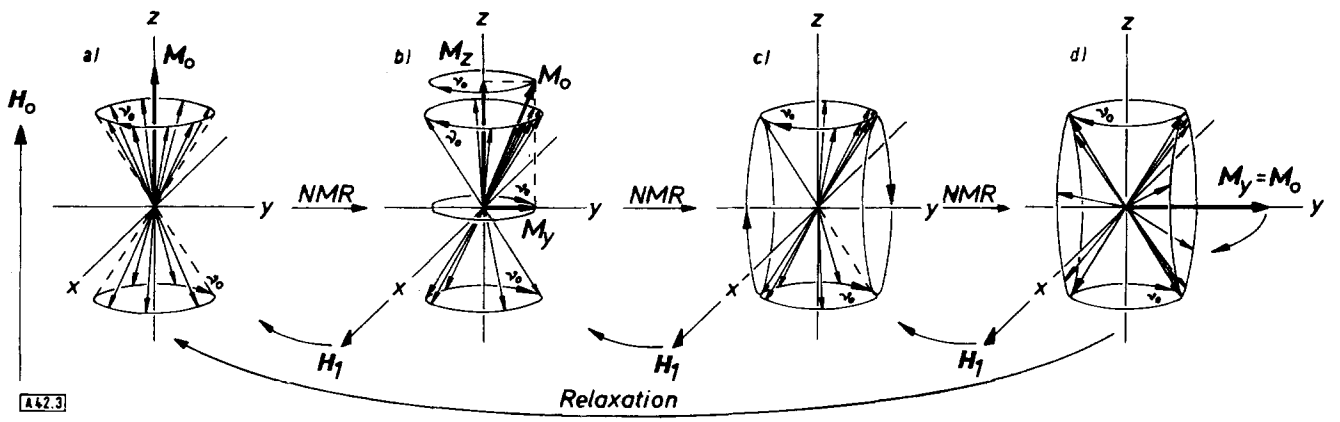


Fig. 3. a) Equilibrium magnetization in the field $\mathbf{H}_0$; b)—d) effect of the alternating field $\mathbf{H}_1$ on the magnetic vectors.

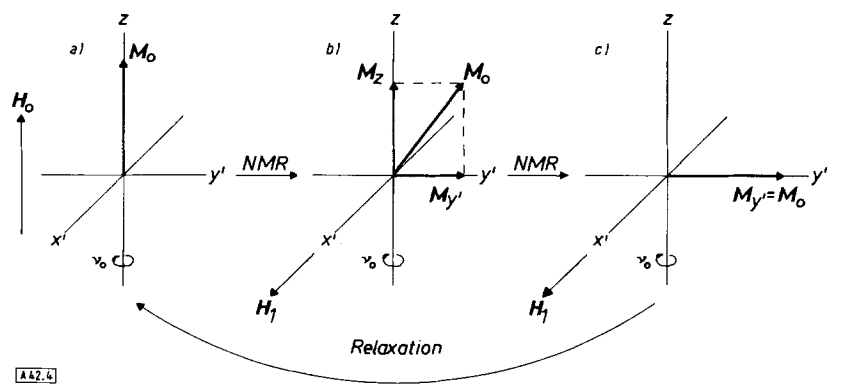


Fig. 4. Motion of the magnetization vector $\mathbf{M}_0$ in a rotating coordinate system under the influence of the alternating field $\mathbf{H}_1$. a) Equilibrium; b) start of deflection; c) deflection by 90° ($\pi/2$ pulse).

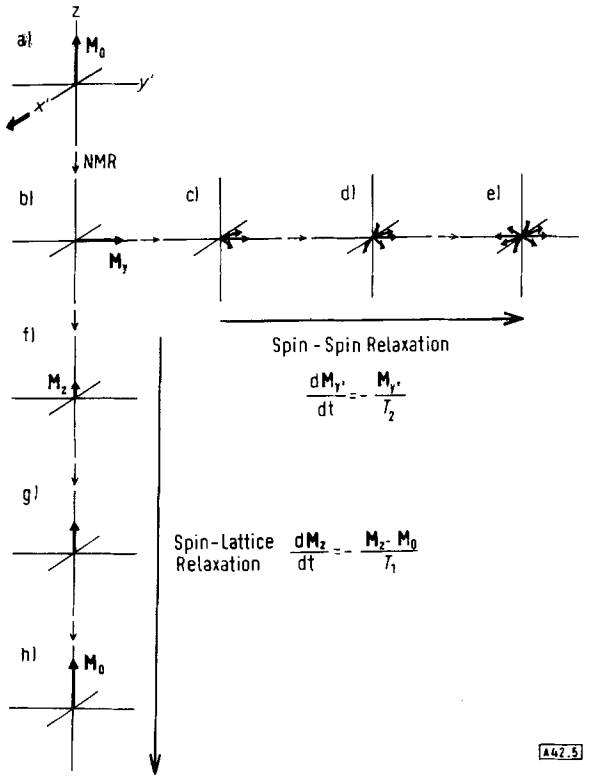


Fig. 5. a) Equilibrium; b) transverse magnetization produced in an NMR experiment; b)—e) decay of transverse magnetization (spin-spin relaxation); f)—h) reestablishment of equilibrium magnetization (spin-lattice relaxation). Shown in a rotating coordinate system.

Fourier transformation $F(t)$ of the FID leads to the frequency function $f(\nu)$, *i.e.* the nuclear magnetic resonance spectrum. This is the basis of pulse Fourier transform (PFT) NMR spectroscopy, shown schematically in Figure 6[2, 5, 6].

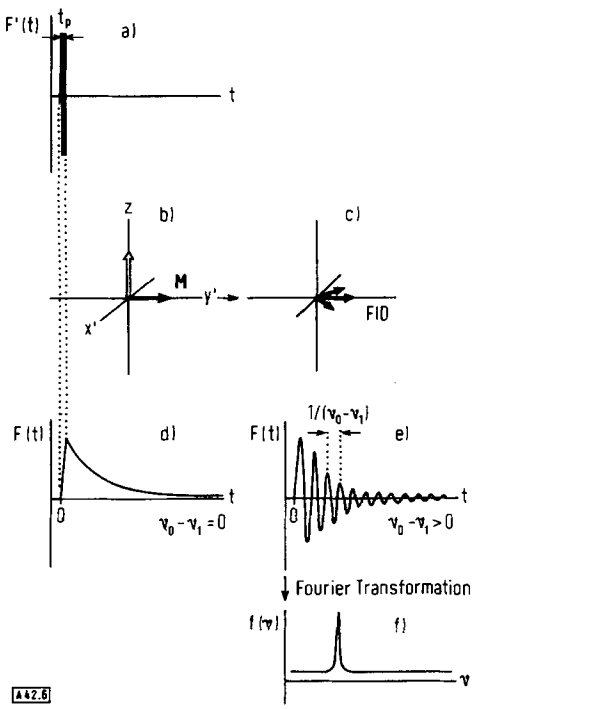


Fig. 6. Pulse Fourier transform (PFT) NMR spectroscopy. a) Radio frequency pulse as input signal; b) and c) rotation of sample magnetization by a 90° pulse and subsequent free induction decay (FID); d) FID signal registered by receiver in case of resonance, e) in case of "off-resonance"; f) Fourier transformed FID signal.

During spin-lattice relaxation, the nuclear spins excited by nuclear resonance return from the more labile to the more stable state (Fig. 2). The Boltzmann spin distribution over the nuclear magnetic energy levels which was disrupted by excitation is reestablished, and the amount of magnetization M_z along the z axis therefore approaches its equilibrium value M_0. This process, which is sketched in Figs. 5f—5h, can be described by eq. (3)[2-4]: spin-lattice relaxation is assumed to be a continuous increase in the longitudinal magnetization M_z to the equilibrium value with a time constant T_1, the spin-lattice relaxation time. T_1 is the time after which M_z has risen to 1/e of the equilibrium value M_0.

$$\frac{dM_z}{dt} = -\frac{M_z - M_0}{T_1} \tag{3}$$

Spin-lattice relaxation liberates energy, which is transferred to the environment of the nuclei. The environment, *e.g.* neighboring or solvating solvent molecules, is designated here as the lattice.

Spin-spin relaxation (decay of transverse magnetization to zero) and spin-lattice relaxation (reestablishment of the equilibrium magnetization $\mathbf{M}_0$) can proceed at different rates for a given kind of nuclei. For instance, spin-lattice relaxation is slower than spin-spin relaxation in the solid state or with macromolecules in solution so that $T_1 > T_2$. In this case, the transverse magnetization has dropped to zero and redistribution of the magnetic vectors over the precession cones is complete before the Boltzmann distribution of the spins between both levels is reached, *i.e.* before the equilibrium magnetization has been restored. With small and medium-sized molecules in the liquid or dissolved state, the relaxation processes often proceed at the same rate, so that $T_1 \approx T_2$. Since the equilibrium magnetization $M_z = M_0$ cannot be attained by a certain number of spins before the transverse magnetization $M_{y'}$ has fallen to zero ($\mathbf{M}_0 = \mathbf{M}_{y'} + \mathbf{M}_z$!), spin-lattice relaxation can proceed slower, but never faster, than spin-spin relaxation. Therefore, in general

$$T_1 \geqslant T_2 \tag{4}$$

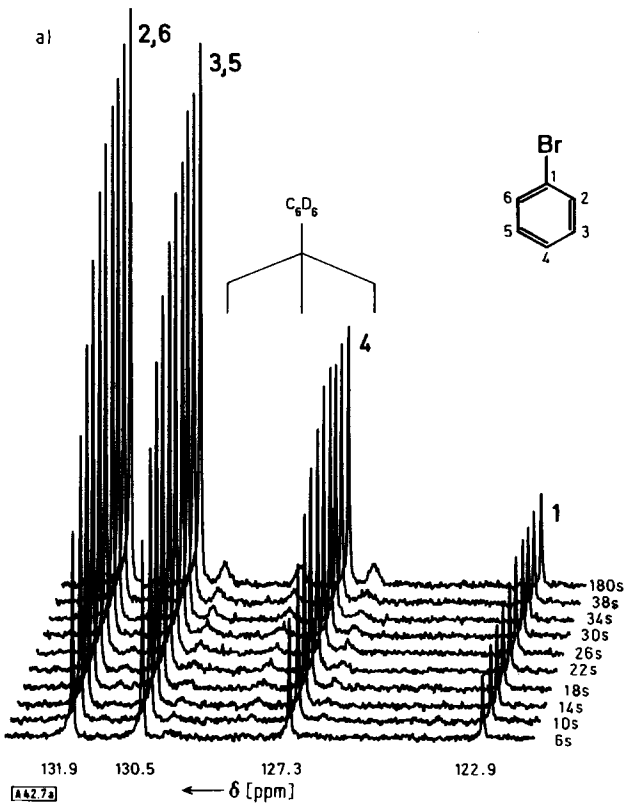
2. Measurement of Spin-Lattice Relaxation Times T_1

Several methods are available for measuring T_1[6-11]. The most important routine methods of Fourier ^{13}C NMR spectroscopy in present use are the "progressive saturation" and "inversion recovery" methods.

The procedure adopted in the "progressive saturation" technique[7] resembles that of Fourier ^{13}C NMR spectroscopy[6]. The signal sequence following a sequence of several 90° pulses is accumulated, and the procedure repeated a number of times for different pulse intervals τ. It is essential that signal summation be undertaken only after a steady-state regime has been obtained where excitation and relaxation balance each other. Therefore, signal accumulation is started for each interval only after the fifth to the tenth pulse. Fourier transformation of the accumulated signals and sequential plotting of the Fourier spectra yield a series of spectra such as that shown in Figure 7a: The signal intensity A_τ asymptotically approaches an equilibrium value A_∞ as the interval τ increases.

T_1 is obtained as the reciprocal slope of a regression line resulting from a semi-logarithmic plot of $A_\infty - A_\tau$ *versus* τ (see *e.g.* Fig. 7b). The signal intensity A is a measure for the amount of the magnetization M.

It is not absolutely necessary to measure the equilibrium value A_∞. Determination of T_1 is already possible with the aid of the averaged signal intensities A_1 and A_2 of only two FT NMR spectra resulting from two sequences of 90° pulses having different intervals τ_1 and τ_2[7b].



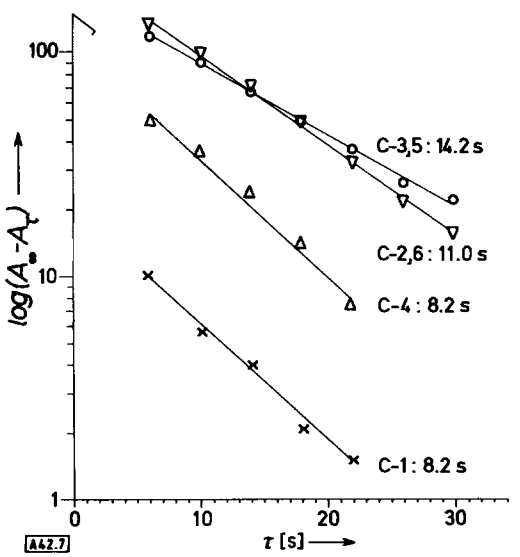


Fig. 7. Measurement of spin-lattice relaxation times T_1 of the ^{13}C atoms of bromobenzene, 85% solution in hexadeuteriobenzene at 28°C and 15.08 MHz. a) Series of measurements (progressive saturation; b) evaluation. T_1 is the reciprocal slope of the straight line.

In the "inversion recovery method" (Fig. 8)[6, 8–11], spin-lattice relaxation is initiated by a 180° pulse, which inverts the Boltzmann distribution of nuclear spins and hence the magnetization vector $\mathbf{M}_0$ (Fig. 8b). After a variable time τ, which determines the extent of spin-lattice relaxation, a 90° pulse is applied to initiate a nuclear induction signal F(t) which affords the NMR spectrum f(ν) on Fourier transformation.

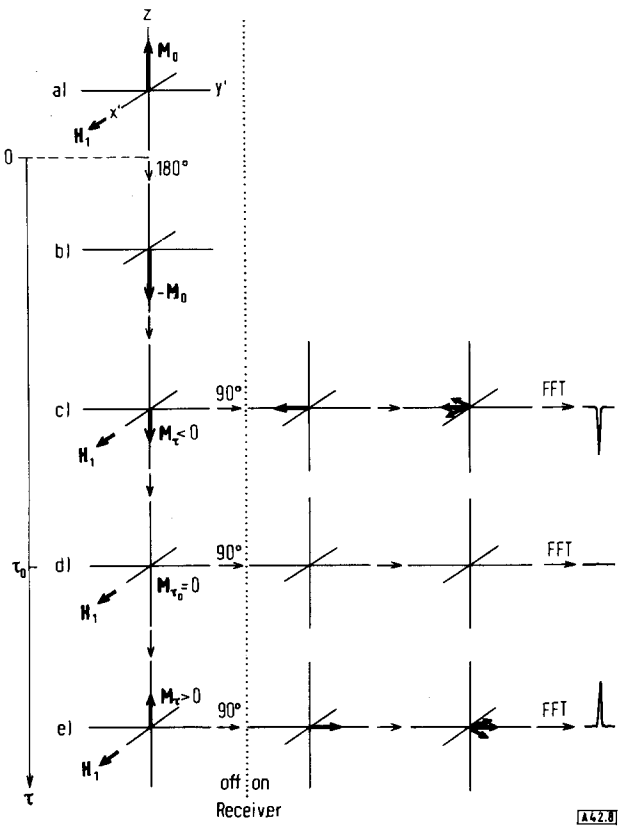


Fig. 8. Inversion recovery or 180°, τ, 90° method: pulse-controlled motion of the magnetization vector in a rotating coordinate system. FFT = fast Fourier transformation. a)–e), see text.

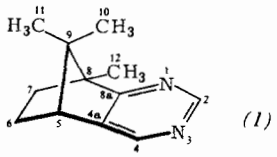
If it follows immediately upon the 180° pulse, the 90° pulse generates an inverted signal (Figs. 8c and 9). This becomes weaker and weaker with increasing interval τ owing to spin-lattice relaxation (Fig. 9). After passing through zero (at τ_0, Figs. 8d and 9), the intensity becomes positive and asymptotically approaches the equilibrium intensity A_∞ as τ increases (Figs. 8e and 9). The resulting series of spectra (Figs. 9a and 9b) are evaluated as for "progressive saturation" (*e.g.* in Fig. 7b), or more simply but less accurately from the interval τ_0, for which the intensity goes through zero, according to eq. (5).

$$T_1 = \tau_0/\ln 2 \qquad (5)$$

The signals following the 180°, τ, 90° pulse sequences usually have to be accumulated in order to increase the sensitivity of the method. One then has to wait after each sequence until all nuclei of the molecule have relaxed.

3. Mechanisms of ^{13}C Spin-Lattice Relaxation[2, 11–13]

In spin-lattice relaxation, the excited nuclei transfer their excitation energy to their environment. They do so *via* interaction of their magnetic vectors with fluctuating local fields of suffi-



(1)

acetylene, and carbonyl compounds (chemical shift anisotropy). The shielding constant σ[1] then possesses spatially oriented components, which can change with time if the molecule moves relative to the field $\mathbf{H}_0$. There arise fluctuating local fields which permit spin-lattice relaxation of the aniso-

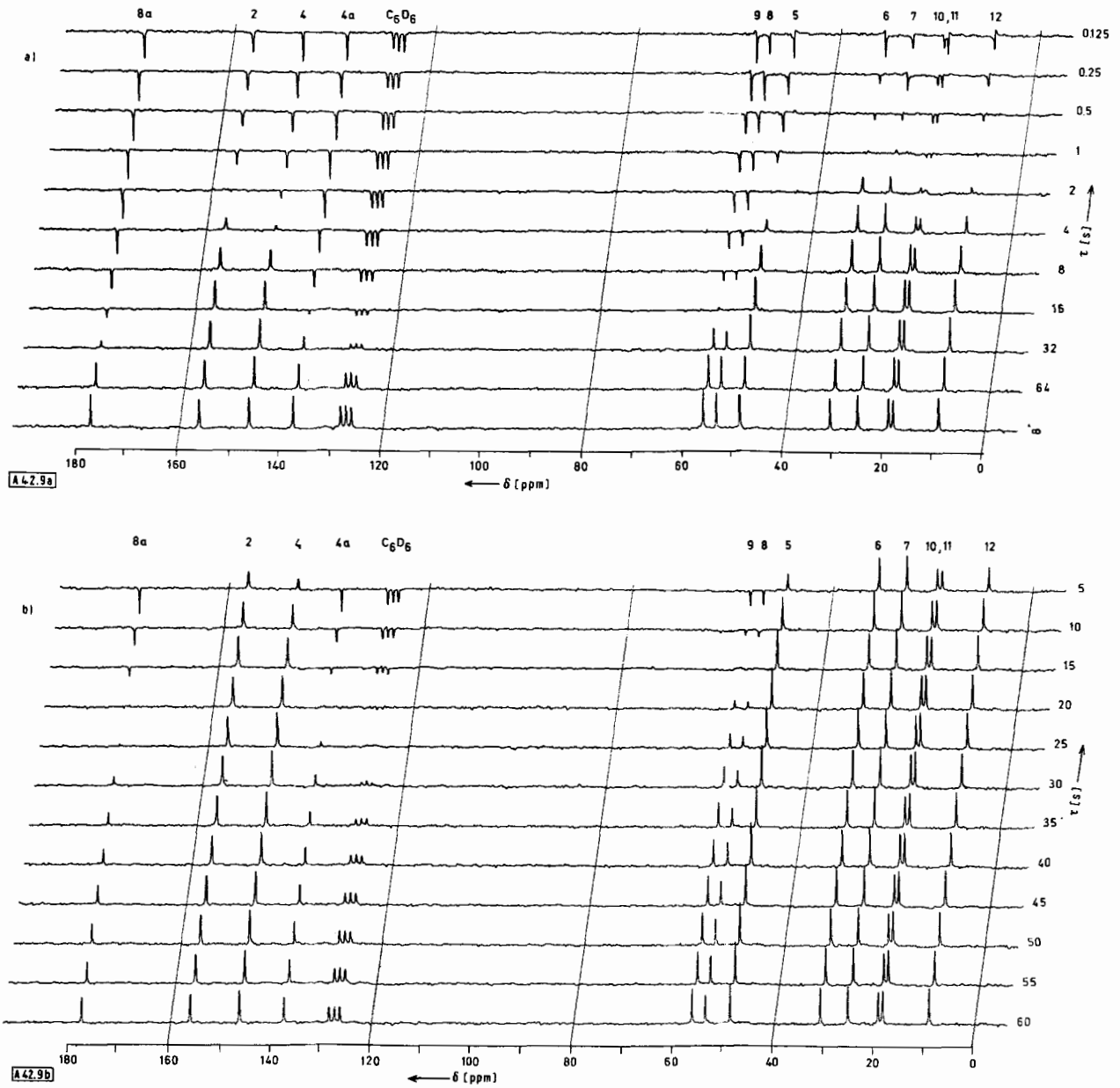


Fig. 9. Measurement of the spin-lattice relaxation times T_1 of the ^{13}C nuclei of 8,9,9-trimethyl-5,8-methano-5,6,7,8-tetrahydroquinazoline *(1)* in hexadeuteriobenzene at 40°C and 22.63 MHz: a) series of measurements with halved intervals; b) series of measurements with subtracted intervals. The series of measurements were evaluated by semilogarithmic plotting of $A_\infty - A_\tau$ *versus* τ (by analogy with Fig. 7b). The T_1 values obtained are given in Section 5.4.1.

cient strength and a fluctuation frequency of the order of the Larmor frequency of the nuclear spin type. Depending upon the atomic and electronic environment of a nucleus in a molecule and the motion of that molecule, there are four potential mechanisms (see Sections 3.1—3.4) contributing to spin-lattice relaxation of the nucleus.

3.1. Relaxation Resulting from Chemical Shift Anisotropy (CSA Mechanism)

The magnetic shielding of a nucleus arising from the surrounding electrons can be anisotropic, *e.g.* in derivatives of benzene, tropically shielded nucleus. A contribution of the CSA mechanism is apparent from a proportionality of the T_1 values measured to the square of the magnetic field strength H_0 applied. This contribution is usually negligible for the ^{13}C nuclei of organic molecules.

3.2. Relaxation by Scalar Coupling (SC Mechanism)

The spins of two proximate nuclei A and X in a molecule undergo coupling, *i.e.* the signals of A and X are split, but only if the lifetime of these nuclei in their nuclear magnetic energy levels (Fig. 2) is sufficiently large (scalar coupling).

If nucleus X relaxes very much faster than nucleus A then no signal splitting is observed. However, the fast relaxation of X generates fluctuating fields which in turn contribute to the relaxation of nucleus A. Quadrupole nuclei having $I \geqslant 1$, *i.e.* nuclei whose charge distribution is not spherically symmetrical, relax so fast, for instance, that they accelerate the relaxation of neighboring nuclei. The contribution of the SC mechanism, which can be recognized from a frequency and temperature dependence of T_1 is particularly large when the coupling nuclei precess with similar Larmor frequencies. This applies to ^{13}C and the quadrupole ^{79}Br. As a consequence ^{13}C nuclei bound to Br relax relatively fast ($CHCl_3$: $T_1 = 32.4$ s; $CHBr_3$: $T_1 = 1.65$ s)[12].

3.3. Relaxation by Spin Rotation (SR Mechanism)

If a molecule or molecular segment rotates, then the magnetic vectors of the bonding electron spins will also rotate. This gives rise to fluctuating local fields which can contribute to spin-lattice relaxation of the nuclei of a rotating molecule or a rotating alkyl group. This SR mechanism plays an important role in small symmetrical molecules (methane, cyclopropane) or in small segments of larger molecules (methyl groups). If the ^{13}C nuclei are not protonated (as in CS_2), spin rotation can even become the predominant relaxation mechanism. In such cases T_1 is found to decrease significantly with increasing temperature[12].

3.4. Relaxation by Internuclear Dipole-Dipole Interaction (DD Mechanism)

Each nuclear spin generates a local magnetic field. If two magnetic nuclei such as ^{13}C and ^{1}H are linked by a bond, then each of the nuclei will "feel" not only the external field $\mathbf{H}_0$, but also the local field of the other nuclear spin (internuclear dipole-dipole interaction). Now molecular motion is very rapid in liquids. Rotations of C—H bonds are correspondingly fast in dissolved organic molecules, and the orientations of ^{1}H and ^{13}C relative to $\mathbf{H}_0$ will be constantly changing. The resulting constantly imposed magnetic reorientation of the two nuclear spins generates fluctuating local fields which contribute to the relaxation of the nuclei. Most of the ^{13}C nuclei in organic molecules, especially those linked to hydrogen (CH, CH_2, CH_3) are relaxed predominantly by internuclear dipole-dipole interaction.

T_1 values of ^{13}C are usually measured with proton noise decoupling[6]. Thus, just one signal, not a multiplet, and consequently only one T_1 value results for each C atom of a molecule. During this decoupling, the protons transfer their excitation energy to the "lattice" primarily by internuclear DD interaction with ^{13}C and consequently forced ^{13}C relaxation. As a result, the population of the energetically more favorable ^{13}C spin states (Fig. 2) increases, and the ^{13}C signal intensities are enhanced on proton-decoupling more than would be expected from the multiplet intensities in the spectra recorded without decoupling (nuclear Overhauser enhancement, NOE[14]).

If ^{13}C relaxation proceeds exclusively by the DD mechanism, the NOE factor η_C, indicating the enhancement of the ^{13}C signal intensity on decoupling, is determined by the gyromagnetic ratios of ^{1}H and ^{13}C according to eq. (6)[14].

$$\eta_C = \frac{\gamma_H}{2\gamma_C} = 1.988 \tag{6}$$

NOE factors of this magnitude are indeed measured for numerous ^{13}C signals of organic molecules, especially for signals of CH and CH_2 carbon atoms, as shown for formic acid in Figure 10[15].

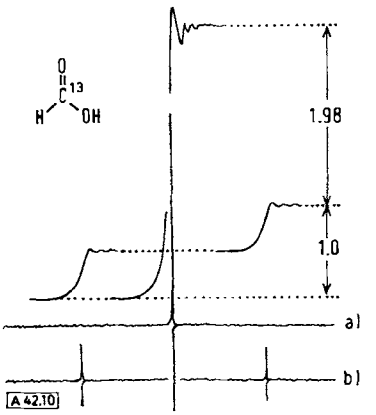


Fig. 10. Nuclear Overhauser enhancement on proton decoupling in the ^{13}C NMR spectrum of ^{13}C-enriched formic acid; a) decoupled, b) coupled (see ref. [15]).

NOE factors smaller than 1.988 indicate participation of other mechanisms in the spin-lattice relaxation of protonated ^{13}C nuclei. The percentage contribution of the DD mechanism can be ascertained from the measured NOE factor according to eq. (7).

$$\%\ \mathrm{DD} = \frac{\eta_C}{1.988} \times 100 \tag{7}$$

Accordingly, the time constant $T_{1(DD)}$ of the DD mechanism can be calculated from the measured η_C and T_1 values [eq. (8)].

$$T_{1(DD)} = T_1 \frac{1.988}{\eta_C} \tag{8}$$

Since the relaxation rates $1/T_1$ on cooperation of several relaxation mechanisms can be assumed to be additive, as shown in eq. (9),

$$\frac{1}{T_1} = \frac{1}{T_{1(DD)}} + \frac{1}{T_{1(SR)}} + \frac{1}{T_{1(SC)}} + \frac{1}{T_{1(CSA)}} + \cdots \tag{9}$$

the measured T_1 value and the value of $T_{1(DD)}$, accessible from the NOE factor η_C *via* eq. (8), can be used to calculate the time constant of a second relaxation mechanism, provided that no further mechanisms are operative. For instance, in benzene the DD mechanism is accompanied only by the SR mechanism. Benzene contains no quadrupole nucleus, and the contribution of the CSA mechanism to ^{13}C relaxation of liquid benzene is so small that the T_1 value can be shown to be independent of the magnetic field strength[16]. Then $T_{1(DD)}$ and $T_{1(SR)}$ can be determined from the experimental values of T_1 and η_C according to Scheme 1[11, 17–19].

Experimental data: Spin-lattice relaxation time $T_1 = 29.3$ s

NOE factor $\eta_C = 1.6$

Percentage of DD relaxation:

$\%\ DD = \eta_C \times 100/1.988 = 80\ \%$

Contribution of DD mechanism:

$T_{1(DD)} = T_1 \times 1.988/\eta_C = 29.3 \times 1.988/1.6 = 36.4$ s

Contribution of SR mechanism:

from $\frac{1}{T_1} = \frac{1}{T_{1(DD)}} + \frac{1}{T_{1(SR)}}$

it follows

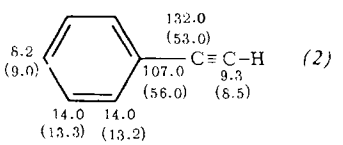
$$T_{1(SR)} = \frac{T_1\, T_{1(DD)}}{T_{1(DD)} - T_1} = \frac{29.3 \times 36.4}{36.4 - 29.3} = 150\ \text{s}$$

Scheme 1. Determination of $T_{1(DD)}$ and $T_{1(SR)}$ from T_1 and η_C measured for benzene.

3.5. Electron Spin-Nucleus Interactions and Consequences

During molecular motion, unpaired electrons generate much stronger fluctuating local fields than the nuclear spins, owing to their considerably greater magnetic moment. As a result, relaxation in the presence of unpaired electrons is dominated by electron spin-nucleus dipole-dipole interactions analogous to internuclear dipole-dipole interactions, especially for non-protonated ^{13}C nuclei. Thus smaller T_1 values are observed for paramagnetic compounds themselves, or in their presence, *e.g.* in solvents containing oxygen. Paramagnetic contaminants, including the oxygen nearly always dissolved in liquids, must therefore be removed if characteristic and reproducible T_1 values are to be measured.

Acceleration of relaxation of a nuclear spin by paramagnetic compounds is the greater the slower the nucleus relaxes. For example, the non-protonated carbon nuclei of phenylacetylene *(2)* in a normally prepared sample (20% in $(CD_3)_2CO$ as solvent) display T_1 values lower by a factor of two (numbers in parentheses)[*] than those for a degassed, *i.e.* largely oxygen-free, solution[18]. In contrast, the faster-relaxing protonated carbon atoms ($T_1 < 20$ s) are affected much less.



(2)

The pronounced relaxation acceleration observed for slowly relaxing nuclei in the presence of paramagnetic compounds is exploited in Fourier transform ^{13}C NMR spectroscopy. On use of the fast pulse sequences that are frequently necessary, the spin-lattice relaxation of "slow" ^{13}C nuclei can no longer follow excitation and the pertinent ^{13}C signals have low intensities. In such cases, addition of small amounts of relaxation accelerators such as radicals or transition metal salts to the sample amplify these signals[20].

It ist quite reasonable that a paramagnetic central ion should accelerate the relaxation of the C atoms of a ligand, and that the magnitude of the acceleration should depend upon the distance between the ion and the C atom being observed.

[*] Unless otherwise stated, the T_1 values in the formulas are given in s.

In such cases, T_1 measurements provide information about the distances between the paramagnetic ion and the ligand. Thus the spin-lattice relaxation times of the ^{13}C nuclei in α- and β-methyl D-glucopyranoside become selectively smaller on binding to the Mn^{2+} complex of the protein concanavalin A[21]. The experimental T_1 values show that the two glucopyranoside anomers retain their C1 chair conformation, but adopt different orientations on binding to the protein complex[21]. The non-reducing end of the α-anomer (C-3, C-4) approaches the Mn^{2+} ion most closely (average separation approx. 10 Å)[21].

4. Influence of Molecular Motion on Dipole-Dipole Relaxation

The majority of ^{13}C NMR measurements are performed with solutions or liquid samples with proton decoupling. Under these conditions, the ^{13}C spin-lattice relaxation times T_1 depend mainly upon the speed of molecular motion relative to ^{13}C Larmor precession. The overall tumbling of molecules in liquids cannot easily be resolved into components such as rotation, vibration, or translation. In order to derive a useful relation with the spin-lattice relaxation, the average time required by a molecule between two reorientations is taken as a measure of molecular motion. This time is referred to the unit circle, *i.e.* divided by 2π, and then designated the effective molecular correlation time τ_C[2, 13, 22–24]. If the molecules are rotating or vibrating, then one revolution or vibration per second (1 Hz) is equal to 2π rad/s. τ_C then corresponds to the average time required by the molecules to rotate through 1 radian.

Only those molecular motions whose "frequencies" lie in the region of the ^{13}C Larmor precession lead to rapid ^{13}C dipolar relaxation. The ^{13}C nuclei are known to precess with a frequency of $\nu_0 \approx 2.26 \times 10^7$ Hz or $\omega_0 = 2\pi\nu_0 \approx 1.42 \times 10^8$ rad/s at a field strength of $H_0 \approx 21$ kG. Most effective DD relaxation then becomes possible owing to molecular motions having correlation times of

$$\tau_C \approx \frac{1}{1.42 \times 10^8} \approx 7 \times 10^{-9}\ \text{s}$$

The correlation function $T_1 = f(\tau_C)$ shown in Figure 11 gives a minimum for such motion; however, this is true only for a field strength of 21 kG. At higher fields the minimum lies at shorter correlation times, *i.e.* the fastest DD relaxation requires even faster motion (Fig. 11).

Very slow molecular motion ($\tau_C > 10^{-9}$ s at $H_0 \approx 21$ kG) leads to an increase in T_1, while T_2 decreases (Fig. 11). The signals then broaden (line width at half-maximum intensity $\Delta\nu_{1/2} \sim 1/T_2$). Therefore the more sluggish macromolecules usually give poorly resolved ^{13}C NMR spectra having a band-like structure.

If the viscosity is sufficiently low, small and medium-sized molecules tumble very fast. The "frequencies" of their motion often even exceed the Larmor frequency $\omega_0 = 2\pi\nu_0$, and the correlation time consequently becomes shorter than the value $\tau_{C(min)}$ leading to the most effective DD relaxation ($\omega_0\tau_C \ll 1$). This situation corresponds to the declining branch of the correlation function (Fig. 11): T_1 and T_2 increase, are approximately equal, and the signals become sharper owing to $\Delta\nu_{1/2} \sim 1/T_2$ (motional narrowing). Under these circumstances

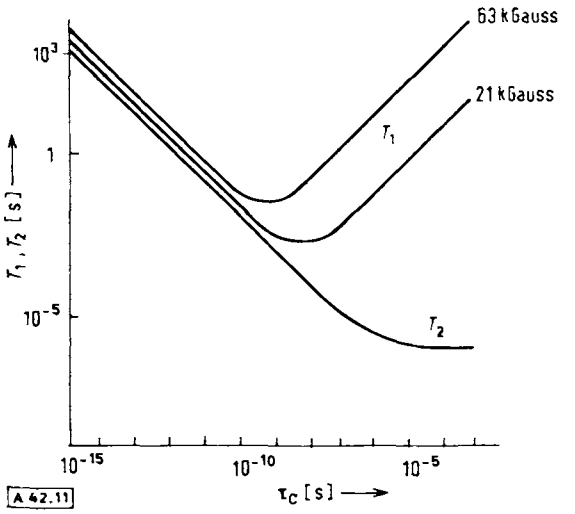


Fig. 11. Relation between the relaxation times T_1 and T_2 and the effective correlation time τ_C. In stronger magnetic fields the T_1 minimum shifts towards smaller correlation times, *i.e.* higher "frequencies" of molecular motion.

the dipolar relaxation time $T_{1(DD)}$ of a ^{13}C nucleus is shown in eq. (10) to be inversely proportional to the number N of directly adjacent protons and to the effective correlation time τ_C[10-13, 22-24].

$$\frac{1}{T_{1(DD)}} = \hbar^2 \gamma_C^2 \gamma_H^2 r_{CH}^{-6} N \tau_C \qquad (10)$$

$\hbar \equiv h/2\pi$; h is Planck's constant; γ_C and γ_H are the gyromagnetic ratios of ^{13}C and ^1H respectively; r_{CH} is C—H internuclear distance, usually about 1.09 Å.

5. Information Content of ^{13}C Spin-Lattice Relaxation Times

5.1. Degree of Alkylation and Substitution of C Atoms

Within rigid molecules the correlation time τ_C is equal for all carbon atoms. Moreover, the C—H bond lengths in nearly all organic compounds are approximately 1.09 Å, except for acetylenes ($r_{CH} \approx 1.06$ Å). Under these conditions, the spin-lattice relaxation time T_1 of a ^{13}C nucleus relaxing by the DD mechanism is shown by eq. (10) to depend solely upon the number N of directly bonded H atoms:

$$T_{1(DD)} = \text{const.}/N \qquad (11)$$

Neglecting the methyl carbons, which do not belong to the rigid skeleton of a molecule owing to internal rotation of the CH_3 groups (Section 5.4.1), the T_1 values for the CH and CH_2 groups of the same molecule give a ratio of 2:1; quaternary C atoms having $N = 0$ relax much more slowly:

$$T_{1(C)} \gg T_{1(CH)} > T_{1(CH_2)} \text{ and } T_{1(CH)} : T_{1(CH_2)} = 2:1 \qquad (12)$$

This relation (12) can be demonstrated for simple rigid molecules, *e.g.* for adamantane having $T_{1(CH)} = 17.0$ s and $T_{1(CH_2)} = 7.8$ s[25]. It is a valuable aid in the assignment of the ^{13}C NMR spectra of large molecules, particularly when signal crowding precludes clear distinction between singlets, doublets, and triplets in coupled or proton off-resonance decoupled ^{13}C NMR spectra[6].

5.2. Molecular Size and Relaxation Mechanisms

The T_1 values of the ^{13}C nuclei generally decrease with increasing molecular size if the molecules are rigid. Thus values in the ms or ns range are observed for the ^{13}C nuclei of the rigid backbone of macromolecules. Medium size molecules (C_{10}—C_{50}) typically show T_1 values between 0.1 s and 20 s. For very small molecules of high symmetry (dumbbells, tetrahedra, pyramids, small regular polyhedra), however, values of up to 100 s and beyond are possible. This applies, *e.g.* to methane derivatives except for bromides (effective SC relaxation, cf. Section 3.2), especially when the molecule contains no H atoms ($^{13}CCl_4$: $T_1 \approx 160$ s[6]). The reason is that the ^{13}C nuclei of very mobile small molecules relax partly, and sometimes even predominantly, by the less effective spin-rotation mechanism. The considerable contribution of SR mechanism to ^{13}C spin-lattice relaxation has already been demonstrated for benzene (Section 3.4).

The relation between molecular size, T_1, and the relaxation mechanisms is apparent from the homologous series of the cycloalkanes. T_1 and NOE data as well as the contributions of the DD and SR mechanisms accessible from these experimental values *via* eqs. (8) and (9) are listed in Table 1. The ^{13}C nuclei of cyclopropane relax almost as fast by spin-rotation as by the DD mechanism ($T_{1(SR)} \approx T_{1(DD)}$). However, in cyclobutane the DD mechanism predominates ($T_{1(DD)} < T_{1(SR)}$), and the carbon atoms of cyclohexane and its higher homologs relax exclusively by the DD mechanism ($T_{1(DD)} \ll T_{1(SR)}$)[26]. The $T_{1(DD)}$ values themselves decrease fairly regularly with increasing ring size (Table 1).

Table 1. Spin-lattice relaxation times T_1 and NOE factors η_C of the ^{13}C nuclei of cycloalkanes containing n carbon atoms [26].

n	T_1 [s]	η_C	DD [%]	$T_{1(DD)}$ [s]	$T_{1(SR)}$ [s]
3	36.7	1.0	50.2	72.2	74.6
4	35.7	1.4	70.5	50.7	121
5	29.2	1.52	76.5	38.2	124
6	19.6	1.9	95.5	20.5	447
7	16.2	1.96	98.5	16.4	> 1000
8	10.3	2.0	100	10.3	> 1000
10	4.7	2.0	100	4.7	> 1000

5.3. Anisotropy of Molecular Motion

Eq. (10) discussed in Section 4 is only valid if the motion of the molecules under study has no preferential orientation, *i.e.* is not anisotropic. Strictly speaking, this applies only for approximately spherical bodies such as adamantane. Even an ellipsoidal molecule like *trans*-decalin performs anisotropic motion in solution: it will preferentially undergo rotation and translation such that it displaces as few as possible of the other molecules present. This anisotropic rotation during translation is accounted for by the three diagonal components R_1, R_2, and R_3 of the rotational diffusion tensor. If the principal axes of this tensor coincide with those of the moment of inertia—as can frequently be assumed in practice—then R_1, R_2, and R_3 indicate the speed at which the molecule rotates about its three principal axes.

The connection between anisotropic molecular motion and nuclear relaxation was derived by *Woessner* as early as 1962[27]. Accordingly, the dipole-dipole relaxation time of a carbon

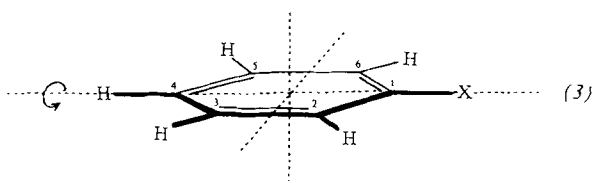
nucleus is a function of the diagonal components R_1, R_2, and R_3 of the rotational diffusion tensor and the cosines λ, μ, and ν of the angles assumed by the C—H bonds relative to the principal axes of this tensor.

$$1/T_{1(DD)} = f(R_1, R_2, R_3, \lambda, \mu, \nu) \quad (13)$$

If the position of the principal axes of the rotational diffusion tensor were known with respect to the molecular coordinates, then the motion of the molecule could be calculated from the measured relaxation times. With simple molecules, however, it is possible to interpret the T_1 values qualitatively in the sense of an anisotropic motion.

Thus the C—H nuclei in the *para* position of monosubstituted benzene derivatives relax faster than those in the *ortho* or *meta* positions (Table 2[18]). The reason for this behavior probably lies in a preferred rotation about the molecular axis passing through the substituent X and the *p*-carbon. In this motion, the *para* C—H bond does not change its direction relative to the field $\mathbf{H}_0$; fluctuating local fields can only arise at the *p*-C nucleus by rotations of the molecule perpendicular to the preferred axis. However, these less preferred rotations still have sufficiently large frequencies to effectively relax the *p*-C atom. The preferred rotation itself continuously changes the orientation of the *ortho* and *meta* C—H bonds with respect to $\mathbf{H}_0$, but too fast for effective dipolar relaxation of the *ortho* and *meta* carbon nuclei.

Table 2. Spin-lattice relaxation times T_1 of the ^{13}C atoms in benzene derivatives *(3)*

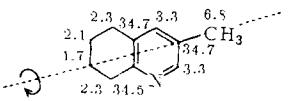


(3)

X	C Atom	T_1 [s]	Ref.
H	1—6	29.3 [a]	[18]
CH_2—CH_3	1	36.0	[28]
	2,6	18.0	
	3,5	18.0	
	4	13.0	
	—CH_2	13.0	
	—CH_3	9.0	
CH=CH_2	1	75.0	[18]
	2,6	14.8	
	3,5	13.5	
	4	11.9	
	—CH=	17.0	
	=CH_2	7.8	
C≡CH	1	107.0 [a]	[18]
	2,6	14.0	
	3,5	14.0	
	4	8.2	
	—C≡	132.0	
	≡CH	9.3	
CH_3	1	58.0	[18]
	2,6	20.0	
	3,5	21.0	
	4	15.0	
	CH_3	16.3	
C_6H_5	1	61.0	[18]
	2,6	5.9	
	3,5	5.9	
	4	3.2	
NO_2	1	56.0	[18]
	2,6	6.9	
	3,5	6.9	
	4	4.8	
OH	1	21.5	[18]
	2,6	4.4	
	3,5	3.9	
	4	2.4	

[a] Degassed.

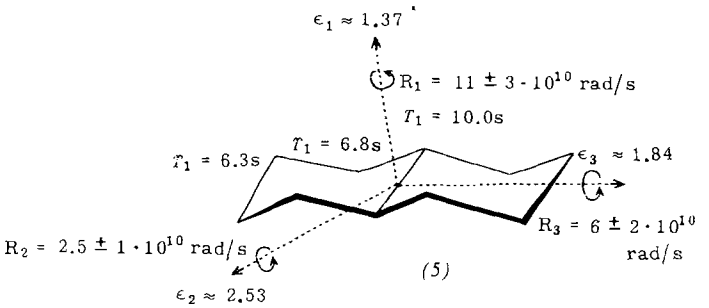
Preferred rotation is also conceivable in 3-methyl-5,6,7,8-tetrahydroquinoline *(4)*, *i. e.* about the axis passing through C-7, C-3, and the methyl group[29]. Accordingly, the C-7 methylene group exhibits a smaller T_1 value than all the other CH_2 groups of this molecule.



(4)

The first quantitative estimate of the rotational diffusion tensor for simple molecules was accomplished by *Grant et al.*[30]. By solving the Woessner equations, they were able to show, *e.g.* for *trans*-decalin *(5)* that the molecule rotates preferentially like a propeller, *i.e.* about the axis perpendicular to the plane of the molecule. The values given as a measure of the rotational frequencies do not correlate with the moments of inertia, but instead with the "ellipticities" of the molecule as defined by *Grant*. They are accessible from the ratios of the interatomic distances perpendicular to the axes of rotation, and can be adopted as a measure of the number of solvent molecules that have to be displaced on rotation about each of the three axes.

The greater the differences between the interatomic distances perpendicular to an axis, the greater will be the ellipticity ε, and the more slowly will the molecule rotate about that axis.

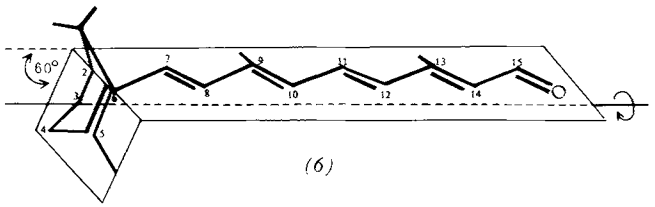


(5)

For less symmetric molecules one has to resort to computer programs[31] to solve the Woessner equations. The orientation of the rotational diffusion tensor is usually defined by assuming that its principal axes coincide with those of the moment of inertia tensor. This assumption is probably a good approximation for molecules of low polarity containing no heavy atoms, since under these conditions the moment of inertia tensor roughly represents the shape of the molecule.

The hitherto most sophisticated application of *Woessner*'s theory has been accomplished for all-*trans*-retinal *(6)* and its isomers[32]. After determination of the components of the rotational diffusion tensor in retinal *(6)* for various dihedral angles between the olefinic chain and the cyclohexene ring, the T_1 values could be calculated for each one of these conformations. The best agreement between experimental and calculated ^{13}C T_1 values results when the 5,6—7,8 dihedral angle

is 60°, in other words when the cyclohexene ring is bent by 60° towards the plane of the olefinic chain[32]. This is the first example of a conformation being determined by measurement of ^{13}C relaxation times.



(6)

Woessner's equations thus permit prediction of spin-lattice relaxation times for the dipole-dipole mechanism, which can be of help in the assignment of ^{13}C NMR spectra. Moreover, the calculations described can be applied to the problem of internal molecular motion.

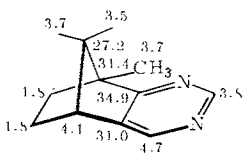
5.4. Internal Molecular Motion

5.4.1. Rotation of Methyl Groups

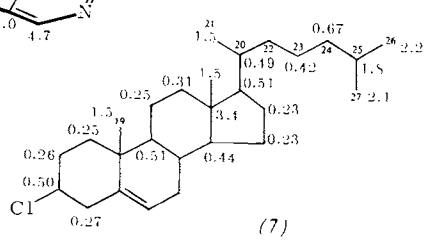
While the skeleton of large molecules is often relatively rigid, the methyl groups bonded to the backbone are highly mobile. Their rotation is thus much faster than the overall motion of the molecule ($\tau_{C(CH_3)} \ll \tau_{C(skeleton)}$). The methyl groups in proton-decoupled ^{13}C NMR spectra therefore exhibit NOE factors that are smaller than the typical value for pure dipolar relaxation (1.988), *i.e.* the signals are relatively weak. At the same time, the spin-lattice relaxation times of the methyl carbon nuclei are usually much longer than permitted by the ratio expected for the DD mechanism according to eq. (10), *i.e.*

$$T_{1(CH)} : T_{1(CH_2)} : T_{1(CH_3)} = 6:3:2$$

The experimental values found for all the methyl carbons in 3-methyl-5,6,7,8-tetrahydroquinoline *(4)*[29], 8,9,9-trimethyl-5,8-methano-5,6,7,8-tetrahydroquinazoline *(1)*[29], and cholesteryl chloride *(7)*[10] may be cited as examples. Lower intensities and longer T_1 values relative to the methylene and methine carbon nuclei thus frequently facilitate detection of methyl resonances in ^{13}C NMR spectra.



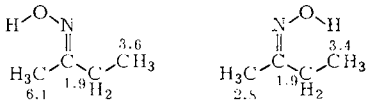
(1)



(7)

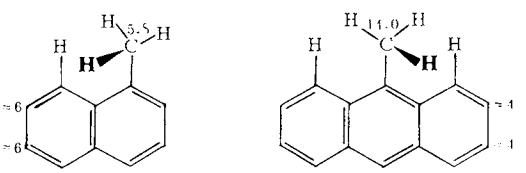
5.4.2. Intramolecular Steric Interactions

Steric interactions can hinder the rotation of methyl groups and thus accelerate methyl relaxation. It can be deduced, *e.g.* from the T_1 values of 2-butanone oxime *(8)*, that the CH_3 group *syn* to the OH group in the more stable *anti* isomer rotates faster ($T_1 = 6.1$ s) than that *anti* to the OH group in the more labile *syn* isomer ($T_1 = 2.8$ s)[33]. As an explanation it is assumed that the van der Waals interactions between the methyl and hydroxyimino groups, and between the methyl and methylene groups are of the same order of magnitude in the *anti* isomer. In contrast, the methyl group in the *syn* isomer adopts an energetically more favorable conformation involving one-sided interaction with the methylene group, with the result that its rotation is hindered[33].



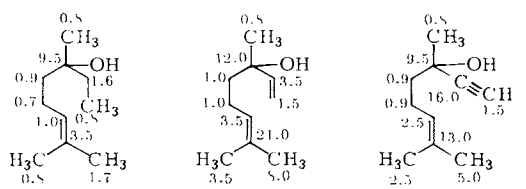
anti (8) *syn*

The T_1 values of the methyl carbon nucleus in 1-methylnaphthalene *(9)* and 9-methylanthracene *(10)* are interpreted accordingly: in *(9)* the *peri* proton forces a preferred conformation of the methyl group and thereby inhibits its rotation. On the other hand, in *(10)* two energetically equivalent *peri* H—CH_3 interactions occur, so that methyl rotation is less hindered because there is no preferred conformation[11].



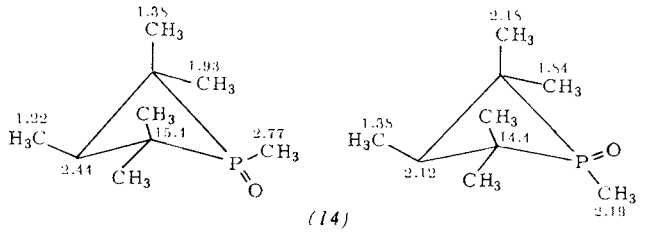
(9) (10)

In the series 6,7-dihydrolinalool *(11)*, linalool *(12)*, and 6,7-dehydrolinalool *(13)* the methyl C atoms of the terminal 1,1-dimethylvinyl group which are located *trans* to the alkyl group show widely differing absolute values of T_1; however, the ratio $T_{1(trans)} : T_{1(cis)}$ is always about 2:1. The rotation of the *trans* methyl groups therefore appears to be less hindered than that of the *cis* methyl groups[28].



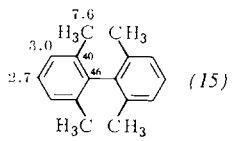
(11) (12) (13)

The T_1 values of the methyl carbon atoms of methylated phosphetanes *(14)* (in s) reveal that the methyl groups attached to C-2 and C-4, as well as to C-3, are subject to greater rotational hindrance than the P—CH_3 group[34]. Surprisingly, the pseudoaxial methyl groups sometimes relax more slowly than their pseudoequatorial counterparts, in spite of the stronger van der Waals repulsion expected for the former[34]. Shorter ^{13}C spin-lattice relaxation times thus do not always constitute proof of hindered rotation. Instead, the effects of methyl mobility found from relaxation time measurements must always be considered in relation to the motion of the entire molecule, which can vary markedly during a change of configuration.



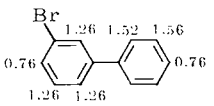
(14)

A more quantitative interpretation of methyl relaxation requires a knowledge of the motional anisotropy of the entire molecule. Thus the activation energy of methyl rotation can be estimated from T_1 data if the rotational diffusion tensor of the molecule, mentioned in Section 5.3, is known[31].

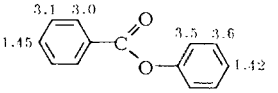


(15)

In biphenyl derivatives and related compounds, substituents can hinder rotation of the phenyl groups. Since phenyl rotation is anisotropic (Section 5.3, $T_{1(o,m)} > T_{1(p)}$), the ratio $T_{1(o,m)} : T_{1(p)}$ of the phenyl carbon nuclei will decrease on rotational hindrance. Hence, a smaller ratio, $T_{1(m)} : T_{1(p)}$ is found in 2,2',6,6'-tetramethylbiphenyl (15)[35] than in biphenyl itself owing to the methyl groups in the *o*- and *o'*-positions (Table 2). In 3-bromobiphenyl (16) and phenyl benzoate (17), the ratio $T_{1(o,m)} : T_{1(p)}$ is significantly larger for the unsubstituted phenyl and phenoxy ring than for the 3-bromophenyl and benzoyl ring[11].



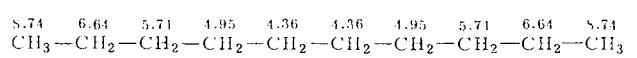
(16)



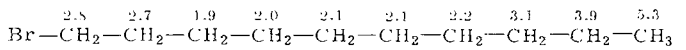
(17)

5.4.3. Molecular Flexibility

Differing T_1 values for CH_3, CH_2, and CH carbon nuclei within a molecule can arise not only by methyl rotation or anisotropic molecular motion, but also from the segmental mobility of partial structures, even when the dipolar mechanism predominates. Thus the spin-lattice relaxation times of methylene carbon atoms in long alkane chains pass through a minimum at the middle of the chain. In the presence of heavy nonassociating substituents, the minimum is displaced somewhat towards the heavier end of the molecule, as is apparent for decane (18)[36] and 1-bromodecane (19)[37]. The molecular periphery is accordingly more flexible than the center.



(18)



(19)

The same behavior of C atoms having the same number of protons is also observed in the side chain of cholesteryl chloride (7)[10]: the methyl carbon atoms C-26 and C-27 relax more slowly than C-21, the methylene carbon C-24 slower than C-23, and the methine carbon atom C-25 slower than C-20. The mobility of the side chain thus increases with increasing distance from the steroidal skeleton.

In the case of such flexible molecules the correlation time τ_C can be different for each C atom. NT_1 is then no longer a constant as for rigid molecules according to eq. (11), but inversely proportional to the correlation time, as can be seen from eq. (10) (N is the number of protons bonded to a carbon atom).

$$NT_1 \propto 1/\tau_C \qquad (14)$$

The product NT_1 can therefore be interpreted as an internal molecular mobility parameter, although only qualitatively and with a certain amount of caution, as was apparent for a correlation of carbon-13 T_1 values with diffusion coefficients[36]. The increase in T_1 or NT_1 with increasing internal mobility is not only a valuable aid in the signal assignment of carbons having the same degree of substitution, but also offers the possibility of determining the geometry and internal dynamics in the liquid and dissolved states, particularly in the case of large molecules. ^{13}C-T_1 measurements with this aim have been performed on phospholipids, peptides, proteins, and synthetic polymers.

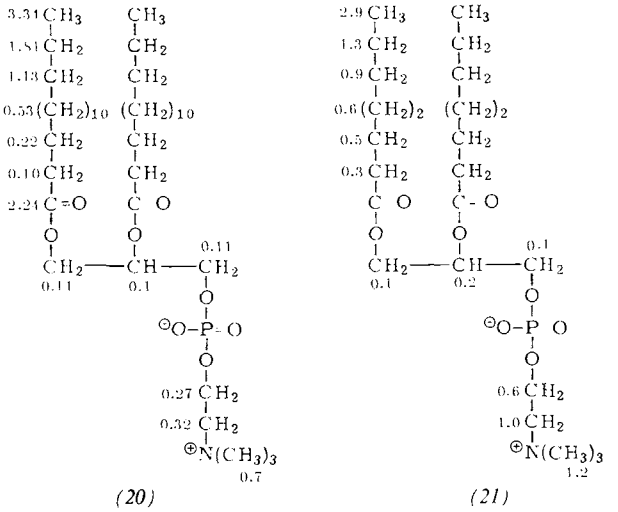
In dipalmitoyllecithin (20) the carbon nuclei relax increasingly slowly going from the central glycerol group to the ends of the two fatty acids, and thence to the tetraalkylammonium end of the choline group[38]. Thus the mobility becomes higher and higher starting from the glycerol skeleton, and proceeding along the fatty acid and choline chains to the molecular periphery. The terminal propyl groups of the fatty acid chains appear to undergo particularly rapid motion. If the fatty acid is shortened or a double bond is introduced, the chain assumes more internal flexibility. This may be seen from a comparison of data for dipalmitoyl-, dioctanoyl-, and dioleyllecithin (20), (21), and (22)[*]: the "central" methylene carbon atoms in (21) and (22) not only relax more slowly than in (20); their T_1 values also differ to a greater degree[39].

Together with proteins, phospholipids are the most important structural components of biological membranes. Since mobility of the lipid segments favors molecular transport through a membrane and thereby increases its permeability, a marked increase in T_1 along a lipid-fatty acid chain also reflects a more efficient molecular diffusion through the lipid layer of a membrane[40].

In methanol, all the α carbons of the cyclic decapeptide antibiotic gramicidin S relax at about the same rate ($T_1 \approx 135$ to 150 ms)[41]. Thus it follows that this molecule undergoes approximately isotropic motion in solution, and that the motion of the α carbons within the peptide ring is slower than the overall molecular motion itself. The mobility parameters NT_1 increase significantly in the order C-α, C-β, C-γ. Thus the side chains become increasingly mobile with increasing length. It is only in the case of the relatively rigid proline skeleton that all carbon nuclei have similar T_1 values. The phenylalanine side chain displays the anisotropy of rotation ($T_{1(o,m)} > T_{1(p)}$) usually encountered in phenyl derivatives. Since the axis of rotation passes through C-β and C-*p*, these

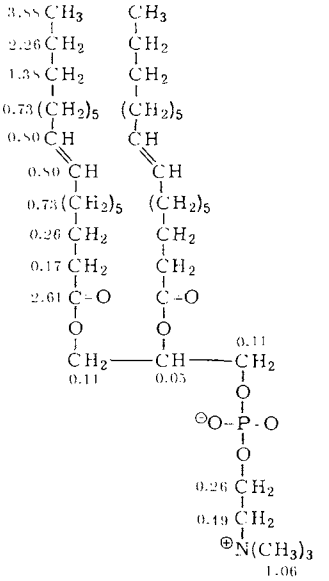
[*] Measured at 52 °C in D_2O solutions that had been treated with ultrasound.

C nuclei should show the same NT_1 values. The differences measured in practice ($NT_{1(\beta)} > NT_{1(p)}$) are possibly due to somewhat different C—H bond lengths (C-β: sp^3 C—H bond; C-p: sp^2 C—H bond)[41].



(20) (21)

η_C are independent of tacticity. These results indicate that internuclear dipole-dipole interaction predominates in the ^{13}C relaxation of polystyrene, but that the polymer chain is also relatively flexible[46].



(22)

In ribonuclease A ^{13}C spin-lattice relaxation of the carbonyl and α and β carbon atoms is slower in the denatured protein than in the native sample[42]. Apparently, the skeleton of this macromolecule becomes more flexible on denaturation, probably owing to conformational changes. However, the ε carbons of lysine in the native protein exhibit relatively large T_1 values which change only insignificantly on denaturation[42]. This behavior is attributed to a considerable segmental mobility of the lysine side chain (Table 3[42]).

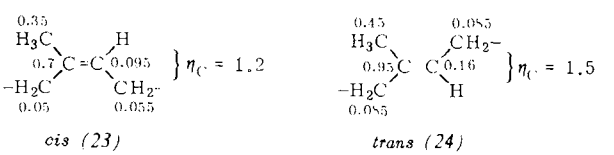
Table 3. ^{13}C spin-lattice relaxation times T_1 of ribonuclease A in aqueous solutions (conc. 0.019 M; 45 °C; 15.08 MHz; maximum deviation ±30 % [42]).

C Atoms	Native T_1 [s]	Denatured T_1 [s]
Carbonyl	0.416	0.539
α-C	0.042	0.120
β-C (Thr)	0.040	0.099
ε-C (Lys)	0.330	0.306

Indeed, ^{13}C spin-lattice relaxation times can also reflect conformational changes of a protein, *i. e.* helix-random coil transitions. This was demonstrated with models of polyamino acids[43–45], in which definite conformations can be generated, *e. g.* by addition of chemicals or by changes in temperature. Thus effective molecular correlation times τ_C of 24—32 ns were ascertained for the α carbons of poly(β-benzyl L-glutamate) in the more rigid helical form and about 0.8 ms for the more flexible "random coil" form[45], from spin-lattice relaxation times and the NOE factors.

A certain segmental mobility of the chains can also be deduced from ^{13}C-relaxation measurements on synthetic polymers. For instance, the ratio of the spin-lattice relaxation times for the methine and methylene carbon atoms of polystyrene is $T_{1(CH)} : T_{1(CH_2)} = 2:1$. The NOE factors η_C lie between 0.8 and 1.1, depending upon the solvent. Both parameters T_1 and

The carbons in amorphous *trans*-polyisoprene (*24*) relax more slowly and display larger NOE factors than the corresponding atoms of amorphous *cis*-polyisoprene (*23*)[47]. Apparently, the "frequency" of internal motion of these molecules lies in the region of the minimum of the correlation function (Fig. 11): the *trans* chain shows slightly shorter and the *cis* chain slightly longer correlation times τ_C; hence the *trans* isomer is more flexible[47]. If carbon black is added as filler to *cis*-polyisoprene (natural rubber), then no significant decrease in T_1 is observed; however, individual line broadening occurs for each carbon atom. The filler therefore appears to impair the mobility of some carbon atoms in the *cis* chain[47]. A situation can then be reached in which segmental motion in the chain becomes so slow that T_1 increases again while the spin-spin relaxation time T_2 continues to decrease (Fig. 11, to right of minimum) so that the signals become broader ($\Delta\nu_{1/2} \propto 1/T_2$).



cis (*23*) *trans* (*24*)

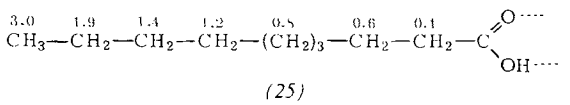
5.5. Association and Solvation of Molecules and Ions

Strong intermolecular interactions such as hydrogen bonds or ion-dipole pairs restrict the motion of molecules and pertinent molecular segments. These interactions increase the correlation time τ_C and accelerate the ^{13}C spin-lattice relaxation. Shorter ^{13}C relaxation times can therefore also indicate that such interactions are operative. The T_1 values of the C atoms of carboxylic acids, phenols, alcohols, and solvated molecular ions behave in this way.

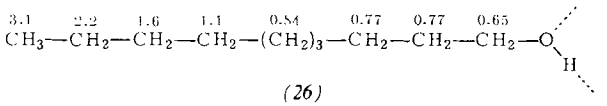
The ^{13}C nuclei in formic and acetic acid relax faster and show larger nuclear Overhauser enhancements than the ^{13}C

Table 4. T_1 and η_C values of ^{13}C nuclei in formic and acetic acid, and their methyl esters[48].

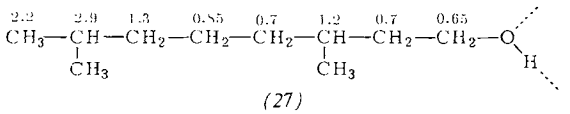
		T_1 [s] at 15 MHz	T_1 [s] at 25 MHz	η_C
Formic acid	—CH=O	10.3±1	10.1±1	2.0 ±0.15
Methyl formate	—CH=O	15.1±2	14.5±1.5	1.55±0.15
	—OCH_3	16.8±2	18.0±2	0.8 ±0.1
Acetic acid	>C=O	29.1±2.2	30.0±3.5	1.08±0.04
	—CH_3	10.5±0.5	9.8±0.6	1.4 ±0.13
Methyl acetate	>C=O	35.0±5	29.0±5	0.25±0.08
	—CH_3	16.3±1.3	17.4±1.5	0.63±0.08
	—OCH_3	17.0±1.5	18.3±2.1	0.93±0.04



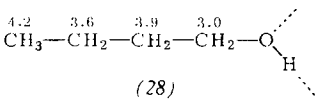
(25)



(26)

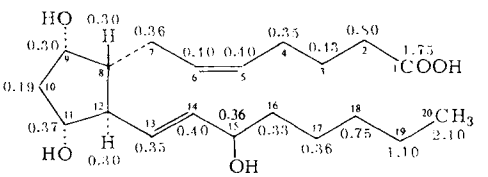


(27)

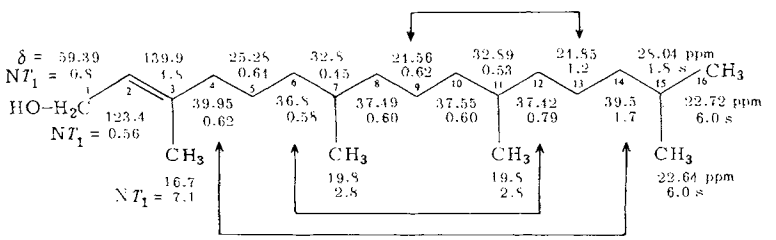


(28)

nuclei of the methyl esters (Table 4)[48]. Hence a methyl ester is more mobile than its parent carboxylic acid, which is dimerized *via* hydrogen bonding. It may also be seen that a pure DD mechanism operates in formic acid, owing to the directly bonded proton ($\eta_C = 2.0$), whereas spin rotation also contributes to ^{13}C relaxation in methyl formate ($\eta_C = 1.55$).



(29)



(30)

Owing to hydrogen bonding, the ^{13}C nuclei of phenol relax faster than the corresponding nuclei of nonassociating benzenes (Table 2). – In decanoic acid *(25)*[37] and 1-decanol *(26)*[37, 49], ^{13}C spin-lattice relaxation becomes progressively slower on going from the associating COOH or CH_2OH group to the hydrophobic end of the molecule. Whereas the hydrocarbon part becomes increasingly mobile towards the exterior, the polar end is rooted by hydrogen bonding. This behavior is also observed in branched alcohols and those having shorter chains such as 3,7-dimethyl-1-octanol *(27)*[28] and 1-butanol *(28)*[11], although it is less pronounced in such cases. In very small alcohols like methanol[50] relaxation is considerably slower ($T_1 = 17.5$ s) as a result of the much faster molecular motion.

In prostaglandin $F_{2\alpha}$ *(29)*, the T_1 values of ^{13}C nuclei in the alkyl side chain increase more significantly towards the periphery than in the associating carboxylic acid chain, thus confirming the assignment of the closely crowded CH_2 signals of the chains in the ^{13}C NMR spectrum[37]. Generally, the increased mobility on going from the associating end of the molecule, and the concomitant increase in T_1 or NT_1 [eq. (14)] can be utilized in signal assignment. Thus in phytol *(30)*, the diterpene alcohol component of chlorophyll, the signals of the carbon atom pairs 4 and 14, 6 and 12, and 9 and 13 defy unequivocal assignment, owing to very similar shifts and equal multiplicities (CH_2 groups). However, the C atoms 12, 13, and 14, which are more removed relative to the associating end of the molecule, undergo faster motion, and the NT_1 values are therefore larger. Signal assignment then follows readily[51].

In weakly solvating solvents interionic interactions between organic molecular ions can lead to fixation of the ionic end of the molecule. The T_1 values of pertinent and neighboring ^{13}C nuclei become smaller. In contrast, strongly solvating solvents such as water and alcohols inhibit interionic interaction and lead to an enhanced mobility of the ions solvated by ion-dipole interactions, and ^{13}C spin-lattice relaxation is consequently slower in such solvents. Thus the T_1 values of *n*-butylammonium trifluoroacetate increase with the polarity of the solvent, as shown in Table 5[11].

Table 5. Solvent dependence of spin-lattice relaxation times of the ^{13}C atoms in *n*-butylammonium trifluoroacetate [11].

Solvent	Conc. [wt.-%]	T_1 [s] CH_3—	—CH_2—	—CH_2—	—$\overset{\oplus}{N}H_3$ $CF_3COO^{\ominus}$
1,4-Dioxane	20	3.35	1.95	1.54	0.88
CH_2Cl_2/acetone	24	3.90	2.41	1.67	0.91
CF_3COOH	15.4	3.98	3.12	2.30	1.54
	28.2	3.46	2.13	1.50	0.97
CD_3OD	20	6.00	5.35	4.52	3.10
D_2O	20	5.00	5.00	4.26	3.75

5.6. Determination of Quadrupole Relaxation Times and Coupling Constants from ^{13}C Spin-Lattice Relaxation Times

While the nuclei ^1H and ^{13}C relax predominantly by the DD mechanism, relaxation of a quadrupole nucleus such as deuterium essentially involves fluctuating fields arising from interaction between the quadrupole moment and the electrical field gradient at the quadrupole nucleus[52]. If the molecular motion is sufficiently fast (decreasing branch of the correlation function, Fig. 11), the ^2H spin-lattice relaxation time is inversely proportional to the square of the quadrupole coupling constant $e^2qQ/\hbar$ of deuterium and the effective correlation time[52]:

$$\frac{1}{T_1} = \frac{3}{8}\left(\frac{e^2qQ}{\hbar}\right)^2 \tau_C \qquad (15)$$

Since ^{13}C and ^2H relaxation are the consequence of intramolecular interactions, the relaxation times T_1 of ^{13}C and ^2H within a given molecule can be subjected to direct comparison according to eqs. (10) and (15):

$$\frac{T_1(^{13}C)}{T_1(^2H)} = \frac{3}{8}\frac{r^6(e^2qQ/\hbar)^2}{N\hbar^2\gamma_C^2\gamma_H^2} \qquad (16)$$

By using the numerical values for the constants (*e.g.* $r_{CH} \approx 1.09$ Å and $e^2qQ/\hbar \approx 170$ kHz for an sp^3 C—H bond) a simple linear relation between the ^{13}C and ^2H relaxation times is obtained:

$$T_1(^{13}C)/T_1(^2H) = 19.9/N \quad (N = 1, 2, 3 \text{ for } CD, CD_2, CD_3) \qquad (17)$$

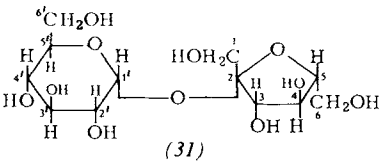
Knowledge of the T_1 values for deuterium thus allows prediction of the ^{13}C relaxation times and *vice versa*[53]. On the other hand, if these data are known the deuterium quadrupole coupling constants can be determined according to eq. (16). Agreement between calculated and experimental quadrupole coupling constants is good, any pronounced deviations indicating that alternative relaxation mechanisms are operative. For instance the quadrupole coupling constant calculated for the terminal acetylene deuteron of phenylacetylene according to eq. (16) is much too large (calc. 254 kHz; exp. 215 ± 5 kHz). This is explained in terms of the chemical shift anisotropy in phenylacetylene[53].

6. Medium and Temperature Effects

Any change in the medium, *i.e.* the solvent, the concentration, the pH value, and the temperature will affect the mobility of the molecules and hence also the spin-lattice relaxation. However, few systematic studies have so far been performed on the concentration dependence or on the precise influence of the macroscopic viscosity, the main reason in the case of ^{13}C lying in the need for highly protracted measurements in concentration studies. Moreover, little is known about the pH dependence of ^{13}C relaxation[54]. Nevertheless, the concentration dependence of ^{13}C relaxation is apparent in the case of saccharose (Table 6)[10], and intramolecular hydrogen bonds can be detected by measuring the concentration dependence of T_1[55]. Solvating solvents appear to facilitate molecular motion, as has already been shown for *n*-butylammonium trifluoroacetate (Table 5)[11].

The ^{13}C nuclei of molecules whose protons undergo exchange relax at different rates in H_2O and D_2O solution. Thus T_1 for the carbonyl carbon of acetamide is 72 s in D_2O, but only 37 s in H_2O[55]. In this context, the influence of paramagnetic impurities should again be mentioned. Traces of paramagnetic ions (*e.g.* Cu^{2+}) no longer detectable by the usual analytical techniques can drastically lower the ^{13}C relaxation times of complexing substrates (*e.g.* amino acids).

Table 6. ^{13}C spin-lattice relaxation times T_1 [s] of saccharose *(31)* in H_2O and D_2O at 42 °C [10].



(31)

	C Atom	0.5 M D_2O	0.5 M H_2O	2.0 M H_2O
C	2	6.0	7.8	2.6
CH	1′	0.54	0.69	0.16
	3	0.51	0.64	0.16
	4	0.52	0.49	0.16
	5	0.58	0.61	0.16
	3′	0.61	0.73	0.15
	2′	0.53	0.69	0.17
	5′	0.60	0.70	0.16
	4′	0.59	0.60	0.17
CH_2	1	0.48	0.40	0.12
	6	0.35	0.30	0.15
	6′	0.34	0.37	0.13

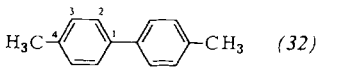
Most previous publications on the temperature dependence of ^{13}C relaxation[56–65] are concerned with simple molecules such as carbon disulfide, iodomethane, and acetonitrile[56–60,63,64]. Any interpretation of the temperature dependence of relaxation times requires a knowledge of the relative contributions of dipole-dipole and spin-rotation relaxation, as the former becomes progressively slower and the latter steadily faster with increasing temperature. In special cases, such as that of cyclopropane[66], the effects of both contributions can almost cancel each other.

The temperature dependence of dipole-dipole relaxation is that of the correlation time, which is usually written in the form of an Arrhenius equation (18):

$$\tau_C = \tau_{C_0} \times e^{\frac{\Delta E}{RT}} \qquad (18)$$

Plotting the logarithm of the dipole-dipole relaxation time $T_{1(DD)}$ *versus* the reciprocal temperature therefore gives an activation energy ΔE for molecular reorientation, which is of the order of 2 kcal/mol for most of the molecules hitherto studied. In the case of 4,4′-dimethylbiphenyl (32) a value of 4 kcal/mol was found from the temperature dependence of T_1 for C-2 and C-3 (Fig. 12)[35]. For T_1 of the methyl carbon atom the Arrhenius plot is curved at lower temperatures since the internal rotation of this group is then probably faster than the overall motion of the molecule.

The temperature dependence of the SR component is more complicated. An Arrhenius relation can again be formulated for the correlation time of spin rotation; however, this function additionally contains a linear temperature term.



(32)

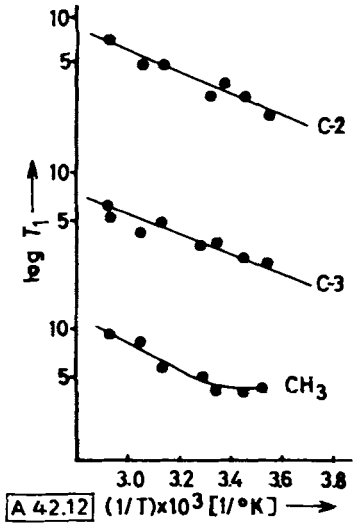


Fig. 12. Temperature dependence of spin-lattice relaxation times T_1 of protonated ^{13}C nuclei in 4,4'-dimethylbiphenyl (32) [35].

7. Outlook

^{13}C relaxation measurements will assume a firm place in the methodology of nuclear magnetic resonance. The principles of the measuring technique have been established[6, 67] and the specific sources of error recognized[67]. On the other hand, the relevant theory is still in a state of flux[68], particularly with regard to the interpretation of T_1 values in terms of the anisotropy of molecular motion and segmental mobility. The organic chemist will profit from relaxation time measurements as a tool for assigning ^{13}C NMR spectra whenever decoupling experiments and shift comparisons fail owing to signal overcrowding. The study of events involving intermolecular motion, such as complexation[69] and micelle formation[70] can now utilize the ^{13}C spin-lattice relaxation time as a new probe. Temperature dependent measurement of T_1 will certainly also be developed into an additional method for the elucidation of internal dynamic processes of molecules. Finally, such measurements will find wide application in biochemistry, for example in active site determination in biomacromolecules[21], the study of lipid double layers[39], or the determination of peptide conformations[71]. Literature for further study is cited in references[72–114].

Received: April 22, 1974;
supplemented: October 18, 1974 [A 42 IE]
German version: Angew. Chem. 87, 152 (1975)

[1] *J. W. Emsley, J. Feeney,* and *L. H. Sutcliffe:* High-Resolution Nuclear Magnetic Resonance Spectroscopy. Vol. 1 and 2. Pergamon Press, Oxford 1965.

[2] *T. C. Farrar* and *E. D. Becker:* Pulse and Fourier Transform NMR, Introduction to Theory and Methods. Academic Press, New York 1971.

[3] *F. Bloch,* Phys. Rev. *70,* 460 (1946).

[4] *F. Bloch, W. W. Hansen,* and *M. Packard,* Phys. Rev. *70,* 474 (1946).

[5] *J. T. Clerc, E. Pretsch,* and *S. Sternhell:* ^{13}C-Kernresonanzspektroskopie. Akademische Verlagsgesellschaft, Frankfurt/M. 1973.

[6] *E. Breitmaier* and *W. Voelter:* ^{13}C NMR Spectroscopy, Methods and Applications. Verlag Chemie GmbH, Weinheim 1974.

[7] a) *R. Freeman* and *H. D. W. Hill,* J. Chem. Phys. *54,* 3367 (1971); b) *R. Freeman, H. D. W. Hill,* and *R. Kaptein,* J. Magn. Resonance *7,* 82 (1972).

[8] *R. L. Vold, J. S. Waugh, M. P. Klein,* and *D. E. Phelps,* J. Chem. Phys. *48,* 3831 (1968).

[9] *R. Freeman* and *H. D. W. Hill,* J. Chem. Phys. *51,* 3140 (1969); *53,* 4103 (1970).

[10] *A. Allerhand, D. Doddrell,* and *R. Komoroski,* J. Chem. Phys. *55,* 189 (1971).

[11] *G. C. Levy,* Accounts Chem. Res. *6,* 161 (1973).

[12] *G. C. Levy* and *G. L. Nelson:* Carbon-13 Nuclear Magnetic Resonance for Organic Chemists. Wiley Interscience, New York 1972, and research papers cited therein.

[13] *J. R. Lyerla, Jr.* and *D. M. Grant,* Int. Rev. Sci. Phys. Chem. Ser. *1,* 4, 155 (1972).

[14] *J. H. Noggle* and *R. E. Schirmer:* The Nuclear Overhauser Effect, Chemical Applications. Academic Press, New York 1971.

[15] *K. F. Kuhlmann* and *D. M. Grant,* J. Amer. Chem. Soc. *90,* 7355 (1968).

[16] *T. D. Alger* and *D. M. Grant,* J. Phys. Chem. *75,* 2538 (1971).

[17] *G. C. Levy, J. D. Cargioli,* and *F. A. L. Anet,* J. Amer. Chem. Soc. *95,* 1527 (1973).

[18] *G. C. Levy,* J. C. S. Chem. Comm. *1972,* 47.

[19] Determination of $T_{1(DD)}$ and $T_{1(SR)}$ of the C atoms of camphor: *J. Grandjean, P. Laszlo,* and *R. Price,* Mol. Phys. *25,* 695 (1973).

[20] *R. Freeman, K. G. R. Pachler,* and *G. N. La Mar,* J. Chem. Phys. *55,* 4586 (1971).

[21] *C. F. Brewer, H. Sternlicht, D. M. Marcus,* and *A. P. Grollmann,* Biochemistry *12,* 4448 (1973).

[22] *D. Doddrell, V. Gluschko,* and *A. Allerhand,* J. Chem. Phys. *56,* 3683 (1972).

[23] *W. T. Huntress, Jr.,* J. Chem. Phys. *48,* 3524 (1968).

[24] *D. E. Woessner,* J. Chem. Phys. *42,* 1855 (1965); *36,* 1 (1962).

[25] *K. F. Kuhlmann, D. M. Grant,* and *R. K. Harris,* J. Chem. Phys. *52,* 3439 (1970).

[26] *S. Berger, F. R. Kreissl,* and *J. D. Roberts,* J. Amer. Chem. Soc. *96,* 4348 (1974).

[27] *D. E. Woessner,* J. Chem. Phys. *37,* 647 (1962).

[28] *E. Breitmaier* and *W. Voelter,* unpublished.

[29] *K. H. Spohn,* Dissertation, Universität Tübingen 1974.

[30] *D. M. Grant, R. J. Pugmire, E. P. Black,* and *K. A. Christensen,* J. Amer. Chem. Soc. *95,* 8465 (1973).

[31] *S. Berger, F. R. Kreissl, D. M. Grant,* and *J. D. Roberts,* J. Amer. Chem. Soc., in press.

[32] *R. S. Becker, S. Berger, D. K. Dalling, D. M. Grant,* and *R. J. Pugmire,* J. Amer. Chem. Soc. *96,* 7008 (1974).

[33] *G. C. Levy* and *G. L. Nelson,* J. Amer. Chem. Soc. *94,* 4897 (1972).

[34] *G. A. Gray* and *S. E. Cremer,* J. Magn. Resonance *12,* 5 (1973).

[35] *M. Imanari, M. Ohuchi,* and *K. Ishizu,* J. Magn. Resonance *14,* 374 (1974).

[36] *N. J. M. Birdsall, A. G. Lee, Y. K. Levine, J. C. Metcalfe, P. Partington,* and *G. C. K. Roberts,* J. C. S. Chem. Comm. *1973,* 757.

[37] *C. Chachaty, Z. Wolkowski, F. Piriou,* and *G. Lukacs,* J. C. S. Chem. Comm. *1973,* 951.

[38] *J. C. Metcalfe, N. J. M. Birdsall, J. Feeney, A. G. Lee, Y. K. Levine,* and *P. Partington,* Nature *233,* 199 (1971).

[39] *Y. K. Levine, N. J. M. Birdsall, A. G. Lee,* and *J. C. Metcalfe,* Biochemistry *11,* 1416 (1972).

[40] *A. G. Lee, N. J. M. Birdsall,* and *J. C. Metcalfe,* Chem. Brit. *9,* 116 (1973).

[41] *A. Allerhand* and *R. A. Komoroski,* J. Amer. Chem. Soc. *95,* 8228 (1973).

[42] *A. Allerhand, D. Doddrell, V. Gluschko, D. W. Cochran, E. Wenkert, P. J. Lawson,* and *F. R. N. Gurd,* J. Amer. Chem. Soc. *93,* 544 (1971).

[43] *L. Paolillo, T. Tancredi, P. A. Temussi, E. Trivellone, E. M. Bradbury,* and *C. Crane-Robinson,* J. C. S. Chem. Comm. *1972,* 335.

[44] *S. Tadorko, S. Fujiwara,* and *Y. Ichihara,* Chem. Lett. *1973,* 849.

[45] *A. Allerhand* and *E. Oldfield,* Biochemistry *12,* 3428 (1973).

[46] *J. Schaefer* and *D. F. S. Natusch,* Macromolecules *5,* 416 (1972).

[47] *J. Schaefer,* Macromolecules *5,* 427 (1972).

[48] *T. D. Alger, D. M. Grant,* and *J. R. Lyerla,* J. Phys. Chem. *75,* 2539 (1971).

[49] *D. Doddrell* and *A. Allerhand,* J. Amer. Chem. Soc. *93,* 1558 (1971).

[50] *T. C. Farrar, S. J. Druck, R. R. Shoup,* and *E. D. Becker,* J. Amer. Chem. Soc. *94,* 699 (1972).

[51] *R. A. Goodman, E. Oldfield,* and *A. Allerhand,* J. Amer. Chem. Soc. *95,* 7553 (1973).

[52] *A. Abragam:* The Principles of Nuclear Magnetism. Clarendon Press, Oxford 1961, Chap. 8.

[53] *H. Saito, H. H. Mantsch,* and *J. C. P. Smith,* J. Amer. Chem. Soc. *95,* 8453 (1973).

[54] *I. M. Armitage, H. Huber, H. Pearson*, and *J. D. Roberts*, Proc. Nat. Acad. Sci. USA *71*, 2096 (1974); *H. Pearson, D. Gust, I. M. Armitage, H. Huber, J. D. Roberts, R. E. Stark, R. R. Vold*, and *R. L. Vold, ibid.*, in press.

[55] *D. D. Gianini, I. M. Armitage, H. Pearson, D. M. Grant*, and *J. D. Roberts*, J. Amer. Chem. Soc., in press.

[56] *J. R. Lyerla, Jr., D. M. Grant*, and *R. B. Bertrand*, J. Phys. Chem. *75*, 3967 (1971).

[57] *K. T. Gillen, M. Schwartz*, and *J. H. Noggle*, Mol. Phys. *20*, 899 (1971).

[58] *H. W. Spiess, D. Schweitzer, U. Haeberlein*, and *K. H. Hausser*, J. Magn. Resonance *5*, 101 (1971).

[59] *A. Olivson* and *E. Lippmaa*, Chem. Phys. Lett. *11*, 241 (1971).

[60] *T. C. Farrar, S. J. Druck, R. R. Shoup*, and *E. D. Becker*, J. Amer. Chem. Soc. *94*, 699 (1972).

[61] *H. W. Spiess, D. Schweitzer*, and *U. Haeberlein*, J. Magn. Resonance *9*, 444 (1973).

[62] *L. J. Burnett* and *S. B. Roeder*, J. Chem. Phys. *60*, 2420 (1974).

[63] *E. Goldammer, H. D. Luedemann*, and *A. Mueller*, J. Chem. Phys. *60*, 4590 (1974).

[64] *T. K. Leipert, J. H. Noggle*, and *K. T. Gillen*, J. Magn. Resonance *13*, 158 (1974).

[65] *E. Goldammer, H. D. Luedemann*, and *O. Roeder*, Chem. Phys. Lett. *26*, 387 (1974).

[66] *S. Berger, F. R. Kreissl, D. M. Grant*, and *J. D. Roberts*, to be published.

[67] a) *I. M. Armitage, H. Huber, D. H. Live, H. Pearson*, and *J. D. Roberts*, J. Magn. Resonance *15*, 142 (1974); b) *G. C. Levy* and *I. R. Peat, ibid.*, in press.

[68] *Y. K. Levine, N. J. M. Birdsall, A. G. Lee, J. C. Metcalfe, P. Partington*, and *G. C. K. Roberts*, J. Chem. Phys. *60*, 2890 (1974).

[69] *M. C. Fedarko*, J. Magn. Resonance *12*, 1985 (1973).

[70] *R. T. Roberts* and *C. Chachaty*, Chem. Phys. Lett. *22*, 348 (1973).

[71] *D. G. Gianini, I. M. Armitage, H. Pearson*, and *J. D. Roberts*, Proc. Nat. Acad. Sci. USA *71*, 4221 (1974).

[72] *T. D. Alger, D. M. Grant*, and *R. K. Harris*, J. Phys. Chem. *76*, 281 (1972): ^{13}C NMR, Relaxation in Hemillitene and Isodurene.

[73] *M. Alexandre, C. Fouchet*, and *P. Rigny*, J. Chim. Phys. *70*, 1073 (1973): NMR Study of Micellar Solutions.

[74] *A. Allerhand* and *D. Doddrell*, J. Amer. Chem. Soc. *93*, 2777, 2779 (1971): Strategies in the Application of Partially Relaxed Fourier-Transform Nuclear Magnetic Resonance Spectroscopy in Assignments of Carbon-13 Resonances of Complex Molecules, Stachyose, D-Fructose, D-Turanose.

[75] *W. A. Anderson, R. Freeman*, and *H. D. W. Hill*, Pure Appl. Chem. *32*, 27 (1972): Fourier Transform Studies of Nuclear Spin Relaxation.

[76] *R. A. Assink*, J. Magn. Resonance *12*, 88 (1973): Elimination of H_1-Inhomogeneity Effects on T_1 Measurements.

[77] *E. D. Becker, R. R. Shoup*, and *T. C. Farrar*, Pure Appl. Chem. *32*, 51 (1972): ^{13}C NMR Spectroscopy: Relaxation Times of ^{13}C and Methods of Sensitivity Enhancement.

[78] *J. P. Behr* and *J. M. Lehn*, Biochem. Biophys. Res. Commun. *49*, 1573 (1972): Molecular Dynamics of Acetylcholine and of Choline.

[79] *S. J. Benkowic, J. J. Villafranca*, and *J. J. Kleinschuster*, Arch. Biochem. Biophys. *155*, 458 (1973): ^{31}P and ^{13}C NMR Measurements of A Fructose-1-phosphate, Mn(II) and Fructose-1,6-diphosphatase Complex.

[80] *S. Boileau, H. Cheradame, N. Spassky, K. Iwiss*, and *E. Lillie*, C. R. Acad. Sci. *C 275*, 535 (1972): ^{13}C NMR Study of Irregularities in the Linking of Polypropylene Sulfide.

[81] *S. Boileau, H. Cheradame, P. Guérin*, and *P. Sigeralt*, J. Chim. Phys. *69*, 1420 (1972): Configurational Study of Polypropylene Sulfide Using ^{13}C NMR.

[82] *J. J. Delpuech* and *C. Bonbel*, J. Chim. Phys. *70*, 578 (1973): NMR Studies of the Solvation of Cations (A)—Solvation of Paramagnetic Cations (Co^{2+}, Ni^{2+}) in Dimethylsulfoxide Studied by Pulsed NMR. Kinetics of the Free Solvent-Bound Solvent Exchange (B).

[83] *R. Deslauriers, I. C. P. Smith*, and *R. Walter*, J. Amer. Chem. Soc. *96*, 2289 (1974): Conformational Flexibility of the Neurohypophysal Hormones Oxytocin and Lysine-Vasopressin. A ^{13}C Spin-Lattice Relaxation Study of Backbone and Side Chains.

[84] *R. Deslauriers, R. Walter*, and *I. C. P. Smith*, FEBS Lett. *37*, 27 (1973): Intramolecular Motion in Peptides Determined by ^{13}C NMR. A Spin-Lattice Relaxation Study on MSH Release Inhibiting Factor.

[85] *R. Deslauriers, C. Garrigou-Lagrange, A. Bellocq*, and *I. C. P. Smith*, FEBS Lett. *31*, 59 (1973): ^{13}C NMR Studies on Thyrotropin Releasing Factor and Related Peptides.

[86] *D. Doddrell* and *A. Allerhand*, Proc. Nat. Acad. Sci. USA *68*, 1083 (1971): Assignments in the Carbon-13 Nuclear Magnetic Resonance Spectra of Vitamin B-12, Coenzyme B-12 and other Corrinoids: Application of Partially Relaxed Fourier Transform Spectroscopy.

[87] *G. G. McDonald* and *J. S. Leigh, Jr.*, J. Magn. Resonance *9*, 358 (1973): A New Method for Measuring Longitudinal Relaxation Times.

[88] *R. E. Echols* and *G. C. Levy*, J. Org. Chem. *39*, 1321 (1974): ^{13}C NMR Spectral Analysis Using Spin-Lattice Relaxation Data and Specific Deuteration. Thiamine Hydrochloride.

[89] *M. C. Fedarko*, J. Magn. Resonance *12*, 30 (1973): The Use of ^{13}C Relaxation Times to Investigate Molecular Motion of Macrocyclic Antibiotics upon Potassium Ion Complex Formation.

[90] *R. Freeman* and *H. D. Hill*, J. Chem. Phys. *55*, 1985 (1971): FT-Study of NMR Spin-Spin Relaxation.

[91] *U. Haeberlein, H. W. Spiess*, and *D. Schweitzer*, J. Magn. Resonance *6*, 39 (1972): Spin-Echo Experiments on ^{13}C, ^{2}H, ^{1}H, and ^{19}F in some Small Molecules in the Liquid Phase.

[92] *R. A. Komoroski* and *A. Allerhand*, Proc. Nat. Acad. Sci. USA *69*, 1804 (1972): Natural-Abundance Carbon-13 Fourier-Transform Nuclear Magnetic Resonance. Spectra and Spin-Lattice Relaxation Times of Unfractionated Yeast Transfer-RNA.

[93] *K. F. Kuhlmann* and *D. M. Grant*, J. Chem. Phys. *55*, 2998 (1971): C^{13} Relaxation and Internal Rotation in Mesitylene and *o*-Xylene.

[94] *Y. K. Levine*, J. Magn. Resonance *11*, 421 (1973): Calculation of Correlation Functions of Internal Motion in Hydrocarbon Chains by Computer Simulation.

[95] *Y. K. Levine, P. Partington*, and *G. C. K. Roberts*, Mol. Phys. *25*, 497 (1973): Calculation of Dipolar NMR Relaxation Times in Molecules with Multiple Internal Rotations I. Isotropic Overall Motion of the Molecule.

[96] *G. C. Levy*, J. C. S. Chem. Comm. *1972*, 352: ^{13}C SLR: Carbon Bromine Scalar and Dipole Dipole Interactions.

[97] *G. C. Levy*, J. C. S. Chem. Comm. *1972*, 768: Carbon Spin Lattice Relaxation and Solvation of Organic Ions: *n*-Butylamine and *n*-Butylammonium Ion.

[98] *G. C. Levy*, J. Magn. Resonance 8, 122 (1972): ^{13}C Spin Lattice Relaxation and Intermolecular Interactions: Phenol and Aniline.

[99] *G. C. Levy*, Tetrahedron Lett. *1972*, 3709: Carbon-13 SLR. Internal Motion in Substituted Ferrocenes.

[100] *G. C. Levy* and *J. D. Cargioli*, J. Magn. Resonance *10*, 231 (1973): Spin Lattice Relaxation in Solutions containing Cr III Paramagnetic Relaxation Agents.

[101] *G. C. Levy* and *R. A. Komoroski*, J. Amer. Chem. Soc. *96*, 678 (1974): Paramagnetic Relaxation Reagents: Alternatives or Complements to Lanthanide Shift Reagents in NMR Spectral Analysis.

[102] *G. C. Levy, R. A. Komoroski*, and *J. A. Halstead*, J. Amer. Chem. Soc. 96, 5456 (1974): Solvation and Segmental Motions of *n*-Alkyl-Ammonium Ions. A ^{13}C Spin Lattice Relaxation Study.

[103] *J. R. Lyerla, D. M. Grant*, and *R. K. Harris*, J. Phys. Chem. *75*, 585 (1971): Dipolar Contributions to Carbon-13 Relaxation Times.

[104] *J. R. Lyerla* and *D. M. Grant*, J. Phys. Chem. *76*, 3213 (1972): The Influence of Internal Motion on the Carbon-13 Relaxation Times of Methyl Carbons.

[105] *J. L. Markley, W. J. Horsley*, and *M. P. Klein*, J. Chem. Phys. *55*, 3604 (1971): SLR Measurements in Slowly Relaxing Complex Spectra.

[106] *R. B. Moon* and *J. H. Richards*, Proc. Nat. Acad. Sci. USA *69*, 2983 (1972): Conformational Studies of Various Hemoglobins by Natural-Abundance ^{13}C NMR Spectroscopy.

[107] *H. Ozawa, Y. Arata*, and *S. Fujiwara*, J. Chem. Phys. *58*, 4037 (1973): Mechanism of ^{13}C NMR Relaxation in Liquid Methanol.

[108] *J. D. Robinson, N. J. M. Birdsall, A. G. Lee*, and *J. C. Metcalfe*, Biochemistry *11*, 2903 (1972): ^{13}C and ^{1}H Nuclear Magnetic Resonance Relaxation Measurements of the Lipids of Sacroplasmic Reticulum Membranes.

[109] *R. Rowan III, J. A. McCammon*, and *B. D. Sykes*, J. Amer. Chem. Soc. *96*, 4773 (1974): A Study of the Distance Obtained from NMR NOE Effect and Relaxation Time Measurements in Organic Structure Determination. Distances Involving Internally Rotating Methyl Groups. Application to *cis* and *trans* Crotonaldehyde.

[110] *C. F. Schmidt* and *S. I. Chan*, J. Magn. Resonance *5*, 151 (1971): Nuclear Spin Lattice Relaxation of the Methyl Carbon in Toluene.

[111] *H. W. Spiess* and *H. Mahnke*, Ber. Bunsenges. Phys. Chem. *76*, 990 (1972): ^{13}C Anisotropic Chemical Shifts and Spin Rotation Constants in Nickel Tetracarbonyl and Iron Pentacarbonyl.

[112] *H. Sternlicht, G. L. Kenyon, E. L. Pacher*, and *J. Sinclair*, J. Amer. Chem. Soc. *93*, 199 (1971): Carbon-13 Nuclear Magnetic Resonance Studies of Heterogenous Systems, Amino Acids Bound to Cationic Exchange Resins.

[113] *F. W. Wehrli*, J. C. S. Chem. Comm. *1973*, 379: ^{13}C NMR Spectral Assignments in Large Molecules with the Aid of SLR Data.

[114] *E. Williams, B. Sears, A. Allerhand*, and *E. H. Cordes*, J. Amer. Chem. Soc. *95*, 4871 (1973): Segmental Motion of Amphipatic Molecules in Aqueous Solutions and Micelles. Application of Natural-Abundance ^{13}C Partially Relaxed FT-NMR-Spectroscopy.

Investigation of Enzyme Mechanisms with Nucleoside Phosphorothioates

By Fritz Eckstein[*]

Nucleoside phosphorothioates are modified nucleotides in which an oxygen atom bound to a phosphorus atom has been replaced by a sulfur atom. These compounds are suitable for the investigation of enzyme mechanisms because, although they are bound by enzymes in many cases just as well as the natural substrate, the enzymatic reactions very often proceed considerably more slowly. Since nucleoside thiophosphate *O*-esters exist as diastereomers these compounds can be used in suitable cases for information about the stereochemistry of enzymatic reactions.

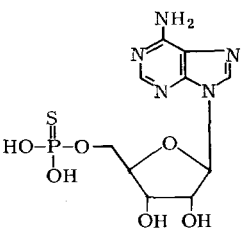
1. Introduction

The rapid development of molecular biology has led, *inter alia*, to the isolation of an ever increasing number of enzymes. Although the functions of these enzymes are known, the understanding of the underlying reactions is often at best fragmentary. It is, therefore, not surprising that many groups are engaged in investigations of enzyme mechanisms.

When the influence of the natural substrate on the enzyme is to be investigated, difficulties can arise from the fact that the enzyme turns over the substrate. Although one can find conditions, *e. g.* by changing the pH and lowering the temperature, under which the rate of reaction is greatly reduced and for the time of the observation very small, one can never completely exclude the possibility that the properties of the enzyme such as its conformation have been drastically affected and that the information thus gained can only be applied with reservation to the proteins' behavior under optimal conditions.

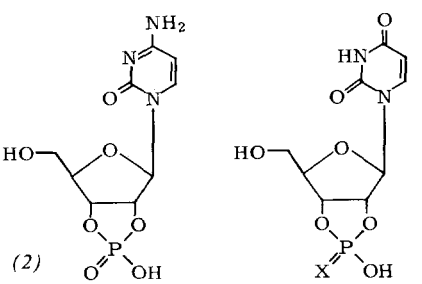
In such cases analogs of the substrate which can be recognized by the enzyme, *i. e.* which can be bound at the substrate binding site, but which cannot be turned over, have been very useful as competitive inhibitors. Using these it has been possible for instance to determine the number of substrate binding sites or conformational changes of an enzyme during the binding of the substrate or an analog as well as to interrupt enzymatic multiple substrate reactions at certain steps. An example for the latter is the utilization of the β,γ-CH_2-analog of guanosine triphosphate (GTP) in protein biosynthesis[1]. As components of the crystalline complex, competitive inhibitors can also be of great value for the determination of the substrate binding site of an enzyme in its crystalline form[2].

Investigations with such competitive inhibitors can always be criticized on the grounds that transformation of the substrate into a non-reactive analog represents such a modification that the experimental results obtained cannot be necessarily extrapolated to the natural substrate-enzyme system. Such investigations will, therefore, be of more value when the alteration in the substrate molecule is small, *i. e.* when the inhibitor is as similar to the substrate as possible. The following discussion will be restricted to a selection of enzyme systems which use nucleotides either as substrates or effectors. It will demonstrate to what extent a class of nucleotide analogs, namely nucleoside phosphorothioates (nucleoside thiophosphates), can be of help in investigations of enzymes. In these analogs an oxygen atom bound to a phosphorus atom is replaced by a sulfur atom; this review will concern itself primarily with analogs in which the oxygen atom that is replaced is not part of an ester bond. The analog of adenosine 5'-phosphate has the structural formula *(1)*.



(1), AMPS

The replacement of such an oxygen atom by a sulfur atom represents a minimal structural change in the natural nucleotide. The base and sugar components as well as the number of negative charges remain completely unchanged. The first dissociation constant is slightly reduced[3]—by about 0.5 p*K* units—from about 5.20 to about 4.70 so that there are no differences to normal nucleotides when working in the neutral pH region or above. The small structural change between nucleoside phosphates and the corresponding nucleoside phosphorothioates is best demonstrated by comparing (Table 1) cytidine 2',3'-cyclic phosphate *(2)*[4] and uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3)*[5] (see Section 3.1) whose structures have been determined by X-ray analysis. Similar values for distances and angles have also been found for a Mg^{2+}-pyridine complex of *O*,*O*-diethylphosphorothioate[6].



(2)

(3), X = S
(4), X = O

X-ray structural analysis of the phosphorothioates shows that the negative charge is localized on the oxygen and not on

[*] Priv.-Doz. Dr. F. Eckstein
Max-Planck-Institut für experimentelle Medizin, Abteilung Chemie
34 Göttingen, Hermann-Rein-Strasse 3 (Germany)

Table 1. Comparison of distances and angles (average values) of cytidine 2',3'-cyclic phosphate *(2)* [4] and uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3)* [5].

	(2)	*(3)*
P—O [Å]	1.47	1.51
P=S [Å]	—	1.94
P—O(C) [Å]	1.61	1.57
	—	1.61
∢ O—P—S [°]	—	117
∢ O—P—O [°]	117	—
∢ S—P—O(C) [°]	—	111
∢ O—P—O(C) [°]	110	—

the sulfur. The electronegativities of oxygen and sulfur are 3.5 and 2.5, and the van-der-Waals radii 1.40 and 1.85, respectively[7]. The difference in chemical reactivity can be seen from a comparison of the apparent first order rate constants of the hydrolysis of uridine 2',3'-cyclic phosphate *(4)* and uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3)*[8] with uridine 2'(3')-phosphate and uridine 2'(3')-phosphorothioate, respectively (Table 2).

Table 2. Apparent first order rate constants k [$10^{-3}s^{-1}$] of uridine 2',3'-cyclic phosphate *(4)* and uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3)*.

	k in 0.15 N $HClO_4$	k in 0.25 N KOH
Cyclicphosphate *(4)*	2.3	1.2
Cyclicphosphorothioate *(3)*	0.011	0.2

The comparatively large change in chemical reactivity makes these compounds interesting for the investigation of nucleotide dependent enzymes. Nucleoside phosphorothioates meet the condition stipulated above for the smallest possible structural difference between substrate analog and substrate. Nucleoside phosphorothioates also appear attractive from another point of view. *O*-Esters of such compounds where the ester group differs from the nucleoside exist as diastereomers. The investigation of the interaction of separate diastereomers with an enzyme should give some insight into the binding of the nucleotide and, in favorable cases, a detailed description of the mechanism of the enzymatic reaction.

Another advantage is that thiophosphate analogs can be synthesized not only of nucleoside monophosphates but also of nucleoside di- and triphosphates with the sulfur localized on the α-, β- or γ-phosphorus atom. Such analogs should be suitable for the investigation of ATP-dependent enzymes.

In this article nucleoside phosphorothioates, -thiodiphosphates and -thiotriphosphates will be discussed separately. In a thorough and excellent review article on ATP-analogs[9] *Yount* has summarized the results of studies with other ATP analogs.

2. Nucleoside Phosphorothioates

The original synthetic preparation of nucleoside 5'-phosphorothioates, the reaction of nucleosides with tris(1-imidazolyl)-phosphane sulfide[10], has been replaced by the reaction of nucleosides with $PSCl_3$[11]. Purine nucleoside 5'-phosphorothioates can be isolated by precipitation as the barium salts which require no further purification over an ion exchanger[12]. ^{35}S-labeled compounds can also be synthesized in this way.

While nucleoside 5'-phosphorothioates are not or are only extremely slowly degraded by phosphatases, they are competitive inhibitors for these enzymes[3], *i.e.* they bind to the substrate binding site. It was this observation which led to the further development of this class of compounds. [^{32}P]AMP is degraded about 2000 times faster than [^{35}S]AMPS by alkaline phosphatase from calf intestine and *E. coli* [see *(1)*][12]. It is known that the rate of hydrolysis of a phosphate ester by alkaline phosphatase is independent of the ester group; esters of alcohols or nucleosides are degraded just as fast as those of phenols[13]. This does not seem to be the case for esters of thiophosphoric acid.

Nucleoside 5'-phosphorothioates are degraded 2000 times more slowly than the corresponding phosphate[12]. However, *p*-nitrophenyl-[14], 4-methylumbelliferyl-[15] and *p*-phenylazophenylphosphorothioate[16] are degraded 100 times, about 300 times and about 200 times, respectively, more slowly than the corresponding phosphate esters, which themselves are all hydrolyzed at similar rates.

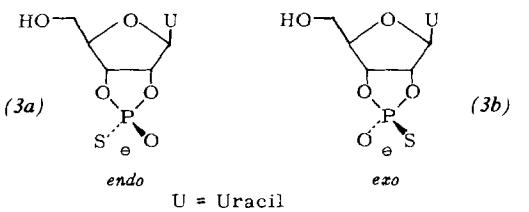
This large difference between phenolic esters of thiophosphoric acid and nucleoside phosphorothioates suggests that the rate determining steps of hydrolysis are possibly different. On hydrolysis of phosphate esters a phosphorylated enzyme intermediate is formed. Whether the formation or the subsequent hydrolysis of this phosphorylated intermediate is rate determining is still in dispute. Investigations on the mechanism of hydrolysis of phosphorothioates might therefore provide clues to enlarge our understanding of this enzyme.

The interactions of adenosine 5'-phosphorothioate *(1)* with enzymes other than phosphatases have been described by *Murray* and *Atkinson*[11]. Also in enzyme reactions where no cleavage of the ester bond occurs, the analog often reacts more slowly than the natural substrate. Thus, adenosine 5'-phosphorothioate is only a poor substrate for myokinase and adenylate desaminase. In the latter system the K_m values for the analog and for AMP are quite similar but the V_{max} values differ by a factor of about 10. Adenosine 5'-phosphorothioate is as active as AMP as an activator for phosphorylase b.

3. Cyclic Nucleoside Phosphorothioates

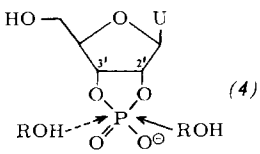
3.1. Uridine 2',3'-*O*,*O*-Cyclic Phosphorothioate *(3)*

Because of the chiral phosphorus this compound exists as the two diastereomers *(3a)* and *(3b)*. Their triethylam-



monium salts can be separated by crystallization[5]. The *endo* (with respect to the ribose ring and sulfur) isomer can be crystallized. Its structure and configuration were determined by X-ray structural analysis. Both isomers are cleaved by RNase A but have different affinities for this enzyme (K_m-*endo* = 6.2×10^{-3} mol/l; K_m-*exo* = 50×10^{-3} mol/l)[8].

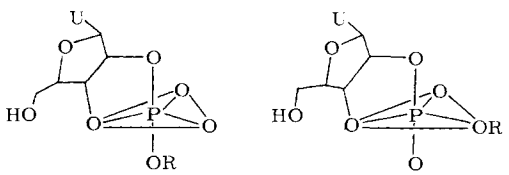
These isomers seemed to be suitable for the elucidation of a disputed step in the hydrolysis catalyzed by RNase A. RNase A hydrolyzes simple esters and polymers of pyrimidine nucleoside 3'-phosphoric acid by a two-step mechanism[2]. In the first, easily reversible step a pyrimidine nucleoside 2',3'-cyclic phosphate is formed by attack of the 2'-OH group on phosphorus (transesterification); in the second step the cyclic ester is hydrolyzed to a pyrimidine nucleoside 3'-phosphate by attack of a water molecule (hydrolysis). The alcoholysis or hydrolysis of uridine 2',3'-cyclic phosphate *(4)* can serve as an example to demonstrate that in principle the alcohol or the water can attack from the opposite side of the leaving group (2'-OH) (in-line, broken arrow) as well as from the same side (adjacent) (solid arrow)[17].



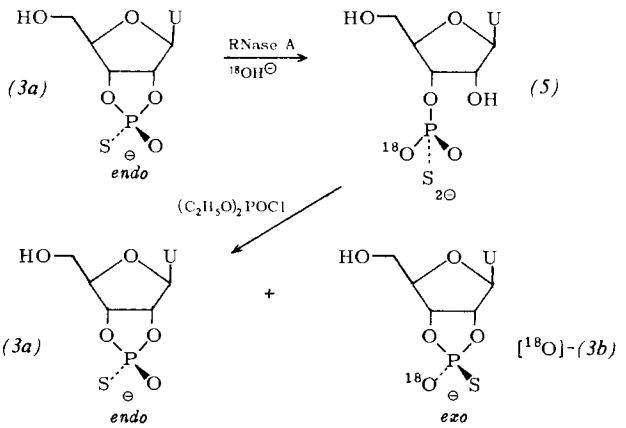
(4)

U = Uracil

Generally it is assumed that the hydrolysis of a five-membered cyclic phosphate ester proceeds *via* a pentacoordinated phosphorus intermediate where the incoming nucleophile as well as the leaving group are in the apical positions of a trigonal bipyramid[18]. The five-membered ring must occupy an apical and an equatorial position, so that the leaving group can always be in an apical position, although this sometimes requires a prior pseudorotation. The adjacent mechanism requires pseudorotation of the pentacoordinated phosphorus intermediate whereas the in-line mechanism does not[19].



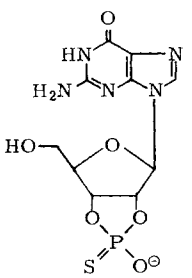
With the known absolute configuration of the diastereomers of uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3)* it should be possible to decide which of the two mechanisms operates. Evidence for the hydrolytic step was obtained by reaction of the *endo* isomer *(3a)* with the enzyme in ^{18}O-containing water. The hydrolysis product, [^{18}O]uridine 3'-phosphorothioate *(5)*, was chemically recyclized to uridine cyclic phosphorothioate (in-line mechanism) and the diastereomers *(3a)* and *(3b)* separated by crystallization and analyzed for their ^{18}O-content[19]. In an in-line mechanism the ^{18}O should be in the *exo* isomer *(3b)*, in an adjacent mechanism in the *endo* isomer *(3a)*. In fact, all the ^{18}O was contained in the *exo* isomer *(3b)*. The second step of the enzymatic hydrolysis can therefore be explained by an in-line mechanism. For investigation of the transesterification step the *endo* isomer *(3a)* was allowed to react with 20% aqueous methanol in the presence of the enzyme to give methyl uridine 3'-thiophosphate. The absolute configuration of this crystallized ester was determined by X-ray structural analysis[20, 21]. In an in-line mechanism this methyl ester should have the *R* configuration, whereas in an adjacent mechanism it should have the *S* configuration. The substance isolated from the enzymatic reaction had the *R* configuration. *Usher* investigated the transesterification reaction of *endo*-uridine 2',3'-cyclic phosphorothioate *(3a)* with cytidine. The product was cleaved under alkaline conditions (in-line), the uridine 3'-phosphorothioate *(5)* thus obtained again undergoing cyclization to uridine cyclic phosphorothioate; the configuration of the isomer obtained was established by crystallization and NMR spectroscopy. This result is also compatible with an in-line mechanism[22].



To what extent can results obtained with phosphorothioates be used to draw conclusions about the mechanism of hydrolysis of the natural substrate, the phosphate? Since the K_m value of the analog is identical with that of the phosphate and the V_{max} value of the analog differs only by a factor of five from that of the phosphate (since the lower value is also to be found on alkaline hydrolysis of the phosphate, it can therefore be explained simply by the phosphorothioates' lower chemical reactivity), there is no reason to believe that the cleavage of both compounds does not follow the same mechanism.

3.2. Guanosine 2',3'-*O*,*O*-Cyclic Phosphorothioate

In analogy to uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3a)*, *(3b)*, guanosine 2',3'-*O*,*O*-cyclic phosphorothioate *(6)* also exists as the *endo* and *exo* isomers[23]. However, attempts to separate the isomers have so far failed.



(6)

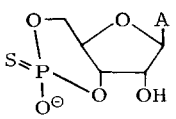
Identification of the isomers was accomplished by comparison of their ^{31}P-NMR spectra with those of the uridine derivatives *(3a)* and *(3b)*, where an assignment of the configuration to the signals was possible. In the reaction of the mixture of diastereomers of *(6)* with RNase T1 in water and methanol only the *endo* isomer undergoes reaction. The chemical shift ($\Delta\delta$) of the methyl guanosine 3'-thiophosphate obtained during the transesterification is just as large as that of the methyl uridine 3'-thiophosphate of the *R* configuration which was

obtained from the reaction of *endo*-uridine 2',3'-*O*,*O*-cyclic phosphorothioate *(3a)* and RNase in aqueous methanol. One can therefore conclude that RNase T1 also follows the in-line mechanism, at least for the transesterification step. Since the chemical shift of the isomeric methyl esters differs only very little, however, this result is not quite as satisfactory as that obtained with RNase A.

3.3. Adenosine 3',5'-*O*,*O*-Cyclic Phosphorothioate

Adenosine 3',5'-cyclic phosphate (cAMP) is apparently one of the most versatile low molecular weight compounds in biology[24]. Apart from the numerous regulatory functions which it exerts and which are of importance for the biochemist, this compound is also of interest for the mechanistically oriented chemist. It is rather stable against alkaline and acid hydrolysis but is degraded in the cell by a specific phosphodiesterase. The mechanism of this enzymatic hydrolysis is of particular interest.

As discussed in connection with uridine cyclic phosphorothioate *(3)* (Section 3.1) the hydrolysis of cyclic phosphate esters proceeds *via* a pentacoordinated phosphorus intermediate where the incoming nucleophile as well as the leaving group are in apical positions[17]. By way of contrast, in six-membered cyclic phosphate esters, a di-equatorial positioning of the ring is preferred for steric reasons[25]. What might be the mechanism of enzymatic hydrolysis of such a structure? Is the structure forced by the enzyme into an apical-equatorial position, possibly involving a pseudorotation process? Here also, the diastereomers of adenosine 3',5'-*O*,*O*-cyclic phosphorothioate *(7)* might be of help.



(7)

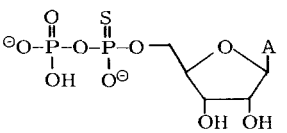
A = Adenine

Judging from the ^{31}P-NMR spectrum both diastereomers are present in a ratio of approx. 1:1. A satisfactory separation by crystallization has not as yet been achieved[26]; however, since the isomers can easily be crystallized this separation should be possible in principle. The results of the hydrolysis of the mixture of isomers with the phosphodiesterases from beef heart and *Dictyostelium discoideum*[27] indicate only a small difference, if any, in rate of hydrolysis of both isomers. The total rate is slower by a factor of about 50—100 than that of adenosine 3',5'-cyclic phosphate.

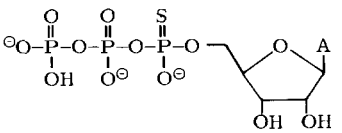
It is also of interest, of course, to see which functions of cAMP the analog can exert. One would hope to be able to differentiate the different cyclic AMP activities in biological systems with the aid of the analog. Analogs which are hydrolyzed slowly enzymatically but which at the same time still undergo reaction are particularly important. Adenosine 3',5'-cyclic phosphorothioate *(7)* belongs to this class of analogs since it is degraded more slowly than cAMP but stimulates for instance protein-kinase almost as well as does cAMP[26] and is also chemotactically as active as cAMP in *Dictyostelium discoideum*[28].

4. Adenosine 5'-*O*-(1-Thiodiphosphate) (ADPαS) and Adenosine 5'-*O*-(1-Thiotriphosphate) (ATPαS)

ADPαS *(8)* and ATPαS *(9)* can be synthesized, contrary to our earlier results[29], without lost of sulfur from adenosine 5'-phosphorothioate by activation with diphenylphosphorochloridate and reaction with pyrophosphate or phosphate[30]. *(8)* and *(9)* also exist as two diastereomers which differ in their reactivity with some kinases[30] and which one can separate analytically by high pressure liquid chromatography[31, 32].



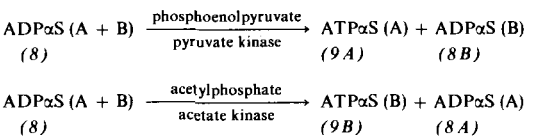
(8), ADPαS



(9), ATPαS

A = Adenine

The reaction of the chemically synthesized mixture of diastereomers A and B of ADPαS *(8)* with phosphoenolpyruvate and pyruvate-kinase leads



to the formation of ATPαS *(9A)*, with about 50% conversion. ATPαS synthesized in this way is readily cleaved to ADPαS by nucleoside diphosphate kinase—in the presence of a nucleoside diphosphate—and by myokinase—in the presence of AMP. Phosphorylation of ADPαS in the presence of acetate kinase and acetyl phosphate leads preferentially to ATPαS *(9B)*, which is only slowly cleaved by nucleoside diphosphate kinase and myokinase. This difference in reactivity of the two ATPαS preparations suggests that they represent the two postulated diastereomers. Indeed only 50% of the chemically synthesized ATPαS *(9)* is cleaved by myokinase and nucleoside diphosphate kinase; in the chemically synthesized ATPαS one can further demonstrate two isomers by high pressure liquid chromatography, but in the enzymatic preparations only one isomer[30-32]. The isomer obtained with pyruvate kinase is designated as isomer A, that obtained with acetate kinase as isomer B. Both isomers of ATPαS exhibit rather similar K_m values with hexokinase but isomer A has a V_{max} value about 100 times larger than that of isomer B[31].

The preferential synthesis of one isomer by different kinases suggests that the substrate binding sites of these kinases have different geometries. By comparison of a series of kinases one can study in this way the similarity of the substrate binding sites. Not only kinases exhibit this stereospecificity. Also phenylalanyl-tRNA synthetase from baker's yeast[33] accepts only isomer A of ATPαS as substrate. DNA-dependent RNA polymerase from *E. coli*[34, 35] and the tRNA-nucleotidyl transferase from baker's yeast[36, 37] however, seem to have a less pronounced stereospecificity towards the isomers of ATPαS. On polymerization of ATPαS and UTPαS with DNA-dependent RNA-polymerase from *E. coli* in presence of poly-d(A-T), one can isolate a double-stranded poly-r(A-U) analog,

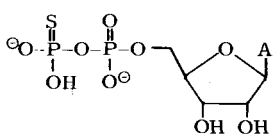
where each phosphate group contains a sulfur atom [poly-r($_S$A$_S$U)][34]. This double-helix is thermally just as stable as the unmodified polymer. It is degraded more slowly by nucleases. Poly-r($_S$A$_S$U) is superior to poly-r(A-U) in the induction of interferon in cell cultures of human fibroblasts and in the rabbit[38]. This also applies to the analog of poly-r(I-C)[39]. It is conceivable that this higher activity is due to the presumably longer lifetime of the modified polymer in cell culture or the animal. However, it cannot be ruled out that other effects, for instance higher affinity of the analog to a receptor, are responsible for it. The toxicity of polynucleotides seems to parallel their ability to induce interferon[40]. The analogs dATPαS and dTTPαS can also be used for the replication of ϕ X174-DNA in ether-treated permeabilized *E. coli cells*[41]. This DNA can be closed by ligase to RFI-particles (circular double strands). It can be demonstrated in spheroblasts that the modified RF-material is apparently also infectious.

The mixture of isomers of ATPαS *(9)* as well as of ATPβS *(11)* (see Section 5) are bound to mitochondrial membranes from rat liver in the absence as well as in the presence of atractyloside[42]. The corresponding diphosphate analogs ADPαS *(8)* and ADPβS *(10)* can not be oxidatively phosphorylated in this system. They are competitive inhibitors for this process.

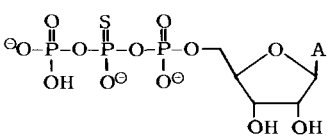
The analogs ADPαS, CDPαS and ADPβS are substrates for the *E. coli* ribonucleotide reductase with similar K_m values to the corresponding natural diphosphates, but strongly decreased rates[43]. This means that the modified substrates are bound just as well as the natural substrates but the reaction proceeds much more slowly even though it occurs on the unmodified part of the molecule. This reduced reaction rate might be due to an incorrect binding which prevents the optimal positioning of the reactive groups.

5. Adenosine 5′-*O*-(2-Thiotriphosphate) (ATPβS)

ATPβS *(11)* also exists as diastereomers A and B which can be synthesized from adenosine 5′-*O*-(2-thiodiphosphate)



(10), ADPβS



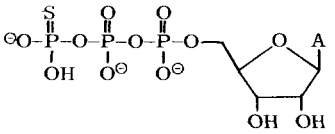
(11), ATPβS

A = Adenine

(ADPβS) *(10)* with pyruvate kinase (isomer A) and creatine kinase (isomer B)[30]. These two isomers differ mainly in their reaction with myosin. Isomer A is cleaved rather rapidly, isomer B extremely slowly. The interaction with other ATPases has not yet been investigated.

6. Adenosine 5′-*O*-(3-Thiotriphosphate) (ATPγS)

ATPγS belongs to the most versatile nucleoside phosphorothioates *(12)*[44]. This ATP-analog is only extremely slowly cleaved by phosphatases. The difference in rate to ATP is about 3 orders of magnitude and is thus similar to the difference in hydrolysis between AMP and adenosine 5′-phosphoro-



(12), ATPγS

A = Adenine

thioate *(1)*. Originally it was hoped that also ATPases would cleave ATPγS extremely slowly and that this analog could therefore be used instead of adenylylimidodiphosphate (AMPPNP) in biological systems where such ATPases interfere. It was found, however, that the ratio of rates of degradation of ATPγS and those of ATP differ for each ATPase. A system in which ATPases notoriously interfere is the ATP-cyclase system. In this reaction ATP is cyclized to cAMP. The ATPases obviously destroy the substrate. ATPγS is also a good substrate in this system of rat brain[45]. However, it is degraded rather rapidly so that it does not offer any decisive advantage over the stable AMPPNP although it is a better substrate apparently in some other cyclase systems. ATPγS is also rapidly cleaved by the ATPase of the sarcoplasmatic reticulum[46].

In contrast ATPγS is hydrolyzed extremely slowly, if at all, by the microsomal Na^+/K^+-ATPase[47]. Of this ATPase it is known that the enzyme is phosphorylated in an initial step and that the phosphorylated enzyme is dephosphorylated in the second step. It should be possible to show with the aid of [^{35}S]ATPγS whether this enzyme is also thiophosphorylated. This would open the possibility to freeze the enzyme in the intermediate stage of thiophosphorylation and to investigate in which ways this differs from the non-phosphorylated enzyme.

This freezing of the phosphorylated intermediate stage has been demonstrated in another system with the aid of ATPγS[46]. Rabbit muscle phosphorylase is phosphorylated by ATP with participation of a phosphorylase kinase to phosphorylase a which then can cleave glycogen. The enzyme is again dephosphorylated to phosphorylase b by a phosphorase a-phosphatase and thus inactivated, *i.e.* its activity is regulated by this mechanism in the cell. The enzymatic transfer of the thiophosphate residue onto phosphorylase can be carried out with ATPγS to obtain a thio-analog of phosphorylase a[46]. This analog is as active as phosphatase a in the cleavage of glycogen but is only extremely slowly degraded if at all by the phosphatase. In addition, the phosphorylase-kinase can be activated by a cAMP-dependent protein kinase through phosphorylation with ATP. Also in this reaction ATP can be replaced by ATPγS. One obtains an activated phosphorylase kinase which presumably cannot be hydrolyzed by the corresponding phosphatase. These are cases in which the thiophosphorylated active enzyme can be investigated separately which is of interest particularly in biological systems such as glycogen particles. Since a series of enzymes is regulated through the cycle of phosphorylation-dephosphorylation one can foresee here interesting applications for ATPγS.

The availability of [^{35}S]ATPγS is important for investigations where the thiophosphate residue is being transferred. The enzymatic method which has been developed for the γ-phosphate exchange of ATP with phosphoglycerate kinase[48] can also be applied to ATPγS. Through changes in the experimental conditions it is possible to introduce [^{35}S]-thiophosphate

into ATPγS in this way[12]. [^{14}C]- or [^{3}H]ATPγS can be synthesized from the correspondingly labeled ADP by thiophosphate transfer with myokinase or nucleoside diphosphate kinase[49]. It should be mentioned here that thiophosphate does not form a blue ammonium molybdate complex like phosphate and that in contrast to phosphate it is adsorbed by charcoal. These methods, therefore, are not available for the determination of data of hydrolysis for ATPγS.

Another system in which the properties of ATPγS have been thoroughly investigated are isolated muscle fibers and the proteins actin and myosin which participate in muscle contraction. Interest is concentrated on this system by many groups at the moment in an effort to establish the relationship between chemical reaction (hydrolysis of ATP by myosin) and mechanical work (contraction of muscle). *Lymn* and *Taylor* have developed a model (Fig. 1)[50], in which actin dissociates

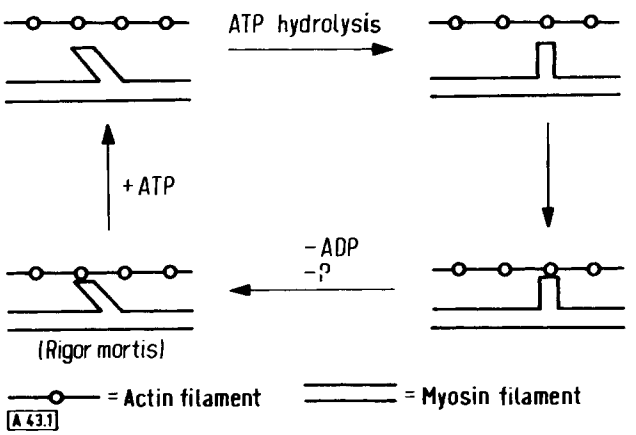


Fig. 1. Lymn-Taylor model for the actin-myosin system. For details see text (after [50]).

from myosin on binding of ATP to the myosin heads without the angles of the heads to the myosin (45°) being changed. The hydrolysis of ATP to ADP and phosphate leads to an extension of the heads and myosin and actin can again combine. In this step the hydrolysis products dissociate and the actual mechanical work—movement of the actin relative to the myosin filament—*i.e.* the contraction occurs. In absence of ATP the muscle returns to the rigor-mortis state. In the presence of ATP the cycle can again start from the beginning, *i.e.* the muscle is in a state of active contraction. The model demands that in this cycle the binding of ATP to the myosin heads causes only dissociation of the actin filament but no extension of the myosin heads. It should be possible to test this idea with ATP analogs which cannot or can only slowly be cleaved by myosin, under the condition that they are being bound similarly to ATP and that the kinetics of the single steps during the hydrolysis of the analogs are known. Moreover a method has to be available to observe such changes in muscle fibers. The latter is possible with X-ray diffraction methods. Of the ATP analogs AMPPNP, $AMPCH_2PP$ and ATPγS, which can be used in principle for such investigations, only ATPγS will be discussed here. In the presence of ATPγS muscle fibers relax (*i.e.* actomyosin dissociation) but cannot contract any more after addition of Ca^{2+} (the physiological contraction stimulator)[51]. As judged from the rates by which ATPγS is being bound to myosin or the myosin subfragment 1 it seems to be more similar to ATP than the other two analogs[52]. Thorough kinetic investigations in *Trentham*'s laboratory in Bristol have shown that the basic difference between ATP and ATPγS is that the actual hydrolysis step of ATPγS is about 1000 times slower than that of ATP. The effect of this is that the dissociation of product is no longer the rate determining step, as it is with ATP itself, but rather the hydrolysis step[53]. In the steady state the complex ATPγS·myosin and not ADP·myosin should be predominant, as in the case of ATP. As discussed above this should allow determination of the orientation of the myosin heads during ATP binding. Such X-ray structural studies are in progress in *Holmes*' laboratory in Heidelberg[54]. Their results[55] are consistent with a 90°-position of the myosin heads and thus would fit only in a modified Lymn-Taylor scheme.

The scheme mentioned above has been refined by *Trentham* and will only be mentioned here in as much as ATPγS was used in this study. On binding of ATP onto the myosin-subfragment 1 the protein fluorescence increases. To decide whether this change of fluorescence is due to the binding of the nucleotide onto the protein or to the conformational change of the binary complex protein-nucleotide or to the hydrolysis of ATP, the slow rate of the hydrolysis step of ATPγS ($k=0.2\,s^{-1}$) in contrast to that of ATP (*ca.* $160\,s^{-1}$) was of help. Since the rates of change of fluorescence ($400\,s^{-1}$) were found to be the same for both substances, while the rates of hydrolysis are largely different, the change of fluorescence could be ascribed to a change of conformation of the binary complex[52]. This can also be of significance for the positioning of the myosin heads as discussed above and thus for the relationship between chemical reaction and mechanical work.

7. Conclusions

These discussions show that nucleoside phosphorothioates exhibit varying properties in their interaction with enzymes. They can be competitive inhibitors but also substrates, in many cases with considerably reduced reaction rates in comparison with normal substrates. This also applies when the actual chemical reaction does not occur on the thiophosphate residue. It seems to be common to all systems studied so far that the affinities of the nucleoside phosphorothioates and of the natural substrates to a given enzyme are rather similar if not identical. Furthermore, in all systems the rate constants of the chemical step seem to be more or less reduced (this has nowhere been shown as unequivocally as in myosin, since with other enzymes only the (steady-state) V_{max} values have been measured) with differences varying from enzyme to enzyme. A prediction about the behavior of nucleoside phosphorothioates towards an enzyme system which has not yet been studied seem to be rather risky at present. This is probably a reflection of our limited understanding of most enzyme systems. The advantage of nucleoside phosphorothioates over other phosphate modified nucleotide analogs is probably that they are not competitive inhibitors in many cases but rather substrates with often reduced reaction rates. These properties, the existance of diastereomers, the ability to transfer the thiophosphate residue of the ATP analog and the possibility of modifying nucleoside mono-, di- and -triphos-

phates open a wide area of application for this group of analogs—as this review hopefully has demonstrated. It remains to be seen whether they can prove as useful in investigations of more complicated systems such as membranes or cell cultures.

I am grateful to many friends and colleagues in this and many other institutes in Germany and abroad for suggestions, criticism, methodical help and the willingness for cooperation without which nucleoside phosphorothioates would never have found such wide distribution and importance. In addition I would like to thank all collaborators for their enthusiastic research which made this work possible. I thank the Deutsche Forschungsgemeinschaft for financial support.

Received: August 1974 [A 43 IE]
German version: Angew. Chem. *87*, 179 (1975)

[1] *P. Lengyel* and *D. Söll*, Biol. Rev. *33*, 264 (1969).

[2] *F. M. Richards* and *H. W. Wyckhoff* in *P. D. Boyer*: The Enzymes, 3rd edition, Vol. 4, Academic Press, New York 1971, p. 647.

[3] *F. Eckstein* and *H. Sternbach*, Biochim. Biophys. Acta *146*, 618 (1967).

[4] *C. L. Coulter*, J. Amer. Chem. Soc. *95*, 570 (1973).

[5] *W. Saenger* and *F. Eckstein*, J. Amer. Chem. Soc. *92*, 4712 (1970).

[6] *C. H. Schwalbe*, *R. Goody*, and *W. Saenger*, Acta Crystallogr. *B29*, 2264 (1973).

[7] *L. Pauling*, Die Natur der chemischen Bindung, Verlag Chemie, Weinheim, 1962.

[8] *F. Eckstein*, FEBS-Lett. *2*, 85 (1968).

[9] *R. Yount*, Method Enzymol., in press.

[10] *F. Eckstein*, J. Amer. Chem. Soc. *92*, 4718 (1970).

[11] *A. W. Murray* and *M. R. Atkinson*, Biochemistry *7*, 4023 (1968).

[12] *F. Eckstein*, unpublished.

[13] *T. W. Reid* and *J. B. Wilson* in *P. D. Boyer*: The Enzymes, 3rd edition, Vol. 4, Academic Press, New York 1971, p. 373.

[14] *R. Breslow* and *J. Katz*, J. Amer. Chem. Soc. *90*, 7376 (1968).

[15] *H. N. Fernley*, Nature New Biol. *241*, 110 (1973).

[16] *P. Mushak* and *J. E. Coleman*, Biochemistry *11*, 201 (1972).

[17] *D. A. Usher*, Proc. Nat. Acad. Sci. USA *62*, 661 (1969).

[18] *F. H. Westheimer*, Accounts Chem. Res. *1*, 70 (1968).

[19] *D. A. Usher*, *D. J. Richardson*, and *F. Eckstein*, Nature *228*, 663 (1970).

[20] *F. Eckstein*, *W. Saenger*, and *D. Suck*, Biochem. Biophys. Res. Commun. *46*, 964 (1972).

[21] *W. Saenger*, *D. Suck*, and *F. Eckstein*, Eur. J. Biochem. *46*, 559 (1974).

[22] *D. A. Usher*, *E. S. Erenrich*, and *F. Eckstein*, Proc. Nat. Acad. Sci. USA *69*, 115 (1972).

[23] *F. Eckstein*, *K. H. Schulz*, *H. Rüterjans*, *W. Haar*, and *W. Maurer*, Biochemistry *11*, 3507 (1972).

[24] *P. Greengard* and *G. A. Robison*, Advances in Cyclic Nucleotide Research, Vol. 1, Raven Press, New York 1972.

[25] *D. Marquarding*, *F. Ramirez*, *I. Ugi*, and *P. Gillespie*, Angew. Chem. *85*, 99 (1973); Angew. Chem. internat. Edit. *12*, 91 (1973).

[26] *F. Eckstein*, *L. P. Simonson*, and *H. P. Baer*, Biochemistry *13*, 3806 (1974).

[27] *D. Malchow* and *F. Eckstein*, unpublished.

[28] *T. Konijn*, personal communication.

[29] *F. Eckstein* and *H. Gindl*, Biochim. Biophys. Acta *149*, 35 (1967).

[30] *F. Eckstein* and *R. S. Goody*, unpublished.

[31] *K. W. Stahl*, *E. Schlimme*, and *F. Eckstein*, FEBS-Lett. *40*, 241 (1974).

[32] *K. W. Stahl*, Habilitationsschrift, Technische Universität Hannover 1974.

[33] *F. von der Haar*, personal communication.

[34] *V. Armstrong* and *H. Sternbach*, personal communication.

[35] *F. Eckstein* and *H. Gindl*, Eur. J. Biochem. *13*, 558 (1970).

[36] *E. Schlimme*, *F. von der Haar*, *F. Eckstein*, and *F. Cramer*, Eur. J. Biochem. *14*, 351 (1970).

[37] *H. Sternbach*, personal communication.

[38] *E. DeClercq*, *F. Eckstein*, and *T. C. Merigan*, Science *165*, 1137 (1969).

[39] *E. DeClercq*, *F. Eckstein*, *H. Sternbach*, and *T. C. Merigan*, Virology *42*, 421 (1970).

[40] *D. R. Black*, *F. Eckstein*, *E. DeClercq*, and *T. C. Merigan*, Antimicrob. Ag. Chemother. *1973*, 198.

[41] *H. P. Vosberg* and *F. Eckstein*, unpublished.

[42] *E. Schlimme*, *W. Lamprecht*, *F. Eckstein*, and *R. S. Goody*, Eur. J. Biochem. *40*, 485 (1973).

[43] *U. v. Döbeln* and *F. Eckstein*, Eur. J. Biochem. *43*, 315 (1973).

[44] *R. S. Goody* and *F. Eckstein*, J. Amer. Chem. Soc. *93*, 6252 (1971).

[45] *H. P. Baer*, *L. P. Simonson*, and *F. Eckstein*, FEBS-Lett. *41*, 199 (1974).

[46] *D. Gratecos* and *E. J. Fischer*, Biochem. Biophys. Res. Commun. *58*, 960 (1974).

[47] *H. Schoner* and *F. Eckstein*, unpublished.

[48] *J. M. Glynn* and *J. B. Chappell*, Biochem. J. *90*, 147 (1964).

[49] *R. S. Goody*, *F. Eckstein*, and *R. H. Schirmer*, Biochim. Biophys. Acta *226*, 155 (1972).

[50] *R. W. Lymn* and *E. W. Taylor*, Biochemistry *10*, 4617 (1971).

[51] *H. J. Mannherz*, *R. S. Goody*, and *F. Eckstein*, unpublished.

[52] *C. R. Bagshaw*, *J. F. Eccleston*, *F. Eckstein*, *R. S. Goody*, *H. Gutfreund*, and *R. Trentham*, Biochem. J. *141*, 351 (1974).

[53] *C. R. Bagshaw*, *J. F. Eccleston*, *D. R. Trentham*, *D. W. Yates*, and *R. S. Goody*, Cold Spring Harbor Symp. Quant. Biol. *37*, 127 (1972).

[54] *J. Barrington Leigh*, *K. C. Holmes*, *H. G. Mannherz*, *G. Rosenbaum*, *F. Eckstein*, and *R. S. Goody*, Cold Spring Harbor Symp. Quant. Biol. *37*, 443 (1972).

[55] *R. S. Goody*, *K. C. Holmes*, *H. G. Mannherz*, *J. Barrington Leigh*, and *G. Rosenbaum*, Biophysical J., in press.

COMMUNICATIONS

Fluorination of Cyanogen Chloride and *N*-Chlorodichloromethyleneamine

By *J. D. Cameron* and *B. W. Tattershall*[*]

Fluorination of cyanogen chloride with potassium fluoride, suspended in tetramethylene sulfone, or in the absence of solvent, yields *N*,*N*-bis(trifluoromethyl)cyanamide *(1)*, along with trifluoromethyl(difluoromethylene)amine *(2)* and cyanuric trifluoride, under mild conditions.

[*] J. D. Cameron and Dr. B. W. Tattershall
Department of Inorganic Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU (England)

The mechanism for increase of the carbon to nitrogen ratio in the formation of *(1)* or *(2)* from ClCN is unknown, but a yield of *(1)* of up to 25% based on carbon of cyanogen chloride can be obtained.

$(CF_3)_2N{-}C{\equiv}N$ *(1)* $CF_3N{=}CF_2$ *(2)* $CF_3N{=}CCl_2$ *(3)*

Compound *(1)* is a colorless gas [vapor pressure (−80° to +10°C) represented by: $\log_{10} p_{(torr)} = 7.267 - 1246/T$; extrapolated b.p. 11°C] identified by its molecular weight and by chemical and spectroscopic analysis. It is thermostable (70 h in Pyrex at 180°C) and stable toward hydrolysis by

water (70 h at 60 °C). The $(CF_3)_2N$ group was diagnosed by ^{19}F-NMR (single peak 58.3 ppm upfield from internal CCl_3F) and by characteristic infrared absorption at 990 cm^{-1} and mass spectral fragment at $m/e = 114$ ($C_2F_4N^+$). The C≡N stretching frequency occurs at 2260 cm^{-1}; further IR bands appear at 1360 vs, 1270 vs, 1230 vs, 1180 s, 1155 s, 990 s, and 728 s cm^{-1}. The mass spectrum shows the molecular ion at $m/e = 177.9971$, and other fragments at 159, 133, 90 (CF_2NCN^+), 69, and 50. Two isomers of *(1)*, $CF_2{=}NCF_2N{=}CF_2$ and $CF_3N{=}C{=}NCF_3$, have been previously reported[1].

Cyanogen chloride reacts with chlorine to give $ClN{\equiv}CCl_2$[2], but the reaction appears to be easily reversed.

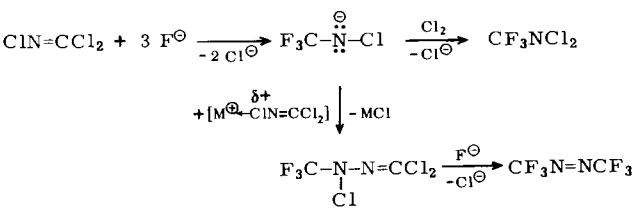
$$ClCN + Cl_2 \rightleftharpoons ClN{=}CCl_2$$

Consequently, reaction of $ClN{=}CCl_2$ with KF in tetramethylene sulfone gives some *(1)*, but the major products are CF_3NCl_2 and $CF_3N{=}NCF_3$, as previously reported for the reaction of ClCN with AgF and chlorine under conditions more conducive to a radical mechanism[3].

$$2\ ClN{=}CCl_2 + 3\ MF \longrightarrow CF_3NCl_2 + ClCN + 3\ MCl$$

$$2\ ClN{=}CCl_2 + 6MF \longrightarrow CF_3N{=}NCF_3 + 6\ MCl$$

We have found that use of KF favors formation of CF_3NCl_2, while AgF favors $CF_3N{=}NCF_3$, suggesting the following scheme which does not involve radicals:



Reaction of $ClN{=}CCl_2$ with SbF_3 gives mainly non-volatile products, but inclusion of CCl_4, CCl_3H, or CCl_3F in the mixture leads to $CF_3N{=}CCl_2$ *(3)*. In contrast to the formation of *(1)* in the basic reactions, the source of the extra carbon atom in *(3)* is clearly the added chloromethane. An acid-catalyzed reaction of $ClN{=}CCl_2$ with CCl_4 has been independently reported[4].

N,N-Bis(trifluoromethyl)cyanamide (1)

KF (20 mmol) is dried in a Pyrex tube at 120 °C in vacuum, then dry tetramethylene sulfone (2 g) is added, and the mixture degassed. ClCN (4.5 mmol) is condensed in from the vacuum system, and the tube is sealed and heated to 60 °C for 60 h. Vacuum fractionation yields *(1)*, which at *ca.* 10^{-3} torr is passed by a trap at −96 °C and stopped at −112 °C. Yield 0.35 mmol (23 %).

Fluorination of N-Chlorodichloromethyleneamine

KF (19 mmol), tetramethylene sulfone (1.8 g), and $ClN{=}CCl_2$ (5.8 mmol) are sealed together in a Pyrex ampoule under the conditions described above, and heated to 60 °C for 70 h. Unreacted $ClN{=}CCl_2$ (0.13 mmol) and ClCN (1.95 mmol) are separated by vacuum fractionation, to yield a mixture of CF_3NCl_2 (1.98 mmol) and $CF_3N{=}NCF_3$ (0.42 mmol) which may be further separated by gas chromatography.

Received: July 29, 1974 [Z 108 IE]
German version: Angew. Chem. 87, 208 (1975)

CAS Registry numbers:
(1), 54657-79-3; CF_3NCl_2, 13880-73-4; $CF_3N{=}NCF_3$, 372-63-4; cyanogen chloride, 506-77-4, *N*-chlorodichloromethyleneamine, 25240-91-9, potassium fluoride 7789-23-3; tetramethylene sulfone, 126-33-0

[1] *P. H. Ogden* and *R. A. Mitsch*, J. Amer. Chem. Soc. *89*, 5007 (1967).
[2] *H. Hagemann, D. Arlt*, and *I. Ugi*, Angew. Chem. *81*, 572 (1969); Angew. Chem. internat. Edit. *8*, 606 (1969).
[3] *W. J. Chambers, C. W. Tullock*, and *D. D. Coffman*, J. Amer. Chem. Soc. *84*, 2337 (1962).
[4] *J. Geevers, W. P. Trompen*, and *J. Th. Hackmann*, Rec. Trav. Chim. Pays-Bas *91*, 331 (1972).

Disilylmercury and Digermylmercury

By *Stephen Cradock, E. A. V. Ebsworth, Narayan S. Hosmane*, and *Kenneth M. Mackay*[*]

We have recently prepared trimethylsilylsilane by the reaction between silyl bromide and bis(trimethylsilyl)mercury. This reaction is very slow in solution. If, however, an excess of *solid* mercurial is treated with silyl bromide, trimethylsilyl bromide is rapidly formed in almost quantitative yield. Trimethylsilylsilane is evolved over a period of days:

$$H_3SiBr + (Me_2Si)_2Hg \rightarrow Me_3SiBr + \underset{(1)}{[Me_3SiHgSiH_3]} \rightarrow Me_3SiSiH_3$$

The solid *(1)* is soluble in benzene. The NMR spectrum of the solution showed new peaks at $\tau \approx 5$ (associated with Si*H*) and $\tau = 10$ (associated with SiC*H*). Each peak had associated ^{199}Hg satellites, and both sets of satellites were collapsed by irradiation at the same ^{199}Hg frequency, showing that the two resonances were due to the same molecular species.

Table 1. NMR data of trimethylsilyl(silyl)mercury and disilylmercury, and of trimethylsilyl(germyl)mercury and digermylmercury. Chemical shifts in ppm, coupling constants in Hz.

	$Me_3SiHgSiH_3$	$(H_3Si)_2Hg$	$Me_3SiHgGeH_3$	$(H_3Ge)_2Hg$
$\tau(SiH_3/GeH_3)$	4.98	5.46	4.54	5.16
$\tau(Me_3Si)$	9.90	—	9.86	—
$\delta(^{199}Hg)$ [a]	+327.1	+196.0	+159.0	−147.45
$\delta(^{29}Si)$ [b] Me_3Si	+ 63.7	—	+ 41.1	—
H_3Si	− 22.1	− 10.3	—	—
$^1J(H^{29}Si)$	178.0	185.0	—	—
$^2J(H^{29}Si)$	6.0	—	6.8	—
$^2J(H^{199}Hg)$	66.0	84.0	92.0	147.0
$^3J(H^{199}Hg)$	54.0	—	62.0	—

[a] In ppm relative to Me_2Hg (positive to high frequency); in $(Me_3Si)_2Hg$ the value is +481.0 ppm.
[b] In ppm relative to Me_4Si (positive to high frequency); in $(Me_3Si)_2Hg$ the value is +64.0 ppm.

[*] Prof. Dr. E. A. V. Ebsworth, Dr. S. Cradock, and N. S. Hosmane
Department of Chemistry, Edinburgh University
West Mains Road, Edinburgh EH9 3JJ (Scotland)
Dr. K. M. Mackay
University of Waikato
Hamilton (New Zealand)

When equimolar proportions of reactants were taken initially, the species could be obtained virtually free of SiH_3Br or $(Me_3Si)_2Hg$; the relative intensities of the Si*H* and the SiC*H* peaks were roughly 1:3, and the ^{29}Si and ^{199}Hg INDOR spectra confirmed the identification of the compound as $Me_3SiHgSiH_3$. Treatment of solid $(Me_3Si)_2Hg$ with excess of SiH_3Br gives Si_2H_6, but if SiH_3Br is added to a solution of $Me_3SiHgSiH_3$ and the solution kept at 50°C for some days, the yellow color fades; trimethylsilyl bromide is formed and the ^1H-NMR spectrum shows a new resonance at $\tau \approx 5$ with ^{29}Si and ^{199}Hg satellites. The ^{199}Hg INDOR spectrum shows the seven-line pattern expected for $(H_3Si)_2Hg$. Both $(CH_3)_3SiHgSiH_3$ and $(H_3Si)_2Hg$ are stable for a matter of days at room temperature in solution, but the compounds are exceedingly reactive as solids towards traces of air and moisture. The NMR parameters for both compounds are given in Table 1.

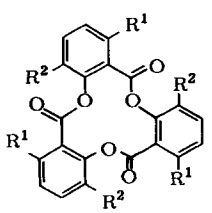
Treatment of bis(trimethylsilyl)mercury with germyl bromide leads similarly to the formation of $(CH_3)_3SiHgGeH_3$ and $(H_3Ge)_2Hg$; these two compounds were identified by their ^{199}Hg INDOR spectra (Table 1). The germyl compounds are much less sensitive than are their silyl analogs to traces of air and moisture, but are somewhat less stable over extended periods in solution.

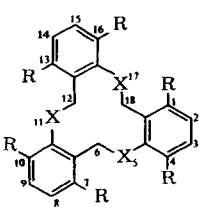
Received: August 1, 1974 [Z 110 IE]
German version: Angew. Chem. 87, 207 (1975)

The Conformational Behavior of 6*H*,12*H*,18*H*-5,11,17-Trithiatribenzo[*a*,*e*,*i*]cyclododecene

By *W. David Ollis*, *J. Fraser Stoddart*, and *Michael Nógrádi*[*]

The trisalicylides *(1)*—*(3)*[1], the hydrocarbon *(4)*[2], and its hexamethyl derivative *(5)*[2] are conformationally mobile in solution. Studies[1, 2] on these compounds suggest that the barrier heights for conformational changes in the twelve-membered rings depend on the nature of the substituent atoms or groups at the *ortho* positions of the aromatic rings. Since the hydrocarbon *(4)* is a rather inconvenient molecule to study by NMR line shape methods due to the complexity of the ^1H-NMR spectrum of its CH_2—CH_2 groups, we have prepared the trithia analog *(6)*, m. p. 197—198 °C, by reaction of 2-(chloromethyl)thiophenol[3] with sodium hydroxide in methanol, in order to investigate a molecule where the *ortho* substituents are hydrogen atoms.

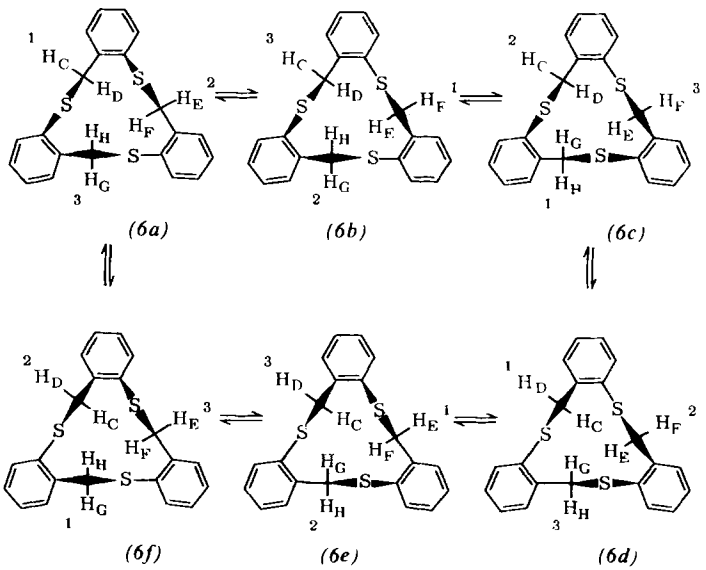




(1), $R^1 = R^2 = CH_3$
(2), $R^1 = CH_3$; $R^2 = CH(CH_3)_2$
(3), $R^1 = CH(CH_3)_2$; $R^2 = CH_3$

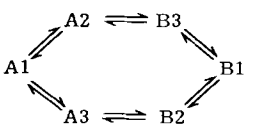
(4), R = H; X = CH_2
(5), R = CH_3; X = CH_2
(6), R = H; X = S

The ^1H-NMR spectrum of this heterocyclic compound *(6)* in CS_2 showed temperature dependence. Three AB systems ($\tau_{A1} = 4.43$, $\tau_{B1} = 6.02$, $\tau_{A2} = 4.61$, $\tau_{B2} = 6.18$, $\tau_{A3} = 5.53$, and $\tau_{B3} = 5.99$; $J_{A1B1} = J_{A2B2} = J_{A3B3} = 9.0$ Hz) for the methylene groups at −106 °C were identified by homonuclear INDOR spectroscopy[4]. They coalesced to a sharp singlet ($\tau = 5.51$) at −36 °C. This observation indicates that the ground state conformation has C_1 symmetry and examination of models suggests that the molecule *(6)* adopts the helical conformation (Scheme 1).



Scheme 1. Helix ⇌ Helix* inversions required to exchange the six methylene protons with six different sites. If *(6a)*, *(6c)*, and *(6e)* correspond to Helix then *(6b)*, *(6d)*, and *(6f)* correspond to Helix*.

The rate constants for Helix ⇌ Helix* inversion at different temperatures were determined by comparing the observed ^1H-NMR spectra with theoretical spectra generated by line shape equations suitable for a six-site exchange process between H_C, H_D, H_E, H_F, H_G, and H_H. Inspection reveals that there are four ways in which three AB systems can be assigned to the pairs of sites represented by 1, 2, and 3. The density matrix approach[5] was used to examine the exchange process *(7)*. Attempts to perform line shape analyses indicated that only the program constructed on the basis of the depicted exchange process provides good matches between computed and experimental spectra over the entire temperature range.



(7)

Thus, like the hydrocarbon *(5)*[2], the trithia compound *(6)* exists in the helical conformation in solution. However, the

[*] Prof. Dr. W. D. Ollis and Dr. J. F. Stoddart
Department of Chemistry, The University
Sheffield S3 7HF (England)
Dr. M. Nógrádi
Institute of Organic Chemistry
Technical University
Budapest XI, Gellert ter 4 (Hungary)

[1] *W. D. Ollis* and *I. O. Sutherland*, Chem. Comm. *1966*, 402; *A. P. Downing*, *W. D. Ollis*, and *I. O. Sutherland*, Chem. Comm. *1967*, 171; *A. P. Downing*, *W. D. Ollis*, *I. O. Sutherland*, *J. Mason*, and *S. F. Mason*, Chem. Comm. *1968*, 329; *A. P. Downing*, *W. D. Ollis*, and *I. O. Sutherland*, J. Chem. Soc. *B 1970*, 24.

[2] *D. J. Brickwood*, *W. D. Ollis*, and *J. F. Stoddart*, J. C. S. Chem. Comm. *1973*, 638.

[3] *G. W. Stacy*, *F. W. Villaescusa*, and *T. E. Wollner*, J. Org. Chem. *30*, 4074 (1965).

[4] We thank Mr. *A. G. Ferrige*, Wellcome Research Laboratories, Beckenham, Kent, for obtaining this result.

[5] *J. I. Kaplan*, J. Chem. Phys. *28*, 278 (1958); *29*, 462 (1958); *S. Alexander*, *ibid. 37*, 967 (1962); *38*, 1787 (1963); *40*, 2741 (1964); *C. S. Johnson*, *ibid. 41*, 3277 (1964); Adv. Magn. Resonance *1*, 33 (1965); J. Magn. Resonance *1*, 98 (1969).

Helix⇌Helix* inversion barrier is very much lower for *(6)* ($\Delta G^{\ddagger}_{H\rightleftharpoons H^*}=9.3\pm0.2$ kcal mol^{-1}) than for *(5)* ($\Delta G^{\ddagger}_{H\rightleftharpoons H^*}=17.1$ kcal mol^{-1}). We believe there are two principal reasons for this difference: (i) the absence of methyl substituents in the *ortho* positions of the aromatic rings, and (ii) conjugative stabilization between the lone pairs on sulfur and the π system of the benzene rings in the inversion transition state.

Received: November 13, 1974 [Z 127a IE]
German version: Angew. Chem. 87, 168 (1974)

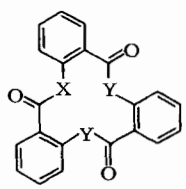
CAS Registry numbers:
(6), 260-08-2; 2-(chloromethyl)thiophenol, 4521-40-8

The Synthesis and Conformational Behavior of *N,N',N''*-Trimethyltrianthranilide

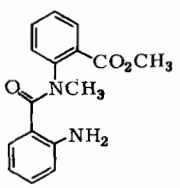
By *W. David Ollis, Jennifer A. Price, Julia Stephanidou Stephanatou*, and *J. Fraser Stoddart*[*]

Although dehydration of salicylic acid and its alkyl-substituted derivatives has been known[1] for over twenty years to yield both disalicylide and trisalicylide derivatives *(1)*, the only anhydro derivative of anthranilic acid which has been reported[2] is dianthranilide. We now wish to report the synthesis of *N,N',N''*-trimethyltrianthranilide *(3)* and discuss its conformational behavior in solution.

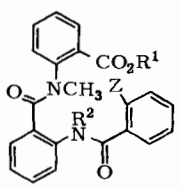
Treatment of a suspension of methyl *N*-anthraniloyl-*N*-methylanthranilate *(4)*[3], m.p. 104—105 °C (88—89 °C[3]) in lithium hydroxide solution with *o*-nitrobenzoyl chloride in benzene afforded the *o*-nitrobenzoyl derivative *(5)* (74%, needles, m.p. 182—184 °C). Conversion into the *N,N'*-dimethyl derivative *(6)* (87%, m.p. 204—206 °C) with methyl iodide and sodium hydride in dimethyl sulfoxide was followed by titanous chloride reduction[4] of the aromatic nitro group. De-esterification was effected by LiOH; the free acid *(7)* (78%) polymerizes on heating.



(1), X = Y = O
(2), X = NH; Y = NCH_3
(3), X = Y = NCH_3



(4)

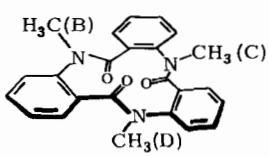


(5), R^1 = CH_3; R^2 = H; Z = NO_2
(6), R^1 = R^2 = CH_3; Z = NO_2
(7), R^1 = H; R^2 = CH_3 Z = NH_2

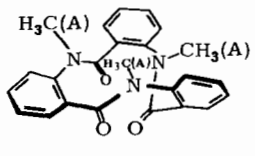
Cyclization was achieved by treatment with dicyclohexylcarbodiimide in dichloromethane to give isomer X (54%, m.p. 182—184 °C; $\tau_{CH_3(A)}=6.90$ and $\tau_{CH_3(B)}=7.29$ in $CDCl_3$) of *N,N'*-dimethyltrianthranilide *(2)*. Quantitative conversion into a second isomer Y (m.p. 251—254 °C; $\tau_{CH_3(A)}=6.73$ and $\tau_{CH_3(B)}=6.83$ in $CDCl_3$) of *(2)* was observed on heating isomer X under reflux in ethanol (3 h). Methylation (CH_3I; NaH; CH_3SOCH_3) of both isomers (X and Y) gave the same compound, *N,N',N''*-trimethyltrianthranilide *(3)* (m.p. >320 °C) on recrystallization from chloroform/ether/light petroleum (b.p. 60—80 °C), in 57% and 76% yields, respectively.

[*] Prof. Dr. W. D. Ollis, J. A. Price, J. S. Stephanatou, and Dr. J. F. Stoddart
Department of Chemistry, The University
Sheffield S3 7HF (England)

When a ^{1}H-NMR spectrum of compound *(3)* was recorded *immediately* after the crystals had dissolved in $CDCl_3$, three equal intensity singlets integrating for three protons each were observed at τ = 6.67, 6.79, and 6.87. After a few minutes a fourth singlet began to appear at τ = 6.51. At equilibrium, the ratio of the peak areas for these singlets was 0.055 : 0.315 : 0.315 : 0.315 (CH_3(A), CH_3(B), CH_3(C), CH_3(D)).



(8), Helix



(9), Propeller

On examination of molecular models, and by analogy with the conformational behavior[5, 6] of the trisalicylides, the spectra of compound *(3)* can be rationalized in terms of two non-planar conformations, the helix (H) *(8)* with C_1 symmetry and the propeller (P) *(9)* with C_3 symmetry, which retain *trans*-amide linkages between the three aromatic rings and which are interconverted by torsion about the Ar—N(CH_3) and Ar—CO single bonds. The interconversion between the H and P conformations, *(8)* and *(9)*, and their enantiomers (denoted by H* and P*) involves the following equilibrium: P⇌H⇌H*⇌P*.

Thus, it may be concluded that *N,N',N''*-trimethyltrianthranilide *(3)* crystallizes in the helical conformation *(8)*. In solution, this conformation is in equilibrium with a small amount (5.5%) of the propeller conformation *(9)*. This finding is to be compared with (i) the observation[5, 6] that tri-*o*-thymotide exists in a propeller conformation in its crystalline clathrate compounds, and with (ii) the observation[5, 6] that in all of the trisalicylides examined to date the propeller conformation is energetically preferred in solution.

The ^{1}H-NMR spectrum of *(3)* in nitrobenzene showed temperature dependence; the four singlets coalesced to a broad singlet at +215 °C. Comparison of the observed ^{1}H-NMR spectra with the theoretical spectra generated by line shape equations[6] based upon a four-site exchange process between CH_3(A), CH_3(B), CH_3(C), and CH_3(D) gave $\Delta G^{\ddagger}_{P\rightarrow H}=21.6$ kcal mol^{-1} and $\Delta G^{\ddagger}_{H\rightarrow H^*}=24.4$ kcal mol^{-1}. The difference in free energy of 1.9 kcal mol^{-1} between the two conformations at +63 °C indicates that the transition states for P⇌H interconversion and H⇌H* inversion must be very similar in their energetic demands.

Received: November 13, 1974 [Z 127b IE]
German version: Angew. Chem. 87, 169 (1975)

CAS Registry numbers:
(2), 54083-70-4; *(3)*, 54083-71-5; *(4)*, 54083-72-6; *(5)*, 54083-73-7; *(6)*, 54083-74-8; *(7)*, 54083-75-9; *o*-nitrobenzoyl chloride, 610-14-0

[1] *W. Baker, W. D. Ollis*, and *T. S. Zealley*, J. Chem. Soc. *1951*, 201; *W. Baker, B. Gilbert, W. D. Ollis*, and *T. S. Zealley, ibid. 1951*, 209; *W. Baker, J. B. Harborne, A. J. Price*, and *A. Rutt, ibid. 1954*, 2042.

[2] *G. Schroeter* and *O. Eisleb*, Liebigs Ann. Chem. *367*, 101 (1909); *G. Schroeter*, Ber. Deut. Chem. Ges. *52*, 2224 (1919).

[3] *D. H. Hey* and *D. G. Turpin*, J. Chem. Soc. *1954*, 2471.

[4] *S. A. Newton, F. J. Stubbes*, and *C. Hinshelwood*, J. Chem. Soc. *1953*, 3384.

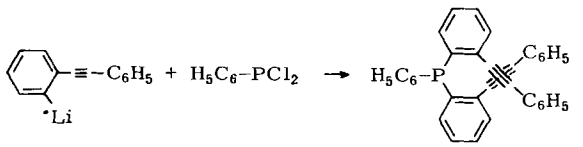
[5] *W. D. Ollis* and *I. O. Sutherland*, Chem. Commun. *1966*, 402; *A. P. Downing, W. D. Ollis*, and *I. O. Sutherland, ibid. 1967*, 171; *A. P. Downing, W. D. Ollis, I. O. Sutherland, J. Mason*, and *S. F. Mason, ibid. 1968*, 329.

[6] *A. P. Downing, W. D. Ollis*, and *I. O. Sutherland*, J. Chem. Soc. *B 1970*, 24.

A Novel Cyclobutadiene-Rhodium(I) Complex

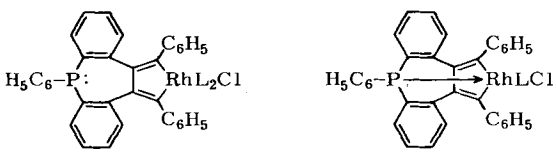
By *Werner Winter*[*]

Alkynylphosphanes of type $R_2P-C\equiv C-R$ behave ambivalently toward transition metals. Thus, reaction of the bis-acetylene compound *(1)* with *e.g.* RhL_3Cl (L = triphenylphosphane) could give, not only a P—Rh-coordination or an acetylene π-complex, but also the compounds *(2)*—*(5)*. Molecular models, however, show that formation of *(3)* can be ruled out, since the length of the bond from the P atom in the angled phosphepin ring would have to be about 5—6 Å.

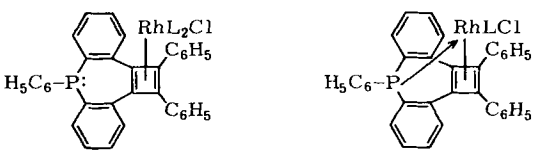


(1)

o,o'-Bis(phenylethynyl)triphenylphosphane *(1)* can be prepared by dropwise addition of dichloro(phenyl)phosphane to *o*-lithiotolan[1] in boiling anhydrous ether under N_2 [*(1)*: 42% yield, m. p. 150—151 °C (xylene); IR (KBr): (C≡C) 2210 cm^{-1} (weak); FT-$^{13}C\{^1H\}$-NMR (in $^{12}CDCl_3$), TMS internal, δ = 96.3 ppm, d, J_{CP} = 5 Hz; δ = 88.7 ppm, d, J_{CP} = 7 Hz (—C≡C); FT-$^{31}P\{^1H\}$-NMR (in $CHCl_3$), H_3PO_4 external, δ = +11.9 ppm; MS = 462].

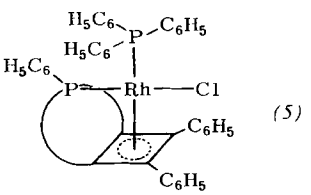


(2) *(3)*



(4) L = $P(C_6H_5)_3$ *(5)*

Heating equimolar quantities of *(1)* and RhL_3Cl in benzene for 15 min under reflux in a nitrogen atmosphere led to almost quantitative precipitation of a fine crystalline, blackish-violet complex (dec. point 211 °C) which is absolutely stable at room temperature. Two triphenylphosphane groups could be detected in the filtrate. Vapor pressure osmometric molecular weight determinations and elemental analysis carried out on the precipitate give the empirical formula $C_{52}H_{38}P_2RhCl \cdot C_6H_6$. No vibrations of the free or of the complexed C≡C groupings could be observed in the IR spectrum.



(5)

[*] Dr. W. Winter
Chemisches Institut der Universität
74 Tübingen, Auf der Morgenstelle 18 (Germany)

The above findings are consistent only with the cyclobutadiene structure *(5)*. Models show that if the Rh—P distance is *ca.* 2.3 Å, the transition metal atom lies almost above the center of the cyclobutadiene ring.

The FT-$^{31}P\{^1H\}$-NMR spectrum of (1,2,7-triphenyl-7*H*-dibenzo[*b,f*]-η-cyclobuta[*d*]phosphepin)(triphenylphosphane)-rhodium(I) chloride *(5)* [in $CH_2Cl_2(N_2)$; 0.1 M H_3PO_4 in D_2O, external; 36.43 MHz] shows an ABX system. Absence of a signal at higher field (δ > 0) clearly indicates that the phosphepin P atom is bound coordinatively to Rh. The δ_1 and δ_2 values are consistent with an Rh^I complex (for comparison: RhL_3Cl, δ = −31.5 and −48.0 ppm; $Rh^{III}L_3Cl_3$, δ = +0.5 and −15.1 ppm[2]). Rh^{III} complexes having a rhodacyclopentadiene structure analogous to *(2)* have δ values between −22 and −27 ppm[3].

The non-equivalent atoms P^1 and P^2 couple with ^{103}Rh (J_{RhP^1} = 158 Hz, J_{RhP^2} = 173 Hz). In contrast, Rh^{III} complexes are found to have coupling constants of 84—115 Hz[2] and 120 Hz (rhodacyclopentadiene complexes)[3].

The coupling constant $^2J_{P^1P^2}$ = 36 Hz is comparable with values for Rh^I complexes (36—38 Hz) (values for Rh^{III} complexes are about 23 Hz)[2]. Assignment of the δ and J_{RhP} values to P^1 and P^2 results from the fact that the signals of the P atoms *trans* to Cl generally lie at lower field than those of the P atoms *cis* to Cl, and that the coupling constants J_{RhP} of the P atom *cis* to Cl is larger than that of the P atom *cis* to Cl[2] (cf. also the "*trans*-effect" in the case of Pt-PR_3 complexes[4]). The *cis* orientation of the two P atoms in *(5)* is also proven by the fact that non-equivalent, *trans* phosphane ligands exhibit $^2J_{PP'}$ values of 300—500 Hz.

Received: October 23, 1974;
revised: November 19, 1974 [Z 130 IE]
German version: Angew. Chem. *87*, 172 (1975)

CAS Registry numbers:
(1), 54100-67-3; *(5)*, 54100-68-4; $Rh(P(C_6H_5)_3)_3Cl$, 14694-95-2; *o*-lithiotolan, 42168-23-0; dichloro(phenyl)phosphane, 644-97-3

[1] *J. E. Mulvaney* and *L. J. Carr*, J. Org. Chem. *33*, 3286 (1968); *E. Müller* and *G. Zounstas*, Chem.-Ztg. *98*, 41 (1974).

[2] *T. H. Brown* and *P. J. Green*, J. Amer. Chem. Soc. *92*, 2359 (1970).

[3] *W. Winter*, J. Organometal. Chem., in press.

[4] *A. Pidcock*, *R. E. Richards*, and *L. M. Venanzi*, J. Chem. Soc. *A 1966*, 1707.

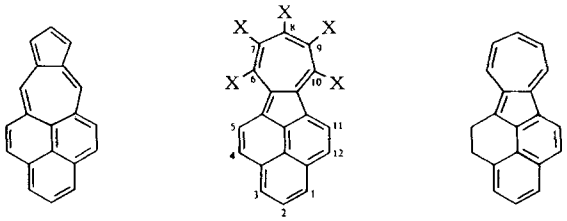
Synthesis and Properties of Azuleno[1,2,3-*cd*]phenalene[1]

By *Ichiro Murata*, *Kazuhiro Nakasuji*, *Kagetoshi Yamamoto*, *Tomoo Nakazawa*, *Yutaka Kayane*, *Akira Kimura*, and *Osamu Hara*[*]

Systems composed of azulene and phenalene rings, *e.g. (1)* and *(2)*, are very interesting, not only because of their unique electronic structures but also because of their expected carcinogenic activities as in the case of the related benzo[*a*]pyrene. The stable, crystalline moss green azuleno[5,6,7-*cd*]phenalene *(1)*[2] exhibits considerable carcinogenic activity[3]. We report here on the synthesis and properties of azuleno[1,2,3-*cd*]phenalene *(2)*.

We have synthesized *(2)* from 2*H*-8,9-dihydrocyclopenta[*cd*]-phenalene *(8)* after the well-known *Ziegler-Hafner* azulene

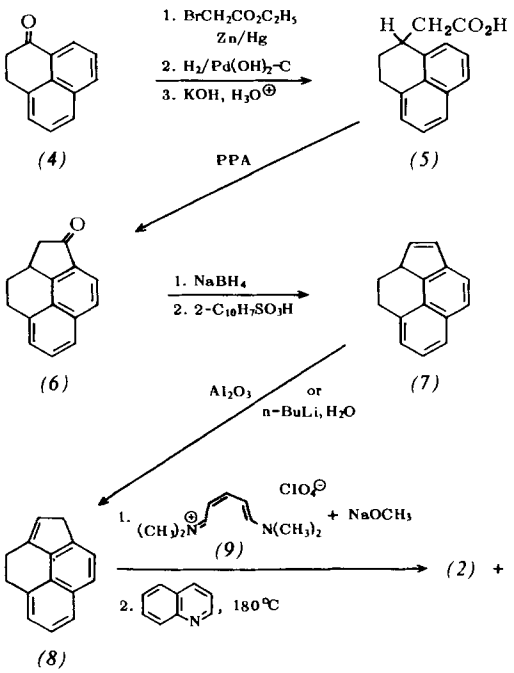
[*] Prof. Dr. I. Murata, Dr. K. Nakasuji, Dr. K. Yamamoto, Dr. T. Nakazawa, Y. Kayane, A. Kimura, and O. Hara
Department of Chemistry, Faculty of Science, Osaka University
Toyonaka, Osaka 560 (Japan)



(1) (2), X = H; D_5-(2), X = D (3)

synthesis[4] and its application to the synthesis of dicyclopenta[*ef*,*kl*]heptalene (azupyrene)[5].

Reformatsky reaction of dihydrophenalenone (4)[6] with ethyl bromoacetate followed by hydrogenolysis and hydrolysis led to the carboxylic acid (5)[7], m.p. 90—91.5°C, which was subjected to cyclization with polyphosphoric acid (PPA) to give the tetracyclic ketone (6)[7], m.p. 143—144°C, $\nu_{C=O}$ (KBr) 1695 cm^{-1}, in 40% overall yield. The ketone (6) was converted by reduction with sodium borohydride into the alcohol[7], m.p. 130—131°C, ν_{O-H} (KBr) 3150 cm^{-1}, in 95% yield; the alcohol was then dehydrated with 2-naphthalenesulfonic acid to give 9a*H*-8,9-dihydrocyclopenta[*cd*]phenalene (7)[7] [colorless crystals, m.p. 93—94°C (from *n*-hexane); *m/e* = 192 (M^+, 100%); ^{1}H-NMR: δ ($CDCl_3$) = 1.0—1.7 (m, 1H), 2.4—2.8 (m, 1H), 3.1—3.7 (m, 3H), 6.70 (dd, *J* = 5.3, 1.7 Hz, 1H), 7.03 (dd, *J* = 5.3, 2.1 Hz, 1H) and 7.2—7.9 (m, 5H).



(4) (5) (6) (7) (8) (9) (2) + (3)

On being passed through an alumina column or treated with *n*-butyllithium in tetrahydrofuran followed by water quenching, the compound (7) was found to convert quantitatively into the isomeric hydrocarbon (8)[7] [colorless crystals, m.p. 101—103°C; *m/e* = 192 (M^+, 100%); ^{1}H-NMR: δ ($CDCl_3$) = 2.8—3.4 (m, 4H), 3.4—3.6 (m, 2H), 6.1—6.3 (m, 1H) and 7.1—7.9 (m, 5H)]. Treatment of (8) (in THF) and dimethyl(5-dimethylamino-2,4-pentadienylidene)ammonium-perchlorate (9) with one equivalent of sodium methoxide in methanol at room temperature gave an intermediate fulvene which was not isolated. To effect the cyclization of the fulvene the solvent was replaced by quinoline and the solution was heated at 180°C for 2h. After usual work-up the crude product was purified by column chromatography (Al_2O_3, benzene/*n*-hexane). The desired azuleno[1,2,3-*cd*]phenalene (2) was eluted from the column as a green band and formed stable dark red plates with metallic luster (yield: 62%; m.p. 183—184°C (benzene)), which showed a green color in solution. 4,5-Dihydroazuleno[1,2,3-*cd*]phenalene (3)[8] (green plates, m.p. 158.0—159.5°C (*n*-hexane)), was also isolated as a minor product in 6% yield.

The unusual electronic spectrum of (2) accords with quantum mechanical calculations by *Zahradnik*[10]. In contrast to the electronic spectrum of (1) which shows the longest wavelength absorption maximum at 739 nm ($\log\varepsilon = 3.26$)[2, 11], the longest wavelength absorption of compound (2) is found at 1010 nm; λ_{max} (cyclohexane) = 1010 nm ($\log\varepsilon = 1.99$), 855 (2.49), 760 (2.52), 694 (2.34), 624 (sh, 2.03), 477 (4.69), 471 (4.34), 465 (4.11), 452 (sh, 4.21), 447 (4.35), 425 (sh, 3.87), 421 (3.90), 390 (3.85), 386 (3.37), 351 (4.85), 284.5 (3.96), 261.5 (4.21), 255.5 (4.16), 249.5 (4.12), 244 (4.12), and 226 (4.21). The ^{1}H-NMR spectrum ($CDCl_3$, 100 MHz) showed a 2H doublet with further small splittings at δ = 9.14 (*J* = 9.5 Hz, H-6,10), an AB-quartet at 8.36 (*J* = 9.0 Hz, 2H, H-5,11 or 4,12) and 7.85 (*J* = 9.0 Hz, 2H, H-4,12 or 5,11), a triplet at 7.50 (*J* = 9.5 Hz, H-7,9), and a multiplet at 7.8—8.1 (H-1,2,3 and 8). Complete assignment of the full ^{1}H-NMR spectrum of (2) could be achieved by comparison with the spectrum D_5-(2), which was prepared by using D_5-pyridine as starting material for (9). Thus, an A_2B-system of H-1,3 and H-2 was found at δ = 7.99 and 7.88 with $J_{1,2} = J_{2,3} = 7.8$ Hz

The structure of (2) was established from these spectral data together with the mass spectrum [*m/e* = 252 (M^+, 100%)] and results of elemental analysis[7]. The ease of dehydrogenation during the preparation of (2) is noteworthy and suggestive of the substantial thermodynamic stability of this compound. The diamagnetic susceptibility (measured with a Cahn balance) is χ_M/χ_M(benzene) = 2.7[12]. The foregoing observations furnish convincing evidence for a definite degree of aromaticity of (2).

Received: November 28, 1974 [Z 132 IE]
German version: Angew. Chem. 87, 170 (1975)

CAS Registry numbers:
(2), 54100-60-6; (3), 54100-61-7; (4), 518-85-4; (5), 54100-62-8; (6), 54100-63-9; (7), 54100-64-0; (8), 54100-65-1; (9), 2506-78-7

[1] The Chemistry of the Phenalenium System, Part 20.—Part 19: *I. Murata, K. Yamamoto*, and *Y. Kayane*, Angew. Chem. *86*, 862 (1974); Angew. Chem. internat. Edit. *13*, 808 (1974).

[2] *C. Jutz* and *R. Kirchlechner*, Angew. Chem. *78*, 493 (1966); Angew. Chem. internat. Edit. *5*, 516 (1966); *C. Jutz, R. Kirchechner*, and *H.-J. Seidel*, Chem. Ber. *102*, 2301 (1969).

[3] *N. P. Buu-Hoi, D. P. Hien*, and *C. Jutz*, Naturwissenschaften *54*, 470 (1967); *N. P. Buu-Hoi, N. B. Giao*, and *C. Jutz, ibid. 57*, 499 (1970).

[4] *K. Ziegler* and *K. Hafner*, Angew. Chem. *67*, 301 (1955), *K. Hafner*, Liebigs Ann. Chem. *606*, 79 (1957); Angew. Chem. *69*, 393 (1957).

[5] *C. Jutz* and *E. Schweiger*, Angew. Chem. *83*, 886 (1971); Angew. Chem. internat. Edit. *10*, 808 (1971); Synthesis *1974*, 193.

[6] *L. F. Fieser* and *M. D. Gates*, J. Amer. Chem. Soc. *63*, 2335 (1940); *V. Boekelheide* and *C. E. Larrabee, ibid.* 72, 1240 (1950); *D. M. Reid* and *R. G. Sutherland*, J. Chem. Soc. *1963*, 3295.

[7] Satisfactory elemental analyses were obtained on all compounds reported herein.

[8] The structure of (3) follows from (i) its ready conversion to (2) (Pd-C in acetic acid at room temperature), (ii) its visible spectrum (λ_{max} (in benzene) = 710 nm, 645 and 590 (sh)), which is closely similar to that of 10-methylbenzo[*a*]azulene [9], and (iii) its MS spectrum [*m/e* 254 (M^+, 100%) and 252 ($M^+ - 2H$, 80%)].

[9] *W. Treibs* and *A. Stein*, Liebigs Ann. Chem. *572*, 165 (1951).

[10] *R. Zahradnik* in *J. P. Snyder*: Nonbenzenoid Aromatics. Vol. 2. Academic Press, New York 1971, p. 59.

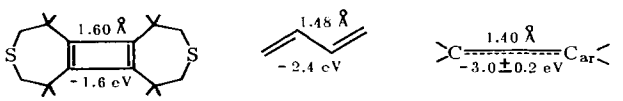
[11] *H. Fischer* and *G. Ege*, Chem. Ber. *100*, 395 (1967).

[12] We thank Prof. *R. Kiriyama* and Dr. *T. Asai*, The Institute of Science and Industrial Research, Osaka University, for carrying out this measurement.

Photoelectron Spectrum and Structure of Tri-*tert*-butylcyclobutadiene[1]

By *Günther Lauer, Claus Müller, Karl-Wilhelm Schulte, Armin Schweig, Günther Maier*, and *Arnaldo Alzérreca*[*]

It has recently been shown[2] that the cyclobutadiene derivative *(1)* has a rectangular structure. This was deduced from a comparison of the resonance integrals determined by PE spectroscopy[3] (lower figures in the following formula) with the known bond lengths[4] (upper figures in the following formula) in *trans*-butadiene and benzene. The rectangular structure of *(1)* has meanwhile been confirmed by X-ray analysis[5]. In the present communication we wish to report that the first cyclobutadiene *(2)* capable of existence at room temperature, which bears only alkyl substituents and is not fixed by rings like *(1)*, is likewise rectangular in structure.



(1)

Since tri-*tert*-butylcyclobutadiene *(2)* was not available as a pure solid owing to its fast dimerization at room temperature our studies were carried out on a mixture of about 2—5% of tri-*tert*-butylcyclopentadienone *(3)*—a by-product of photosynthesis[6] of *(2)*—with *(2)* and its dimeric reaction product *(4)* in a specially constructed glass inlet system. Comparison of the photoelectron (PE) spectrum thus obtained with those of the pure compounds *(3)* and *(4)* showed that band ① (at 6.83 eV, Fig. 1), which precedes all the other bands in the PE spectrum, is a pure cyclobutadiene band. This is in full accord with its complete disappearance within about 60—90 minutes in the course of a series of measurements, although the sample mixture was cooled with liquid air during all intermediate operations connected with the recording of the spectra (such as instrumental adjustment and calibration of the spectra). Previous investigations[2] on *(1)* indicate that band ① must be assigned to the $D(\pi_2)$ ionic state (Fig. 1) of *(2)*.

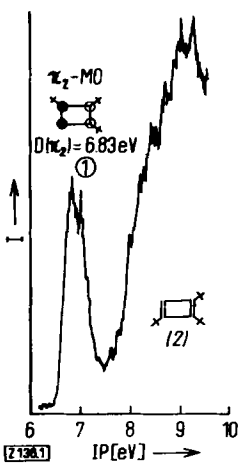


Fig. 1. Photoelectron spectrum of tri-*tert*-butylcyclobutadiene *(2)* in admixture with *(3)* and *(4)* (see text).

[*] Prof. Dr. A. Schweig, Dipl.-Chem. G. Lauer, Dipl.-Chem. C. Müller, and Dipl.-Chem. K.-W. Schulte
Fachbereich Physikalische Chemie der Universität
355 Marburg, Biegenstrasse 12 (Germany)
Prof. Dr. G. Maier and Dipl.-Chem. A. Alzérreca
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

The $D(\pi_2)$ ionic states of *(1)* (at 6.89 eV[2]) and of *(2)* (at 6.83 eV) are of virtually *equal energy*. CNDO/S[7] calculations on *(1)* with the experimentally determined geometry[5], and on *(2)* with the same rectangular geometry (1.600 Å/1.344 Å) largely concur in yielding *equal* $D(\pi_2)$ Koopmans ion energies[8] (Fig. 2). A corresponding calculation for square (1.425 Å[9]) *(2)* expectedly predicts a considerably (0.7 eV) more stable $D(\pi_2)$ Koopmans ion[8]. Rectangular tetra-*tert*-butylcyclobutadiene *(5)* should be more readily ionized (by 0.2 eV) than its rectangular relations *(1)* and *(2)*. These results suggest that *(2)*—just like *(1)*—has a rectangular structure.

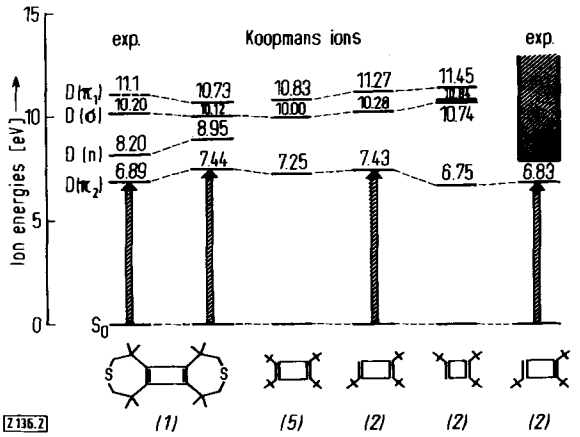


Fig. 2. Comparison of measured and/or calculated ion energies of the cyclobutadiene derivatives *(1)*, *(2)*, and *(5)*.

These findings are confirmed by a semiempirical LCMO estimate according to which π_2 is to be regarded as an antibonding linear combination of a localized *tert*-butylethylene πMO (energy = −9.7 eV[10]) and the corresponding *cis*-di-*tert*-butylethylene πMO (energy = −8.80 eV[11]). The interaction $H_{\pi\pi}$ between the two basis MOs is given by

$$H_{\pi\pi} = \sqrt{\delta E(\delta E + \Delta E)}$$

where ΔE is the energy difference between the two MOs, and δE is the destabilization of the higher-energy MO. If $\Delta E = 0.9$ eV and $\delta E = 1.97$ eV, and it is borne in mind that only 72%[2] of the interaction $H_{\pi\pi}$ can take place by way of the newly formed bonds, we calculate from $0.72\,H_{\pi\pi} = 2c^2\beta_{\pi\pi}$ ($c = 0.7$, where c denotes the $2p_\pi$ AO coefficient in the basis MO) that the resonance integral $\beta_{\pi\pi}$ of these bonds is −1.7 eV, which agrees well with the value of −1.6 eV determined for *(1)*. Accordingly, tri-*tert*-butylcyclobutadiene is rectangular and probably has a geometry resembling that of *(1)*.

Received: August 12, 1974 [Z 136 IE]
German version: Angew. Chem. 87, 194 (1975)

[1] Theory and Applications of Photoelectron Spectroscopy, Part 54. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 53: *A. Schweig*, Nachr. Chem. Tech. *22*, 370 (1974).—Presented at the Second International Symposium on the "Chemistry of Nonbenzenoid Aromatic Compounds", Lindau, 23—27 Sept., 1974.

[2] *G. Lauer, C. Müller, K. W. Schulte, A. Schweig*, and *A. Krebs*, Angew. Chem. *86*, 597 (1974); Angew. Chem. internat. Edit. *13*, 544 (1974).

[3] *M. Beez, G. Bieri, H. Bock*, and *E. Heilbronner*, Helv. Chim. Acta *56*, 1028 (1973); *R. Gompper, F. Holsboer, W. Schmidt*, and *G. Seybold*, J. Amer. Chem. Soc. *95*, 8479 (1973).

[4] *A. Almenningen, O. Bastiansen*, and *M. Traetteberg*, Acta Chem. Scand. *12*, 1221 (1958); *A. Langseth* and *B. D. Stoicheff*, Can. J. Phys. *34*, 350 (1956).

[5] *H. Irngartinger* and *H. Rodewald*, Angew. Chem. *86*, 783 (1974); Angew. Chem. internat. Edit. *13*, 740 (1974).

[6] *G. Maier* and *A. Alzerreca*, Angew. Chem. *85*, 1056 (1973); Angew. Chem. internat. Edit. *12*, 1015 (1973).

[7] *K. W. Schulte* and *A. Schweig*, Theor. Chim. Acta *33*, 19 (1974).

[8] According to preliminary estimates of the Koopmans defects for rectangular (1.600 Å/1.344 Å) and square (1.425 Å) unsubstituted cyclobutadiene, Koopmans' theorem is fulfilled satisfactorily in the former case and less well in the latter case. As a consequence, the difference between the $D(\pi_2)$ ion energies (0.7 eV) of rectangular and square *(2)* given in the text will be somewhat smaller.

[9] *M. J. S. Dewar, M. C. Kohn*, and *N. Trinajstic*, J. Amer. Chem. Soc. *93*, 3437 (1971).

[10] *U. Weidner* and *A. Schweig*, J. Organometal. Chem. *39*, 261 (1972).

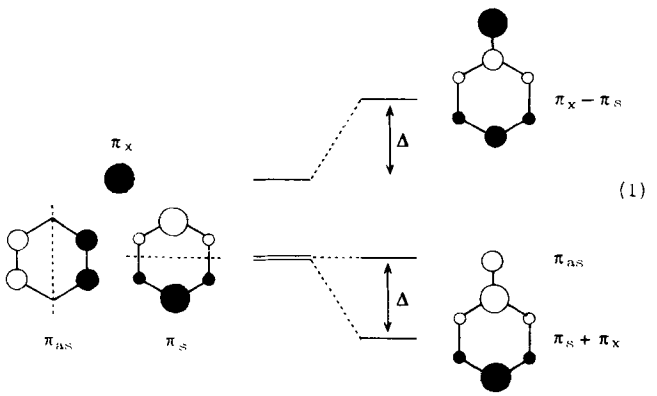
[11] In the case of *trans*-1,2-di-*tert*-butylethylene = 8.85 eV [*W. Schäfer* and *A. Schweig* unpublished]. According to *P. Masclet, D. Grosjean, G. Mouvier*, and *J. Dubois* [J. Electron Spectr. *2*, 225 (1973)] the difference between the adiabatic ionization potentials of *cis*- and *trans*-di-*tert*-butylethylene amounts to 0.05 eV. We therefore assume the vertical IP of the *cis* isomer to be 8.80 eV.

Extreme Perturbation of π-Systems by Ylidic Substituents[1,2]

By *Karl-Heinz A. Ostoja Starzewski, Hans Bock*, and *Heindirk tom Dieck*[*]

The simplest phosphorus ylide $(H_3C)_3P{=}CH_2$[3] reacts with explosive violence when exposed to air or water, in accord with the low-lying first ionization energy of 6.81 eV[2] and the high-field $^{13}CH_2$ NMR signal[4]. These exceptional properties prompted us to examine the interactions between the ylidic π_{PC} bond and the π-system of benzene.

Benzene derivatives are particularly suitable for characterization of substituent effects since the highest occupied π levels π_s and π_{as}, degenerate in benzene itself, are affected to different extents[5]:



(1)

While π_s can undergo mixing with a substituent orbital π_X os like symmetry, π_{as} remains unperturbed (1), since its nodal plane passes through the substitution site, and thus permits the splitting Δ to be read off[5a,b].

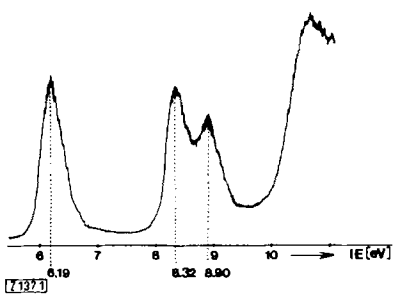


Fig. 1. PE spectrum (5–12 eV) of benzylidenetrimethylphosphorane, calibrated with the $^2P_{3/2}Xe$ band at 12.13 eV.

Although the first ionization energy of benzene is known to be 9.24 eV[5], no band is observed between 9.0 and 10.5 eV in the photoelectron (PE) spectrum of benzylidenetrimethylphosphorane (Fig. 1), contrary to what would be expected from (1).

Various approaches were adopted to solve the riddle of the "missing" benzene π-ionizations, and simultaneously to assign the benzylidene PE spectrum: calculations with a modified CNDO/2 program, reparametrized to achieve an optimum fit with PE data[6], reveal the compositions shown in Figure 2 for the three highest occupied molecular orbitals ψ_{30}, ψ_{29}, ψ_{28}.

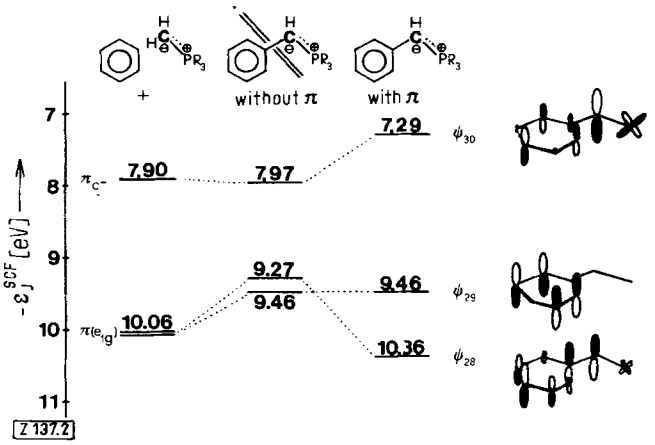


Fig. 2. CNDO correlation diagram for the highest occupied π-orbitals of benzene and methylenetrimethylphosphorane, and of benzylidenetrimethylphosphorane with and without π-interactions.

The calculated orbital sequence is also expected from qualitative perturbation arguments, as is apparent from (1). Particular attention should be directed to ψ_{29} (Fig. 2), which resembles the unperturbed benzene orbital π_{as} in (1). Furthermore, the correlation diagram (Fig. 2) shows how the individual orbitals move on stepwise coupling of the partial systems: if π-interactions are initially neglected[7] then the different inductive raising of the two benzene orbitals is clearly to be seen. Inclusion of π-interactions in a further calculation shows that mixing occurs almost exclusively between π_s and the "carbanion" orbital $\pi_{C\ominus\cdots P\oplus}$. Thus the π_{as} orbital which is raised by about 1 eV relative to benzene reflects the extreme inductive perturbation[5c] by the "carbanion" center.

Since the quality of semiempirical calculations is frequently rather modest, the CNDO/2 eigenvalues $-\varepsilon_j^{SCF}$ (Fig. 2) can be regarded as correlating satisfactorily *via* Koopmans'

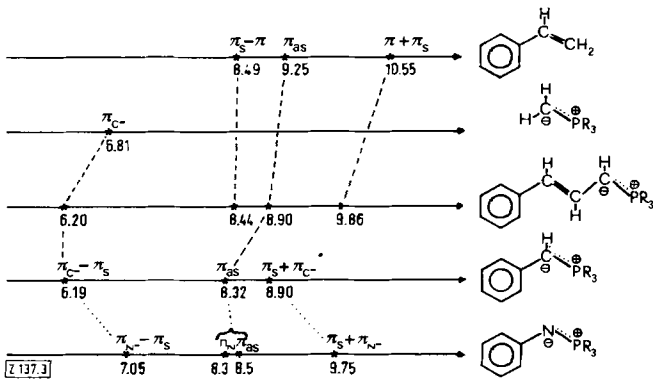


Fig. 3. Ionization energy correlation diagram for the highest occupied π-levels of benzylidenetrimethylphosphorane and appropriate model compounds.

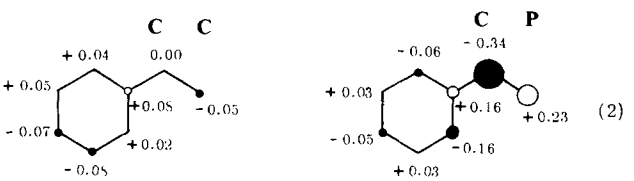
[*] Dipl.-Chem. K. A. Ostoja Starzewski, Prof. Dr. H. Bock, and Prof. Dr. H. tom Dieck
Institut für Anorganische Chemie der Universität
6 Frankfurt am Main 70, Theodor-Stern-Kai 7 (Germany)

theorem $-\varepsilon_n^{SCF} = IE_n$[8] with the PE ionization energies IE_n (Fig. 1). However, since Koopmans' theorem can fail in cases of extreme charge redistribution in the resulting cation radical[8], as is conceivable for ylides, it was important to accomplish an independent assignment by comparing the PE spectra of related compounds (Fig. 3).

The starting points for the comparison are styrene[5b, 9], whose π-orbital sequence having a constant $\pi_{as} = 9.25$ eV is to be derived by mixing $\pi_s \pm \pi_X$ (X:C=C) according to (1), and the simplest ylide with $IE_1 = 6.81$ eV. Even in cinnamylidenephosphorane, where the phenyl ring and the ylide site are separated by three bonds, the π_{as} ionization energy is lowered by 0.35 eV owing to the relatively high charge density in the neighboring "allyl anion". The π-interaction with the ylide system is manifested in the lowered first ionization energy, $\Delta IE_1 = -0.6$ eV. However, the most important feature of the cinnamylidene comparison substance is that there is no steric reason for any change in styrene geometry. Finally, in benzylidenephosphorane, charge concentration at the ylidic carbon leads to a further shift of π_{as} to 8.32 eV.

Figure 3 also shows the ionization energies of the isoelectronic phenyliminophosphorane: the π_{as} destabilization once again indicates a high negative charge on the neighboring nitrogen; the much greater π-splitting shifts π_s to 9.75 eV, and thus beyond the corresponding ionization energy of the unperturbed benzene system.

Summarizing, replacement of the terminal CH_2 group of styrene by the $(CH_3)_3P$ unit drastically perturbs the original charge distribution and confers considerable benzyl anion character. This is readily seen from the CNDO total atomic charges:



(2)

Comparable charge shifts are also calculated for all the other ylide systems mentioned—in full accord with measured ^{13}C-NMR shifts[10].

Received: August 6, 1974 [Z 137 IE]
German version: Angew. Chem. 87, 197 (1975)

[1] Photoelectron Spectra and Molecular Properties, Part 40.—Part 39: *H. Bock*, "Photoelectron Spectra and Bonding in Phosphorus compounds", Pure Appl. Chem., in press.

[2] Also, Electronic Structure and Reactivity of Ylide Systems, Part 3.—Part 2: *K. A. Ostoja Starzewski, H. tom Dieck*, and *H. Bock*, J. Organometal. Chem. 65, 311 (1974).

[3] *H. Schmidbaur* and *W. Tronich*, Chem. Ber. *101*, 595 (1968).

[4] The ^{13}C chemical shift of $\delta = +200$ ppm relative to CS_2 [*H. Schmidbaur, W. Buchner*, and *D. Scheutzow*, Chem. Ber. *106*, 1251 (1973)] is comparable with that of H_3CMgI ($\delta = +207$ ppm) or $LiCH_3$ ($+206$ ppm).

[5] A general survey of perturbations due to substituent effects is given by *L. Libit* and *R. Hoffmann*, J. Amer. Chem. Soc. *96*, 1370 (1974). Characteristic individual cases are described by: a) *H. Bock, G. Wagner*, and *J. Kroner*, Chem. Ber. *105*, 3850 (1972); b) *J. P. Maier* and *D. W. Turner*, J. C. S. Faraday II *69*, 521 (1973); c) *C. Batich, E. Heilbronner, V. Hornung, A. J. Ashe III, D. T. Clark, U. T. Cobley, D. Kilcast*, and *I. Scanlan*, J. Amer. Chem. Soc. *95*, 928 (1973). See also references cited in these publications.

[6] *J. Kroner, D. Proch, W. Fuss*, and *H. Bock*, Tetrahedron *28*, 1585 (1972).

[7] By putting the off-diagonal elements in the CNDO-Hartree-Fock matrix equal to zero, cf., *e.g. W. Ensslin, H. Bock*, and *G. Becker*, J. Amer. Chem. Soc. *96*, 2757 (1974).

[8] Cf., *e.g., E. Heilbronner, R. Daudel* and *B. Pullman*: Proc. First Int. Congr. Quantum. Chem. D. Reidel Publ. Co., Dordrecht/Holland 1974.

[9] Cf., *e.g.*, [5b] or *T. Kobayashi, K. Yokata*, and *S. Nagakura*, J. Electron Spectry. *2*, 449 (1973).

[10] *K. A. Ostoja Starzewski*, unpublished.

[Bis(diphenylphosphino-η-benzene)chromium]tetracarbonylmetal Complexes of Chromium, Molybdenum, and Tungsten[1][**]

By *Christoph Elschenbroich* and *Felix Stohler*[*]

Bidentate phosphane chelate ligands are considered to be a well-studied class of compounds[3]. However, a new aspect of their chemistry consists in the transformation of such a ligand into a paramagnetic form. In the case of bis(diphenylphosphino-η-benzene)chromium(0)[2] (bdpc), this transformation can be accomplished by prolonged air-oxidation and renders the behavior of this "ligand" in substitution and solvolysis reactions accessible to study by ESR spectroscopy.

We now report the synthesis of dinuclear bis(arene)chromium-tetracarbonylmetal complexes which are obtained according to eq. (1) as reddish brown crystals displaying only little

$$[(C_6H_5)_2P\text{-}\eta\text{-}C_6H_5]_2Cr^0 + M(CO)_6 \xrightarrow{-2\,CO} \{[(C_6H_5)_2P\text{-}\eta\text{-}C_6H_5]_2Cr^0\}M(CO)_4 \quad (1)$$

(bdpc)

M = Cr, Mo, W

sensitivity to air exposure. Their composition was confirmed by elemental analysis and molecular weight determination; spectroscopic data are listed in Table 1.

In the range of CO stretching vibrations the IR spectra of the dissolved complexes (bdpc)$M(CO)_4$ exhibit four bands that are characteristic of C_{2v} local symmetry of the $M(CO)_4$ group in compounds of type *cis*-$L_2M(CO)_4$[4]. Hence (and also on the basis of ESR data, see below) it is possible to distinguish between the alternative structures *(1a)*[5] and *(1b)*, and to ascribe structure *(1b)* to the new complexes.

(1a) R = C_6H_5 *(1b)*

M = Cr, Mo, W

π-Coordination of Cr^0 to one phenyl group each of the triphenylphosphane ligands in *cis*-$[(C_6H_5)_3P]_2Mo(CO)_4$ (ν(CO): 2022, 1929, 1911, 1899 cm^{-1}[4]) has virtually no effect on the CO stretching frequencies (cf. Table 1), although it raises the electron density in the aromatic rings[6, 7]. However, the ν(CO) frequencies undergo considerable shifts ($+10$ to $+30$ cm^{-1}) if the chelate ligand is oxidized to its cation radical. This increase in CO bond order connected with the oxidation (bdpc)$M(CO)_4 \rightarrow [(bdpc)M(CO)_4]^{\ddagger}$ can be explained in terms of reduced σ-donor and increased π-acceptor character of the cationic ligand relative to neutral bdpc. The green cation radicals $[(bdpc)M(CO)_4]^{\ddagger}$ obtained by passage of O_2 for several hours through solutions of the corresponding neutral complexes reveal, *via* ESR spectroscopy, that oxidation entails removal of an electron from the bis(arene)chromium part of the molecule, and the spin density is largely localized in this part of the molecule. Thus the ESR spectra of the species

[*] Priv.-Doz. Dr. Ch. Elschenbroich and Dipl.-Chem. F. Stohler
Physikalisch-chemisches Institut der Universität
CH-4056 Basel, Klingelbergstrasse 80 (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds (Project No. 2.477.371). We thank Ciba-Geigy AG, Basel, for performing the elemental analyses.

Table 1. Spectroscopic data for bdpc, bdpc^{+}, (bdpc)M(CO)$_4$, and [(bdpc)M(CO)$_4$]$^{+}$.

	IR: ν(CO) [cm^{-1}]		^{1}H-NMR [ppm] [c]		ESR [G] [d]			
	[a]	[b]	τ(C$_6$H$_5$)	τ(η-C$_6$H$_5$)	a(10 ^{1}H) [e]	a(2 ^{31}P)	a(1 ^{53}Cr)	⟨g⟩
bdpc	—	—	2.7 m (10H)	5.7 m (5H)	—	—	—	—
(bdpc)Cr(CO)$_4$	1893 B_1 1900 B_2 1921 A_1(2) 2019 A_1(1)	1863 1885 1904 2012, 2020 [f]	2.6 m (10H)	5.5 m (5H)	—	—	—	—
(bdpc)Mo(CO)$_4$	1898 B_1 1911 B_2 1928 A_1(2) 2028 A_1(1)	1865 1898 1916 2021, 2035 [f]	2.5 m (10H)	5.4 m (5H)	—	—	—	
(bdpc)W(CO)$_4$	1894 B_1 1900 B_2 1921 A_1(2) 2024 A_1(1)	1862 1891 1908 2019, 2030 [f]	2.6 m (10H)	5.6 m (5H)	—	—	—	—
[(bdpc)Cr(CO)$_4$]$^{+}$	—	1880 sh 1894 1925 sh 2020	—	—	3.27	≤0.8	18.1	1.9871
[(bdpc)Mo(CO)$_4$]$^{+}$	—	1895 sh 1910 1935 2036	—	—	3.22	0.87	18.0	1.9869
[(bdpc)W(CO)$_4$]$^{+}$	—	1885 sh 1900 1929 sh 2034	—	—	3.24	1.12	17.9	1.9864
bdpc^{+}	—	—	—	—	3.25	<0.7	17.7	1.9866

[a] Solution in methylcyclohexane; assignment as for *cis*-[(C$_6$H$_5$)$_3$P]$_2$Mo(CO)$_4$ [8].
[b] KBr disc; counterion I$^-$
[c] In [D$_8$]THF, TMS as internal standard. In order to avoid line broadening and contact shifts caused by the presence of small amounts of isostructural cation radicals [9], the sample solutions were reduced on a K mirror until the ESR signal had disappeared prior to recording the ^{1}H-NMR spectra.
[d] In THF at +25°C.
[e] Equivalent within the limits of resolution (protons attached to π-bonded phenyl groups).
[f] Splitting due to intermolecular interactions.

[(bdpc)M(CO)$_4$]$^{+}$ closely resemble that of the ligand cation radical bdpc^{+}, and no coupling is observed with ^{53}Cr, ^{95,97}Mo, or ^{183}W of the M(CO)$_4$ group. In contrast, replacement of an H atom in each of the π-bonded benzene rings by a P(C$_6$H$_5$)$_2$ group leads to a triplet splitting (2 ^{31}P, $I = 1/2$) of each ^{1}H hyperfine component.

Coordination of a M(CO)$_4$ group to bdpc modifies the latter's properties in a characteristic manner: whereas bdpc exhibits considerable thermal stability[2] (can be melted and sublimed without decomposition), (bdpc)M(CO)$_4$ begins to lose triphenylphosphane at 140°C/10^{-3} torr; the M(CO)$_4$ group in (bdpc)M(CO)$_4$ therefore weakens the Cr—arene π bond. On the other hand, the resistance of the C(η-arene)—P bond to solvolysis is enhanced when bdpc^{+} assumes the role of a chelating ligand on M(CO)$_4$.

$$[(C_6H_5)_2P\text{-}\eta\text{-}C_6H_5]_2Cr^{+} \xrightarrow[50\,^\circ C]{THF/5\%\ H_2O} (C_6H_6)_2Cr^{+} + 2\ (C_6H_5)_2PHO \qquad (2)$$

$$\{[(C_6H_5)_2P\text{-}\eta\text{-}C_6H_5]_2Cr\}M(CO)_4^{+} \xrightarrow[50\,^\circ C]{THF/5\%\ H_2O} \text{no reaction}$$

Reaction *(2)* can be conveniently followed by observing the change in ESR hyperfine structure—transition from 10 to 12 equivalent protons with a different coupling constant (a^1H = 3.25 G, bdpc^{+}, and 3.46 G, (C$_6$H$_6$)$_2$Cr^{+} resp.). The differing reactivity of bdpc^{+} and (bdpc)M(CO)$_4^{+}$ in solvolyses of the C(η-arene)—P bond is probably attributable to the forced *syn* orientation of the two C(η-arene)—P bonds in (bdpc)M(CO)$_4$. While *endo* attack by solvent molecules is clearly impossible in this form, an *exo* attack would require the P-containing fragment to depart in the *endo* direction, which would be opposed by the presence of the second C(η-arene)—P(C$_6$H$_5$)$_2$ group.

Procedure:

All reactions are carried out with dry, air-free solvents under inert gas (N$_2$). [(C$_6$H$_5$)$_2$P-η-C$_6$H$_5$]$_2$Cr^0[2] (600 mg, 1.04 mmol) and Mo(CO)$_6$ (317 mg, 1.20 mmol) are refluxed for 2 h in diglyme (25 ml) at 170°C with mechanical re-introduction of sublimed carbonylmetal. After removal of solvent by distillation at oil-pump vacuum, the residue is extracted with a boiling mixture of methylcyclohexane and tetrahydrofuran (2:1, 75 ml). Reddish brown {[(C$_6$H$_5$)$_2$P-η-C$_6$H$_5$]$_2$Cr^0}-Mo(CO)$_4$ crystallizes from the extract, yield 410 mg (51%).

The corresponding Cr and W complexes are prepared in similar manner although in somewhat lower yields, despite prolonged reaction (4 h).

Received: July 26, 1974; revised: August 16, 1974 [Z 138 IE]
German version: Angew. Chem. 87, 198 (1975)

[1] Metal π-Complexes of Benzene Derivatives, Part 4.—Part 3: ref. [2]. Part 5: *Ch. Elschenbroich* and *F. Stohler*, Chimia *28*, 730 (1974).

[2] *Ch. Elschenbroich* and *F. Stohler*, J. Organometal. Chem. 67, C51 (1974).
[3] *W. Levason* and *C. A. McAuliffe*, Advan. Inorg. Chem. Radiochem. *14*, 173 (1972).
[4] *R. Poilblanc* and *M. Bigorgne*, Bull. Soc. Chim. Fr. *1962*, 1301.
[5] *J. A. Bowden* and *R. Colton*, Aust. J. Chem. *26*, 43 (1973).

[6] *R. P. Barinsky*, Zh. Strukt. Khim. *1*, 200 (1960).

[7] *H. Binder* and *Ch. Elschenbroich*, Angew. Chem. *85*, 665 (1973); Angew. Chem. internat. Edit. *12*, 659 (1973).

[8] *F. T. Delbeke*, *E. G. Claeys*, *G. P. Van der Kelen*, and *Z. Eeckhaut*, J. Organometal. Chem. *25*, 213 (1970).

[9] *Ch. Elschenbroich*, J. Organometal. Chem. *22*, 677 (1970).

Optical Activity of Oriented Molecules[**]

By *Hans-Georg Kuball* and *Ties Karstens*[*]

Measurement of the optical rotatory dispersion (ORD) and the circular dichroism (CD) of isotropic solutions has proved to be valuable in structural elucidation. Since it follows from the theory[1] of optical activity that ORD and CD depend upon the direction of radiation of the light in the molecule, investigations on oriented molecules should yield additional structural information. So far, this effect has only been detected in flowing media or in electrical fields with oriented molecules of high polymers[2].

Small molecules cannot be oriented sufficiently by these methods[3, 4]. However, a very high degree of orientation can be achieved by their inclusion in liquid crystals—especially in nematic phases—and orientation of the nematic phase in electrical or magnetic fields. Incorporated optically active molecules convert nematic phases into cholesteric phases[5], and the optical activity of the solution is then determined by the liquid crystal and no longer by the included molecule[3, 4] (induced optical activity).

However, this optical activity induced in solution can be compensated by a further optically active component. For this purpose a solvent mixture of two compounds is used which on their own give cholesteric phases of opposite helicity. At a certain temperature (T_{nem}), this mixture, which normally forms a cholesteric phase, behaves as a nematic phase[6] (compensated nematic phase). T_{nem} is a function of the mixing ratio (in present case cholesteryl chloride and cholesteryl laurate in weight ratio 1.8:1; $T_{nem} \approx 36$ °C, depending upon additive). If the optically active substance is dissolved then the nematic phase is transformed into a cholesteric phase owing to the induced optical activity. A change in temperature to T'_{nem} compensates this effect, *i.e.* the nematic phase is restored ($|T_{nem} - T'_{nem}| \approx 3$—4 °C). After orientation of the molecules of this nematic phase in an electrical field (20—30 kV/cm) the optical activity can be measured with a light ray that propagates along the optical axis[7].

Investigations were performed on the steroids 4-cholesten-3-one *(1)* and 3β-acetoxy-5-cholesten-7-one *(2)* in the nematic phase at T'_{nem} and at a temperature ($T = 80$ °C) at which the mixture is isotropic (Figs. 1 and 2). From the degree of polarization $P \neq 0$ (Figs. 1a, 2a) it follows that the molecules in the liquid crystal do not display an isotropic distribution. Since P is larger for *(1)* than for *(2)*, either the orientation must be greater for *(1)* than for *(2)* or, as is more likely, the direction of the transition moment describes a smaller angle with respect to the orientation axis in the case of *(1)* than in the case of *(2)*. The orientation axis is the longest molecular axis, since in this case the dissolved molecules are included in the liquid crystals in similar manner to the molecules of the liquid crystals themselves.

[*] Prof. Dr. H.-G. Kuball and Dr. T. Karstens
Fachbereich Chemie der Universität
675 Kaiserslautern, Postfach 3049 (Germany)

[**] Optical Activity of Oriented Molecules, Part 1. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

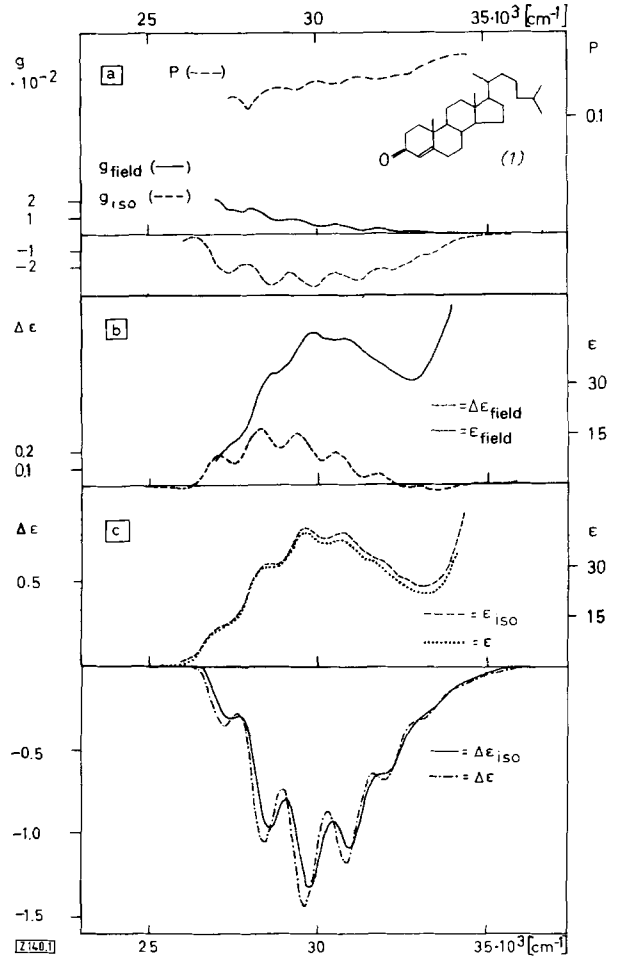


Fig. 1. 4-Cholesten-3-one *(1)*, dissolved in cholesteryl chloride/cholesteryl laurate (cf. text).—a) Degree of polarization $P = (\varepsilon_{\parallel} - \varepsilon_{\perp})/(\varepsilon_{\parallel} + \varepsilon_{\perp})$; $\varepsilon_{\parallel}$ and $\varepsilon_{\perp}$ are the molar decadic absorption coefficients of the sample for light polarized parallel and perpendicular, respectively, to the optical axis. $g_{field} = \Delta\varepsilon_{field}/\varepsilon_{field}$ and $g_{iso} = \Delta\varepsilon_{iso}/\varepsilon_{iso}$ are the dissymmetry factors.—b) Circular dichroism $\Delta\varepsilon_{field}$ and molar decadic absorption coefficient $\varepsilon_{field} = 1/3\,(\varepsilon_{\parallel} + 2\varepsilon_{\perp})$, measured at T_{nem}.—c) Circular dichroism $\Delta\varepsilon_{iso}$ and $\Delta\varepsilon$ and molar decadic absorption coefficient ε_{iso} and ε, measured in the mixture in the isotropic state ($T = 80$ °C) and in *n*-heptane ($T = 20$ °C).

In all cases, the $\Delta\varepsilon$ and ε spectra (Figs. 1c, 2c) are practically identical in the isotropic mixture and in *n*-heptane ($T = 20$ °C), *i.e.* the mixture displays no anomalous solvent effects. Moreover, the absorption spectrum ε_{field} does not deviate significantly from the spectrum in the isotropic medium. In contrast, the CD is completely different when recorded for the solution in the field. Whereas the CD signal is merely enhanced for *(2)* and its frequency dependence remains the same (Fig. 2b), the sign and the frequency dependence change for *(1)* (Fig. 1b). This effect can be seen clearly from the dissymmetry factors (Figs. 1a, 2a).

The optical activity of *(1)* and *(2)* is largely determined by the chromophore C=C—C=O. Since this group has approximately mirror symmetry in *(1)* and *(2)*[8], the circular dichroism of isotropic solutions will differ in sign. On the basis of these assumptions, the difference between $\Delta\varepsilon_{field}$ in *(1)* and *(2)* should arise from the differing arrangement of the chromophore in the molecule. When measurements are performed in the oriented state, the direction of the light ray runs parallel to the longest molecular axis. However, the chromophore is arranged differently relative to the longest molecular axis in *(1)* and *(2)*, and is therefore traversed differently by the light ray.

The results described here indicate that measurement of optical activity on oriented systems yields not only information about absolute configurations but also provides further structural

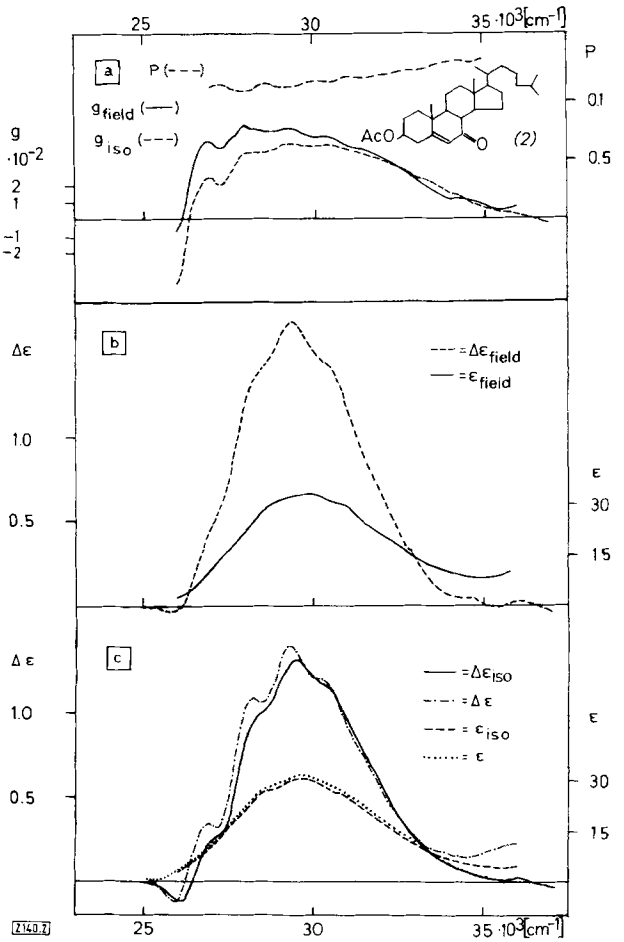


Fig. 2. 3β-Acetoxy-5-cholesten-7-one *(2)*, dissolved in cholesteryl chloride/-cholesteryl laurate (cf. text and legend to Fig. 1).

information, *e.g.* regarding the arrangement of the chromophore relative to the molecular axis. Theoretical evaluation and the consequences of applying the sector rules, *etc.*, will be reported later.

Received: September 16, 1974 [Z 140 IE]
German version: Angew. Chem. 87, 200 (1975)

CAS Registry numbers:
(1), 601-51-0; *(2)*, 809-51-8

[1] *I. Tinoco, Jr.* and *W. G. Hammerle*, J. Phys. Chem. *60*, 1619 (1956); *N. Go*, J. Chem. Phys. *43*, 1275 (1965); J. Phys. Soc. Jap. *23*, 88, 1094 (1967); *Y. N. Chiu*, J. Chem. Phys. *52*, 1042 (1970); *A. D. Buckingham* and *M. B. Dunn*, J. Chem. Soc. *A 1971*, 1988.

[2] *I. Tinoco, Jr.*, J. Amer. Chem. Soc. *81*, 1540 (1959); *R. Mandel* and *G. Holzwarth*, J. Chem. Phys. *57*, 3469 (1972); Biopolymers *12*, 655 (1973); and references cited therein.

[3] *J. Kunz* and *A. McLean*, Nature *136*, 795 (1935); *J. Kunz* and *A. Babkock*, Phil. Mag. *23*, 616 (1936); *J. Kunz* and *R. G. La Baw*, Nature *140*, 194 (1937).

[4] *A. D. Buckingham, G. P. Caesar*, and *M. B. Dunn*, Chem. Phys. Lett. *3*, 540 (1969).

[5] *E. Friedel*, C. R. Acad. Sci. Paris *1923*, 475; *H. Stegemeier, K. J. Mainusch*, and *E. Steigner*, Chem. Phys. Lett. *8*, 425 (1971).

[6] *J. M. Pochan* and *P. F. Erhardt*, Phys. Rev. Lett. *27*, 790 (1971); *E. Friedel*, Ann. Phys. Paris *18*, 273 (1922); *H. Baessler* and *M. M. Labes*, J. Chem. Phys. *51*, 1846 (1969); *52*, 631 (1970); *E. Sackmann*, Chem. Phys. Lett. *3*, 253 (1969); J. Amer. Chem. Soc. *90*, 3569 (1968).

[7] Owing to the orientation with an electrical field, the phase has a symmetry axis in the direction of the field (optical axis of system). Measurement perpendicular to the optical axis is impossible at present because the linear dichroism is very large. On filling the cells care should be taken that no additional linear dichroism arises at the cell windows.

[8] *C. Djerassi, R. Riniker*, and *B. Riniker*, J. Amer. Chem. Soc. *78*, 6377 (1956); *H. Ziffer* and *C. H. Robinson*, Tetrahedron *24*, 5803 (1968).

Isolation of Tetrazene, N_4H_4[1]

By *Nils Wiberg, Heiner Bayer*, and *Heinz Bachhuber*[*]

The only hydrogen compounds of nitrogen that have previously been unambiguously characterized are ammonia (NH_3), hydrazine (N_2H_4), diimine (N_2H_2)[2] and hydrogen azide (N_3H). We have now succeeded in preparing a further nitrogen hydride, namely tetrazene (N_4H_4), which, unlike the previously known compounds containing a one-, two- or three-membered nitrogen chain, is based on a skeleton of four nitrogen atoms.

For *synthesis* of this compound, tetrakis(trimethylsilyl)tetrazene[4] which is readily accessible by acid-catalyzed dimerization of bis(trimethylsilyl)diimine[3] is treated with trifluoroacetic acid in methylene dichloride at −78 °C. The tetrazene, being only sparingly soluble in methylene dichloride, is thus precipitated as a colorless solid; it can be purified by sublimation.

$$(Me_3Si)_2N{-}N{=}N{-}N(SiMe_3)_2 \xrightarrow[-4\ F_3C{-}COOSiMe_3]{+4\ F_3C{-}COOH} H_2N{-}N{=}N{-}NH_2$$

The following facts indicate that the nitrogen hydride isolated has the structure of a *trans*-2-tetrazene: 1. Quantitative analysis of the thermolysis products (see below) yields a nitrogen/hydrogen ratio of 1 : 1, *i.e.* the nitrogen hydride has the molecular formula $(NH)_x$.—2. The mass spectrum obtained for the isolated compound at an ionization energy of 70 eV in the gas phase at 5×10^{-7} torr shows the molecular ion $N_4H_4^+$ as an intense line at $m/e = 60$. If the ionization energy is lowered from 70 to 10 eV, then, as expected, the mass groups of ionic fragments $N_mH_n^+$ with one, two or three nitrogen atoms disappear almost completely and there remains only the signal of the molecular ion. Thus x in the molecular formula $(NH)_x$ that follows from the analytical investigations must be replaced by the number 4.—3. By germylation with *N,N*-diethyl(trimethylgermyl)amine the nitrogen hydride N_4H_4 can be converted by the reaction (E = Ge)

$$N_4H_4 \xrightarrow[-4\ H{-}NEt_2]{+4\ Me_3E{-}NEt_2} (Me_3E)_2N{-}N{=}N{-}N(EMe_3)_2$$

into the derivative, tetrakis(trimethylgermyl)-2-tetrazene which could be synthesized by an independent route[5]. N_4H_4 also reacts analogously with *N,N*-diethyl(trimethylstannyl)-amine (E = Sn). Thence we conclude that N_4H_4 has the structure 2-tetrazene.—4. The synthetic route leading to tetrazene consists of protolysis of tetrakis(trimethylsilyl)-2-tetrazene which according to X-ray structure analysis[6] has the *trans*-configuration; and, since a change of configuration during protolysis is unlikely, the 2-tetrazene prepared in this way probably also has the *trans*-configuration[7].

Thermolysis of tetrazene

$$H_2N{-}N{=}N{-}NH_2 \longrightarrow N{\equiv}N + H_2N{-}NH_2$$
$$\qquad\qquad\qquad\qquad\quad \longrightarrow NH_4^{\oplus}\ N{=}N{=}N$$

[*] Prof. Dr. N. Wiberg, Dipl.-Chem. H. Bayer, and Dr. H. Bachhuber
Institut für Anorganische Chemie der Universität
8 München 2, Meiserstr. 1 (Germany)

leads by decomposition to nitrogen and hydrazine and by isomerization to ammonium azide[8]. If pure tetrazene is thus decomposed, the decomposition and isomerization products are formed in about 75 and 25% yields, respectively (*e.g.* found: 1.18 mmol of N_2, 1.18 mmol of N_2H_4, 0.39 mmol of NH_3, 0.38 mmol of HN_3). However, decomposition and isomerization of tetrazene in methanol affords about 40 and 60%, respectively. Thermolysis of solid tetrazene begins only at *ca.* 0 °C (gaseous tetrazene is metastable even at room temperature); *trans*-2-tetrazene is thus unexpectedly thermostable.

Experimental:

Trifluoroacetic acid (6.00 mmol) in methylene dichloride (15 ml) is dropped very slowly into a well-stirred solution of tetrakis(trimethylsilyl)tetrazene[3] in methylene dichloride (25 ml) cooled to −78 °C. The tetrazene is isolated by condensation: the reaction mixture is warmed slowly to 0 °C and the vapor is passed in a high vacuum through a glass trap cooled to −78 °C into one cooled to −196 °C. All the methylene dichloride then collects in the second trap (−196 °C) together with trimethylsilyl acetate; the 2-tetrazene remaining in the first trap (−78 °C) is purified by repeated sublimation in a high vacuum from −15 °C into a tube cooled to −78 °C (yield 90%).

Received: August 15, 1974 [Z 143a IE]
German version: Angew. Chem. *87*, 202 (1975)

CAS Registry numbers:
Tetrakis(trimethylsilyl)tetrazene, 52164-24-6; trifluoroacetic acid, 76-05-1; *trans*-tetrazene, 54410-57-0

[1] Part 3 of Tetrazene and Its Derivatives. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 2: *N. Wiberg* and *W. Uhlenbrock*, Chem. Ber. *105*, 63 (1972); Part 1: [4].

[2] *N. Wiberg, H. Bachhuber*, and *G. Fischer*, Angew. Chem. *84*, 889 (1972); Angew. Chem. internat. Edit. *11*, 829 (1972). *N. Wiberg, G. Fischer*, and *H. Bachhuber*, Chem. Ber. *107*, 1456 (1974).

[3] *N. Wiberg* and *W. Uhlenbrock*, J. Organometal. Chem. *70*, 239 (1974).

[4] *N. Wiberg* and *W. Uhlenbrock*, Angew. Chem. *82*, 47 (1970); Angew. Chem. internat. Edit. *9*, 70 (1970).

[5] *N. Wiberg* and *S. K. Vasisht*, unpublished work.

[6] *M. Veith*, Acta Crystallogr., in press.

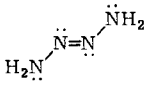
[7] The amine nitrogen atoms in *trans*-2-tetrazene are most probably sp^3- and not sp^2-hybridized (cf. *J. Kroner, N. Wiberg*, and *H. Bayer*, Angew. Chem. *87*, 203 (1975); Angew. Chem. internat. Edit. *14*, 178 (1975)).

[8] For decomposition, isomerization and other possible degradations of azo-compounds cf. [3].

Photoelectron Spectrum of Tetrazene[1]

By *Jürgen Kroner, Nils Wiberg*, and *Heiner Bayer*[*]

The nitrogen hydride N_4H_4 recently isolated for the first time has the geometrical structure of a *trans*-2-tetrazene[1].



To obtain the first preliminary information about its electronic structure we have measured the photoelectron (PE) spectrum of tetrazene[2]. In the energy range up to 21.21 eV it shows eight bands (Fig. 1), which can be assigned by qualitative MO considerations (Fig. 2).

[*] Dr. J. Kroner, Prof. Dr. N. Wiberg, and Dipl.-Chem. H. Bayer
Institut für Anorganische Chemie der Universität
8 München 2, Meiserstr. 1 (Germany)

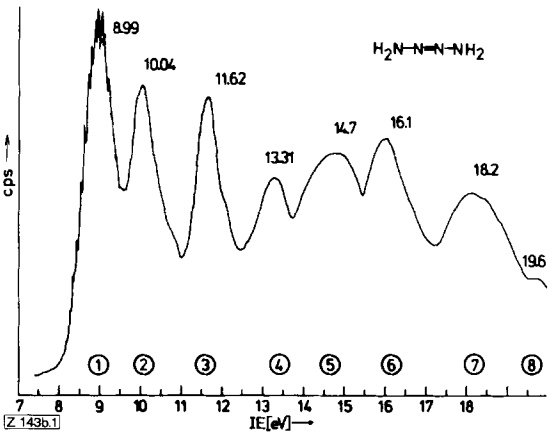


Fig. 1. Photoelectron spectrum of *trans*-2-tetrazene.

Derivation of the orbital sequence of tetrazene (Fig. 2) is based on the vertical ionization energies of *trans*-azomethane[3a] and ammonia[3b] together with consideration of the inductive effects of azo ($-I$) and amino groups ($+I$).

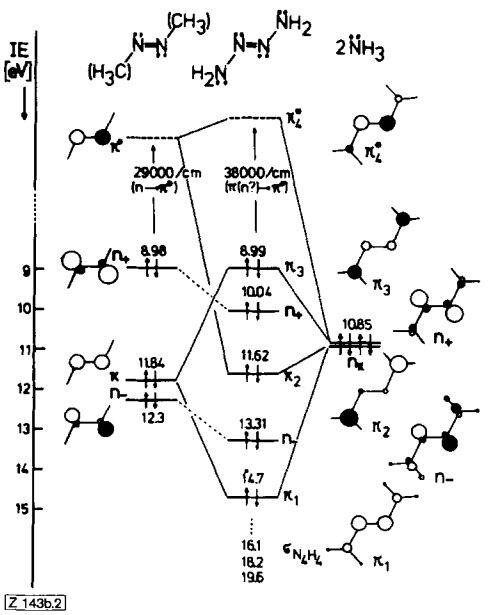


Fig. 2. MO scheme of n- and π-interactions in *trans*-2-tetrazene (vertical ionization energies in eV).

The first PE bands of tetrazene is undoubtedly to be assigned to ionization of the π_3-orbital because of its shape and vibrational fine structure ($\nu^{\oplus} = 650\ cm^{-1}$, *ca.* 15 progressions; cf. also ammonia[3b] and cyanamide[3c]). In view of the inductive effect ($CH_3 \rightarrow NH_2$) and of a small interaction effect between the n-orbital of the azo group and the energetically low-lying σ-orbitals of the amino group ($IE_{\sigma}^{NH_3} = 15.8$ eV[3b]), the second band should refer to ionization of the n_+-orbital of the azo group. If as an approximation one assumes an equal inductive decrease in n_+ and n_- on going from azomethane to tetrazene (≈ 1 eV), the fourth band can be assigned to ionization of the corresponding n_- combination[4]. Thus the third PE band must be assigned to π_2 which mixes symmetry-correctly with the π*-orbital of the azo group. For π_1 there remains the fifth PE band.

The qualitatively derived interaction diagram (Fig. 2) has been confirmed by CNDO/S calculations[5] on the assumption of "pyramidal" amino-nitrogen atoms: π_3 (8.51), n_+ (10.13), π_2 (11.67), n_- (13.92), π_1 (14.44 eV); it was impossible to

obtain comparable agreement between orbital and ionization energies for "planar" amino-nitrogen. The utility of the model used for calculations is further shown by prediction of the three σ-orbital ionizations of the tetrazene [σ_{NNNN} (15.50), σ_{NH_2} (19.88, 19.89 eV)], which correlate satisfactorily with the vertical ionization energies (Fig. 1).

The following, *inter alia*, can be derived from the photoelectron spectrum and the molecular orbital scheme:

1. A tetrazene orbital of π-type advances to the highest occupied orbital owing to π-interaction of π-orbitals of the azo group and n_π-orbitals of the amino groups. This finding is in contrast with previous findings that in compounds of type X—N=N—X the positions of the n- and π-orbitals are indeed appreciably influenced by electronic interactions of the azo group and substituents X but that the highest occupied orbital is always of n_σ-type. Thus the orbital sequence derived by PE spectroscopy for tetrazene contributes also to understanding of the UV spectra of amino-substituted π-electron systems: whereas n→π* transitions of low intensity occur in azo compounds X—N=N—X ($X \neq NR_2$)[6], the low ionization energies of the highest occupied π-orbitals of substituted tetrazenes[7] and triazenes[7] cause coincidence of π→π* and n→π* bands. Corresponding results are valid for azobenzene/aminoazobenzenes[7, 8] and quinone/aminoquinones[3b, 6b, 9].

2. The surprisingly great π-conjugation along the nitrogen chain of the tetrazene (cf. Fig. 2)[10] need not necessarily produce a marked shortening of the N—N single bonds or a lengthening of the N=N double bonds, since the equally strong delocalization of the electron pair in the π_3-orbital opposes this change in the bond lengths. A tetrazene cation $N_4H_4^{\oplus}$ should, however, show appreciably shorter single and longer NN double bonds[11] and should thus be more stable than tetrazene towards radical decomposition. The opposite is to be expected for a tetrazene anion $N_4H_4^{\ominus}$.

3. The structuring of the first PE band of the tetrazene (Fig. 1) and the finding that no satisfactory agreement can be achieved between calculation and experiment for an sp^2-hybridized amino-nitrogen atom can be regarded as showing the occurrence of sp^3-hybridized nitrogen atoms in the amino groups of the tetrazene.

Received: October 2, 1974
Revised: November 14, 1974 [Z 143b IE]
German version: Angew. Chem. 87, 203 (1975)

CAS Registry numbers:
trans-2-Tetrazene, 54410-57-0

[1] Part 4 of Tetrazene and Its Derivatives. This work was supported by the Deutsche Forschungsgemeinschaft. — Part 3: *N. Wiberg, H. Bayer*, and *H. Bachhuber*, Angew. Chem. *87*, 202 (1975); Angew. Chem. internat. Edit. *14*, 177 (1975).

[2] PS 16 spectrometer, Perkin-Elmer Ltd., Beaconsfield [He(I) lamp, Ar/Xe calibration]; recorded at *ca.* −20 °C.

[3] a) *E. Haselbach* and *E. Heilbronner*, Helv. Chim. Acta *53*, 684 (1970); b) *D. W. Turner, C. Baker, A. D. Baker*, and *C. R. Brundle*: Molecular Photoelectron Spectroscopy. Wiley-Interscience, London 1970; c) *H. Stafast* and *H. Bock*, Chem. Ber. *107*, 1882 (1974).

[4] The n_+/n_--orbital energy difference in tetrazene (≈3.3 eV) corresponds exactly to that in azomethane [3a].

[5] *J. Kroner, D. Proch, W. Fuss*, and *H. Bock*, Tetrahedron *28*, 1585 (1972).

[6] a) *H. Suzuki*: Electronic Absorption Spectra and Geometry of Organic Molecules. Academic Press, New York 1967; b) *E. Haselbach* and *A. Schmelzer*, Helv. Chim. Acta *54*, 1575 (1971); *55*, 1745 (1972).

[7] *J. Kroner*, unpublished work.

[8] *J. Kroner* and *H. Bock*, Chem. Ber. *101*, 1922 (1968).

[9] *K. Wallenfels* and *W. Draber*, Tetrahedron *20*, 1889 (1964); *M. Klessinger*, Theor. Chim. Acta *5*, 251 (1966).

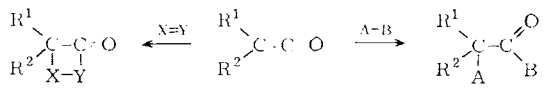
[10] Marked π-interaction between azo- and amino-nitrogen atoms is indicated also by the energy barriers of 10—16 kcal/mol for rotation of the amino groups around the N—N single bond in substituted phenyltriazenes: *N. P. Marullo, C. B. Mayfield*, and *E. H. Wagener*, J. Amer. Chem. Soc. *90*, 510 (1968); *N. Wiberg* and *H. J. Pracht*, Chem. Ber. *105*, 1399 (1972).

[11] *W. M. Tolles, D. W. Moore*, and *W. E. Thun*, J. Amer. Chem. Soc. *88*, 3476 (1966).

Additions to the C=O Group of Ketenes: β-Substituted α-Trimethylsiloxyacrylonitriles[**]

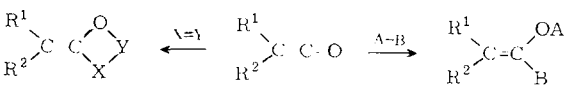
By *Ulrich Hertenstein* and *Siegfried Hünig*[*]

The numerous additions to the cumulated double bond system of the ketenes *(2)* take place almost without exception at the C=C bond with formation of acyl derivatives *(3)* or of four-membered *(1)* or six-membered cycloadducts having a carbonyl function[1]. A—B = R_3^1Si—NR^2R^3 is also added to *(2)* with formation of a Si—C bond[2].



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

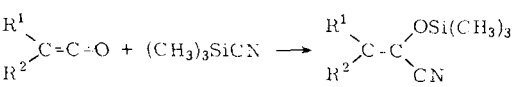
In contrast, there are very few additions to the C=O function of ketenes yielding *(4)* or *(5) with retention of the C=C*



(4) *(2)* *(5)*

bond[3]. The dimerization of aldoketenes to *(4)* is well known (X=Y is the CO function of the ketene)[1]. Compounds of type *(5)* are formed on thermal addition of oxiranes (= A—B) to ketene acetals: however, this reaction has only been investigated in the case of diphenylketene[4].

Looking for a reaction *(2)*→*(5)* of maximum generality we found that trimethylsilyl cyanide[5] *(6)* adds cleanly to the C=O bond of ketenes to give β-substituted α-trimethylsiloxyacrylonitriles *(7)*. Thus compound *(7)* does not follow the



(2) *(6)* *(7)*

Table 1. 2-Trimethylsilyloxyacrylonitriles *(7)* prepared *via* ketene intermediates.

	R^1	R^2	Yield [%]	B.p. [°C/torr]
(7a)	H	H	96	58—59/40
(7b)	H	CH_3	71	76/40
(7c)	CH_3	CH_3	85	71—73/16
(7d)	H	$n\text{-}C_{16}H_{33}$	95	140—142/0.005
(7e)	—$(CH_2)_5$—		82	122—125/15
(7f)	H	C_6H_5	90	76/0.005
(7g)	H	OCH_3	75	96—97/20
(7h)	CH_3	Cl	60	71—75/18
(7i)	Cl	Cl	60	78/20
(7j)	F_3C	F_3C	90	62/38

[*] Dipl.-Chem. U. Hertenstein and Prof. Dr. S. Hünig
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and BASF, Ludwigshafen.

scheme *(2)*→*(3)* like trialkylsilylamines, but behaves as in additions to aldehydes and ketones[6–8], and to certain acyl chlorides[6, 9].

Adducts *(7)* are produced both from free ketenes and from those formed *in situ*. Generation of ketene intermediates from acyl chlorides with tertiary amines in the presence of *(6)* seems to be a particularly versatile approach. The adducts *(7)* are apparently formed very rapidly since many ketenes are known to undergo fast dimerization under these conditions[1]. Good yields are even obtained with dichloroketene, which polymerizes so fast in the presence of ammonium salts that it can only be trapped with highly reactive enes[10]. The significance of the ketene intermediate is clear from the finding that no adduct *(7)* is obtained from cyclopropanecarbonyl chloride, which forms no ketene with tertiary amines[11].

Table 1 illustrates the versatility of the reaction, whose scope is limited practically only by the existence of ketene intermediates. The colorless compounds *(7)* can be distilled without decomposition up to ≈120 °C. The stretching vibration of the nitrile function appears largely independent of R^1 and R^2 at 2220–2210 cm^{-1}, and that of the C=C bond at 1645–1620 cm^{-1}.

According to the NMR spectra, mixtures are formed in the cases of unequal β-substitution. Surprisingly however, *(7f)* is homogeneous, the phenyl group probably being *cis* to the nitrile group.

We are presently examining whether the reactivity of the cycloadducts *(7)* more closely resembles that of enol silyl ethers or that of acrylonitriles. Apart from the reactions with cycloaddends and nucleophiles known for other α-substituted acrylonitriles[12], a directed attack at the trimethylsiloxy group and at the nitrile group appears to be of interest.

2-Trimethylsiloxyacrylonitrile (7) from acyl chlorides:

A solution of acyl chloride (0.10 mol) in anhydrous ether (20 ml) is added dropwise under N_2 to a mixture of *(6)* (0.11 mol), triethylamine (0.30 mol), and ether (60 ml) at 0 °C in a carefully dried apparatus over 1.5 h. The reaction mixture is then stirred for 1 h at room temperature and for 1 h at 50 °C. The precipitated ammonium salt is filtered off under suction and washed thoroughly with ether. After removal of the solvent the residue is distilled.

2-Trimethylsiloxyacrylonitrile (7) from free ketenes:

Hexafluorodimethylketene[13] or pyrolytically generated ketene is passed into *(6)* (*e.g.* 10—40 g) at room temperature until the IR band of *(6)* at 2190 cm^{-1} has largely disappeared. The crude product is purified by distillation.

Received: December 2, 1974 [Z 145 IE]
German version: Angew. Chem. *87*, 195 (1975)

[1] See the excellent survey by *D. Borrmann* in Houben-Weyl-Müller: Methoden der Organischen Chemie Thieme, Stuttgart 1968, Vol. 7/4, p. 55.

[2] *V. D. Sheludyakovetal*, Zh. Obshch. Khim. *37*, 2141 (1967).

[3] Special cases (cf. [1]), *e.g.* $(F_3C)_2C{=}C{=}O + (C_2H_5)_3SiH$ or $(C_6H_5)_2C{=}C{=}O + (C_6H_5)_2CN_2$, need not be considered.

[4] *K. Gulbins* and *K. Hamann*, Chem. Ber. *94*, 3287 (1961).

[5] Preparation of $(CH_3)_3SiCN$: *W. Sundermeyer*, Z. Anorg. Allg. Chem. *313*, 290 (1961), and literature cited therein.

[6] *W. Lidy* and *W. Sundermeyer*, Chem. Ber. *106*, 587 (1973).

[7] *H. Neef* and *R. Müller*, J. Prakt. Chem. *315*, 367 (1973).

[8] *D. A. Evans* and *L. K. Truesdale*, Tetrahedron Lett. *1973*, 4929.

[9] *W. Lidy* and *W. Sundermeyer*, Tetrahedron Lett. *1973*, 1449.

[10] *L. Ghosez*, *R. Montaigne*, and *P. Mollet*, Tetrahedron Lett. *1966*, 135.

[11] *H. W. Walkovsky*, J. Amer. Chem. Soc. *74*, 4962 (1952); *J. L. E. Erickson*, *F. E. Collins*, and *B. L. Owen*, J. Org. Chem. *31*, 480 (1966).

[12] *P. S. Wharton* and *B. T. Aw*, J. Org. Chem. *31*, 3787 (1966); *E. J. Corey* and *N. M. Weinsheuter*, J. Amer. Chem. Soc. *91*, 5675 (1969); *A. W. Ashton*, Tetrahedron *30*, 559 (1974); *G. Ege* and *Ph. Arnold*, Angew. Chem. *86*, 237 (1974); Angew. Chem. internat. Edit. *13*, 206 (1974); *A. R. Martin*, J. Org. Chem. *39*, 1808 (1974).

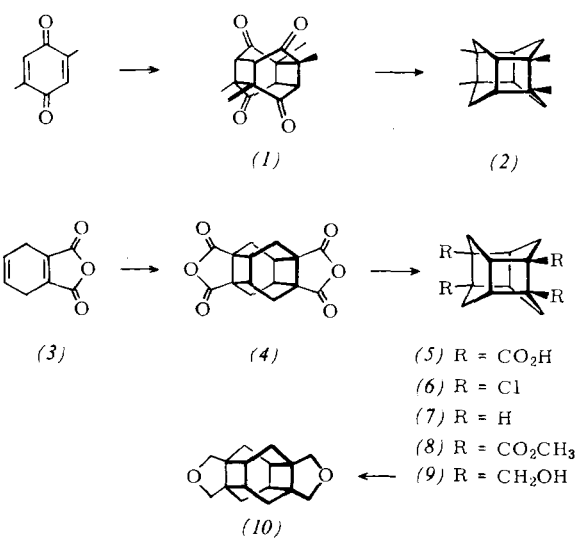
[13] We are grateful to Dr. *D. C. England*, Du Pont de Nemours & Co., Central Research Department, for kindly providing this ketene.

Tetraasterane, Pentacyclo[6.4.0.0^{2,7}.0^{4,11}.0^{5,10}]-dodecane[1][**]

By *Hans-Martin Hutmacher*, *Hans-Günter Fritz*, and *Hans Musso*[*]

The cage dimers of dimethyl-*p*-benzoquinones, *e.g.* *(1)*[2], can be converted into tetramethyltetraasteranes, *e.g.* *(2)*[3, 4], by Wolff-Kishner reduction. We now report the synthesis of the parent hydrocarbon *(7)*, which was first conceived in 1965[3]; all former attempts met with failure[4, 5].

The sparingly soluble cage dimer anhydride *(4)* is accessible in 9–10 % yield in addition to other products by irradiation of 3,6-dihydrophthalic anhydride *(3)* in dioxane[6]. Degradation of the tetracarboxylic acid *(5)* obtainable from *(4)* in 86 % yield initially ran into difficulties. Finally, repeated application of lead tetraacetate and *N*-chlorosuccinimide in dimethylformamide/glacial acetic acid (5 : 1) according to *Grob*[7] gave *ca.* 20 % of tetrachlorotetraasterane (1,2,5,10-tetrachloropentacyclo[6.4.0.0^{2,7}.0^{4,11}.0^{5,10}]dodecane) *(6)*, which is reduced to tetraasterane *(7)* in 74 % yield by sodium in boiling alcohol. The composition and structure of *(6)* and *(7)* can be deduced unequivocally from their spectra (Table 1).



As expected, *(7)* is thermally quite stable. It is unchanged on heating at 500 °C *in vacuo* for 1 h, and only begins to decompose to three major products, which are presently being investigated, above 530 °C. The proximity of the 1,2- and 5,10-substituents on the tetraasterane skeleton accounts for the extreme ease with which *(5)* regenerates *(4)* on heating or on treatment with $SOCl_2$, and with which the tetraalcohol *(9)* [accessible from the tetramethyl ester *(8)* (m.p. 221 °C) with $LiAlH_4$ in ether] reacts with tosyl chloride in pyridine to form "astera-propellane" (6,17-dioxaheptacyclo-

[*] Dr. H.-M. Hutmacher, Dr. H.-G. Fritz, and Prof. Dr. H. Musso
Institut für Organische Chemie der Universität
75 Karlsruhe, Richard-Willstätter-Allee (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are indebted to Dr. *U. I. Záhorszky* and Miss *I. Gerhardt* for recording numerous spectra.

[9.4.3.0.0^{2,10}.0^{4,8}.0^{4,14}.0^{8,13}]octadecane *(10)*. In the NMR spectrum of *(10)* the large shift difference from the signals of the anisochronous protons in the CH_2O and CH_2 groups is particularly striking.

Table 1. Compounds *(6)*—*(10)* prepared.

(6), m.p. 305—310°C; molar mass, calc. 298 [8] exp. (MS) M^+ 302 (1%), 300 (5), 298 (12), 296 (8); NMR (chlorobenzene): $\delta = 2.81$ (m, 4 tert. H), AB-qt 1.99, $\Delta\delta_{AB} = 14.3$ Hz, $J_{AB} = 15.5$ Hz, $J = 1.5$ Hz (4 CH_2).

(7), readily sublimable colorless crystals, m.p. 324—325°C; molar mass, calc. 160, exp. (MS) 160 M^+ (38%), 131 (9), 117 (13), 104 (15), 91 (25), 79 (100), 67 (42); NMR ($CDCl_3$): pseudosinglets at $\delta = 1.69$ (8 tert. H) and 2.61 (4 CH_2), $J_{HH} < 0.5$ Hz; IR (CCl_4): 2923, sh 2905, 2843 (ν_{CH}), 1439 m, 1362, and 926 cm^{-1}.

(8), m.p. 221°C (acetone); yield 82%; molar mass, calc. 392, exp. 392 (MS); NMR ($CDCl_3$): $\delta = 3.67$ (s, 4 OCH_3), 3.19 (t, 4 tert. H, $J = 1.5$ Hz), AB-q 2.14 and 1.87 (4 CH_2, $J_{AB} = 15.0$ and $J = 1.5$ Hz); IR (KBr): $\nu_{C=O}$ 1718 and 1732 cm^{-1}.

(9), m.p. 234—236°C (ethanol); yield 65%; molar mass, calc. 280, exp. 280 (MS); NMR (D_6-DMSO): $\delta = 4.68$ (dd, 4 OH, $J = 6.5$ and 4.0 Hz), two AB-dd 3.75 (4 H, $J_{AB} = 11.0$ and 4.0 Hz), 3.16 (4 H, $J_{AB} = 11.0$ and 6.5 Hz) (4 CH_2—O), 2.00 (pseudo-s, 4 CH, $J < 0.5$ Hz), two AB-q 1.82 and 1.32 (4 CH_2, $J_{AB} = 14.0$ and $J < 0.5$ Hz).

(10), m.p. 206—208°C (acetone); yield 63%; molar mass, calc. 244, exp. 244 (MS); NMR ($CDCl_3$) δ: AB-q 3.87 and 3.19 (—CH_2—O, $J_{AB} = 9.0$ Hz), 2.35 (t, 4 tert. H, $J = 1.2$ Hz), AB-q 1.84 and 1.43 (4 CH_2, $J_{AB} = 14.0$ and $J = 1.2$ Hz).

All new compounds gave correct elemental analyses. Only that of *(6)* showed a small content of trichlorotetraasterane which could not be unequivocally determined in the mass spectrum.

Received: December 3, 1974 [Z 147 IE]
German version: Angew. Chem. 87, 174 (1975)

[1] Asteranes, Part 12.—Part 11: see ref. [5].

[2] *R. C. Cookson, D. A. Cox*, and *J. Hudec*, J. Chem. Soc. *1961*, 4499; *H. Hopf* and *H. Musso*, Chem. Ber. *106*, 143 (1973).

[3] *U. Biethan, U. v. Gizycki*, and *H. Musso*, Tetrahedron Lett. *1965*, 1477; *U. Biethan* and *H. Musso*, Chem. Ber. *100*, 119 (1967).

[4] *J. P. Chesick, J. D. Dunitz, U. v. Gizycki*, and *H. Musso*, Chem. Ber. *106*, 150 (1973).

[5] *H.-G. Fritz, H. Henke*, and *H. Musso*, Chem. Ber. *107*, 3164 (1974).

[6] *G. Ahlgren, B. Åkermark*, and *R. Karlson*, Acta Chem. Scand. *25*, 753 (1971); *G. Ahlgren* and *B. Åkermark*, Tetrahedron Lett. *1973*, 987; *H.-G. Fritz*, Dissertation, Universität Karlsruhe 1972.

[7] *K. B. Becker, M. Geisel, C. A. Grob*, and *F. Kuhnen*, Synthesis *1973*, 493.

[8] Based on $^{35}Cl_3{}^{37}Cl$.

Fatal Accident During Work with 2-(Perfluoroalkyl)-ethyl Iodides

By *Klaus Ulm* and *Walter Weigand*[*]

During the isolation of 2-(perfluoroalkyl)ethyl iodides *(1)* prepared by known procedures[1-3] a fatal accident occurred following circulatory collapse by pulmonary edema.

The cause of the accident was most probably inhalation of toxic substances appearing on isolation of *(1)* from the crude product.

$$RI + C_2H_4 \xrightarrow{1\%\ \text{radical catalysts}} R{-}CH_2{-}CH_2{-}I \quad (1)$$

$R = C_2F_5, C_4F_9, C_6F_{13}, C_8F_{17}, C_{10}F_{21}$

[*] Dr. K. Ulm and Dr. W. Weigand
Hoechst AG
8261 Gendorf/Obb., Werk Gendorf (Germany)

A screening test of acute inhalation toxicity in mice (one hour's exposure) afforded an LC_{50} of 400 to 500 ppm for *(1)*, $R = C_2F_5$, and an LC_{50} of about 4000 ppm for *(1)*, $R = C_4F_9$. Formation of perfluoroisobutylene on isolation of *(1)* could not be detected, even in trace amounts. Perfluoroalkylethylenes prepared from *(1)* are not significantly toxic.

Received: January 2, 1975 [Z 148 IE]
German version: Angew. Chem. 87, 171 (1975)

[1] *R. N. Haszeldine*, J. Chem. Soc. *1949*, 2856.

[2] *R. N. Haszeldine*, J. Chem. Soc. *1953*, 3761.

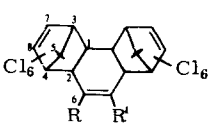
[3] *N. O. Brace*, J. Org. Chem. *31*, 2879 (1966).

Benzene as Dienophile in the Diels-Alder Reaction[1]

By *Wolfgang Jarre, Dieter Bieniek*, and *Friedhelm Korte*[*]

Furan, thiophene and naphthalene behave towards hexachlorocyclopentadiene as dienophile components in the Diels-Alder reaction[2]. No similar reaction with benzene has previously been described.

Since the course of the Diels-Alder reaction is strongly influenced by pressure, we have tried to cause benzene, chlorobenzene and *o*-dichlorobenzene to react with hexachlorocyclopentadiene at 10 kbar (1 kbar = 987 atm) and 220—240°C (reaction time 20 h). Along with the cage dimer of hexachlorocyclopentadiene, namely dodecachloropentacyclo-[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane[3], we obtained the Diels-Alder adducts *(1)*, always in the ratio 1:1.



(1a): R = R' = H
(1b): R = H, R' = Cl
(1c): R = R' = Cl

On the basis of physical data (UV, IR, MS, ^{1}H-NMR, ^{13}C-NMR) and elemental analyses the new compounds have structures *(1a)*, *(1b)* and *(1c)*. As a representative example, the characteristic data of compound *(1a)* may be cited: m.p. 237—238°C (from methanol). Mass spectrum (70 eV): M^+ 618, rel. int. 0.03%; $[M-Cl]^+$ 583, 0.27%; $[C_5Cl_6]^+$ 270, 100%; $[C_5Cl_5]^+$ 235, 19.4%; $[C_6H_6]^+$ 78, 18.8%. IR spectrum ($CHCl_3$): 1600, 1320, 1250, 1170, 1070, 915, 850 cm^{-1}. ^{1}H-NMR ($CDCl_3$): $\tau = 4.15$ (br), 2H; 6.85 (s), 4H. ^{13}C-NMR ($CDCl_3$, TMS int.): $\delta = 40.11, 44.99$ (C-1,2), 82.44, 82.78 (C-3,4), 101.34 (C-5), 124.88 (C-6), 128.86, 133.19 ppm (C-7,8)[4].

The physical data for compounds *(1b)* (m.p. 212—213°C) and *(1c)* (m.p. 225—227°C) accord with the structures proposed.

[*] Dr. W. Jarre, Dr. D. Bieniek, and Prof. Dr. F. Korte
Institut für Ökologische Chemie der Gesellschaft für Strahlen- und Umweltforschung mbH, München
5205 St. Augustin 1, Postfach 1260 (Germany)

[1] Part 10 of High-pressure Reactions. This work was supported by the Deutsche Forschungsgemeinschaft.—Part 9: *J. Roemer-Mähler, D. Bieniek*, and *F. Korte*, Z. Naturforsch., Part B, in press.

[2] *J. Hyman* and *A. A. Danish*, US-Pat. 2658926; Chem. Abstr. *48*, 12177 (1954); *N. Neeman* and *A. Modiano*, 131. Meeting Amer. Chem. Soc. (Miami 1957), Abstr. Pap. p. 83-O; *R. Riemschneider* and *A. Kühnl*, Monatsh. Chem. *86*, 879 (1955); *A. A. Danish, M. Silverman*, and *Y. A. Tajima*, J. Amer. Chem. Soc. *76*, 6144 (1954).

[3] *H. J. Prins*, Rec. Trav. Chim. Pays-Bas *65*, 455 (1946).

[4] We thank Dr. *R. Matusch*, Marburg, and Dr. *B. Novotny*, Darmstadt, for measuring and discussing the ^{13}C-NMR spectra.

[5] *H. G. Drickamer*, Angew. Chem. *86*, 61 (1974); Angew. Chem. internat. Edit. *13*, 39 (1974).

Addition of a third molecule of hexachlorocyclopentadiene is impossible because of steric hindrance.

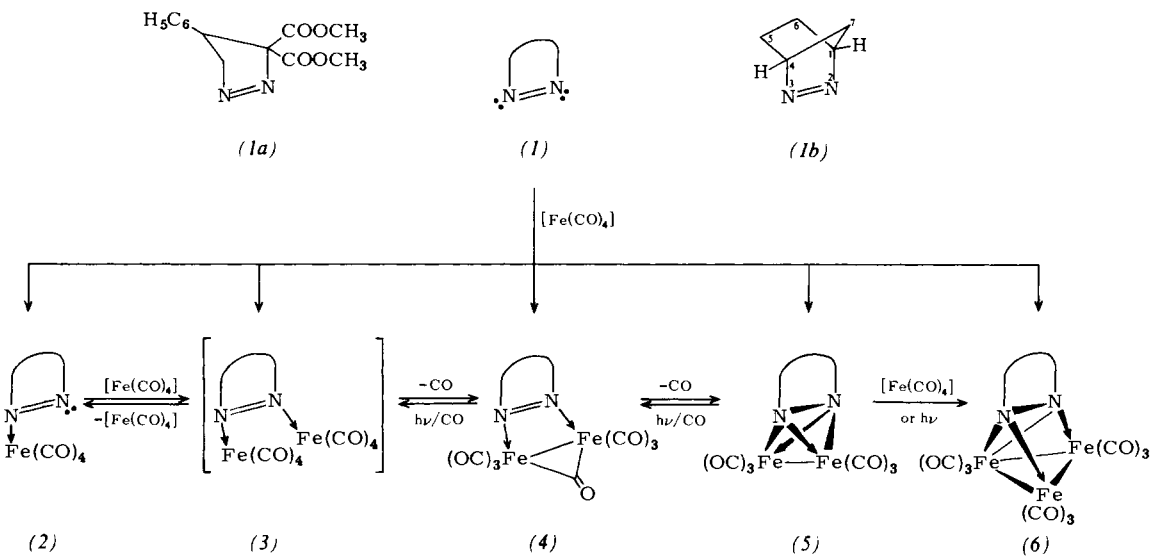
The relative shift of orbital energies occasioned by high pressure, which often leads to a new molecular ground state, may be responsible for the increased reactivity of benzene in the reactions described here[5].

Received: September 19, 1974 [Z 150 IE]
German version: Angew. Chem. 87, 201 (1975)

$(C_5H_8N_2)Fe_3(CO)_9$—An Iron Cluster Containing a *cis*-Diimine Unit[1]

By *Angelo Albini* and *Horst Kisch*[*]

Cyclic azoalkanes of medium ring size *(1)* are more suitable than open-chain azoalkanes for study of the complex-chemical behavior of the *cis*-azo group because they contain the isolated N=N double bond always in the *cis*-configuration. We recently showed that on irradiation of a mixture of $Fe(CO)_5$ and *(1a)* the mononuclear complex *(2a)* is formed in the first step of the reaction and that this combines with further carbonyliron fragments to afford the more stable binuclear complex *(5a)*[1]. To find whether the observation on this system is of general importance we have now investigated the reaction of iron carbonyls with 2,3-diazabornene *(1b)* and then isolated, besides the previously known $Fe_2(CO)_6$ complex *(5b)*[2,3], also an $Fe(CO)_4$ complex of type *(2)* and a trinuclear compound of the previously unknown structural type *(6)*.



(6b) crystallizes from acetone/*n*-hexane in shiny black prisms which sublime unchanged at 60 °C/0.04 torr. The mass spectrum, oxidative degradation and elemental analysis lead to the molecular formula $(C_5H_8N_2)Fe_3(CO)_9$. In the ^{1}H-NMR spectrum (C_7D_8) the bridgehead-protons appear as an apparent singlet with about the same chemical shift (7.0 τ) as for *(5b)* (7.2 τ); further, the ^{13}C-NMR spectrum ($CDCl_3$, TMS = 0 ppm) gives for C^1, C^4 and C^5, C^6 only one signal for each pair, at 66.6 and 31.5 ppm, respectively, whose positions again agree well with the data for *(5b)* (62.8 and 30.3 ppm, respectively). *(6b)* can be converted by dilute nitric acid into *(5b)*, in which the presence of an N—N bond is proved by X-ray structure analysis[4]. The IR spectrum (*n*-hexane) contains absorptions of the terminal CO groups at 2072 (s), 2021 (vs), 2012 (vs), 1993 (s), 1976 (s) and 1949 (vw) cm^{-1} and indicates C_{3v} local symmetry of the $Fe_3(CO)_9$ skeleton. On the basis of this finding the novel structure *(6b)* is proposed for the complex, with the *cis*-azo group bound to an $Fe_3(CO)_9$ cluster[5].

The mononuclear compound *(2b)* forms yellow-brown crystals that melt at 38—40 °C without decomposition. The mass spectrum contains the molecular ion and fragment ions that indicate successive removal of CO. The CO stretching vibrations (*n*-hexane) at 2055 (s), 1977 (vs), 1958 (vs) and 1940 (vs) cm^{-1} are largely the same as those of *(2a)* whose structure is proved by X-ray structure analysis[6]. The ^{1}H-NMR spectrum (C_7D_8) shows two broad apparent singlets at 5.65 and 5.45 τ for H^1, H^4 and confirm the unsymmetrical coordination of the ligand; further, for C^1, C^4 and C^5, C^6 the ^{13}C-NMR spectrum (C_7D_8) shows two signals for each pair, at δ = 89.3, 79.0 and 23.6, 22.4 ppm, respectively. When the temperature is lowered to −60 °C the bridgehead-protons yield only a single signal, at 5.8 τ, while the chemical shift for the carbon atoms and the IR absorptions of the CO groups remain unchanged[7]. We presume that rotation around the Fe—N bond is hindered and that at −60 °C a mixture of conformations exists whose ^{1}H-NMR spectrum appears fortuitously to indicate a symmetrical coordination of the ligand; the dependence of the UV spectra of *(2a)* and *(2b)* on temperature and on solvent provide indications in the same direction[8].

The mononuclear complex *(2b)* reacts with further carbonyliron, presumably by way of intermediates of type *(3)* that have not yet been isolated[11], thus giving the stable end products *(5b)* and *(6b)*. Irradiation of *(5b)* ($\lambda \geq 300$ nm) also provides *(6b)*, which is stable under these conditions. Recently a further binuclear complex was reported, for which structure *(4b)* is proposed; decarbonylation at room temperature affords *(5b)*, whence *(4b)* is regenerated on UV-irradiation in presence of CO[9]. IR spectroscopic investigation of this irradiation of *(5b)* shows that it yields also *(2b)* and *(6b)*.

The variety of the complexes isolated reflects the ability of the *cis*-azo group to function as a 2-, 4- or 6-electron donor. Preliminary study of the chemical reactivity of the Fe—N bond in these compounds was carried out with alkynes and

[*] Dr. H. Kisch and Dr. A. Albini [**]
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
433 Mülheim-Ruhr, Stiftstrasse 34—36 (Germany)

[**] A. A. thanks the Humboldt-Stiftung for a grant.

both *(5a)* and *(5b)*; alkyne is inserted, yielding three new types of complexes, which in the case of diphenylacetylene can be converted into tricarbonyl(tetraphenylcyclobutadiene)iron[10].

Experimental:

(2b): (1b) (6 g, 0.063 mol) and $Fe_2(CO)_9$ (6 g, 0.016 mol) are stirred in *n*-hexane (120 ml) until all the $Fe_2(CO)_9$ is consumed. Column chromatography at −10 °C (silica gel Serva 100—200 nm; *n*-hexane/toluene) and crystallization from ether/*n*-hexane afford analytically pure *(2b)* (1.4 g, 32%), m.p. 38—40 °C.—*(6b)*: Analogous to the preparation[2] of *(5b)*; chromatographic separation (neutral Al_2O_3; *n*-hexane/benzene) affords *(5b)*, and further elution with benzene affords *(6b)* in 20% yield; sublimes at 130 °C in a closed tube.

Received: September 30, 1974 [Z 152 IE]
German version: Angew. Chem. *87*, 206 (1975)

CAS Registry numbers:
(2a), 54515-75-2; *(2b)*, 54517-20-3; *(5b)*, 32507-01-0; *(6b)*, 54575-93-8; $Fe_2(CO)_9$, 15321-51-4

[1] Transition-metal Complexes of Azo Compounds, Part 3.—Part 2: *H. Kisch*, J. Organometal. Chem. *38*, C19 (1972).

[2] *R. P. Bennett*, Inorg. Chem. *9*, 2184 (1970).

[3] *M. Herberhold* and *W. Golla*, J. Organometal. Chem. *26*, C27 (1971).

[4] *R. G. Little* and *R. J. Doedens*, Inorg. Chem. *11*, 1392 (1972).

[5] X-ray structure analysis *(C. Krüger)* not yet complete.

[6] *C. Krüger*, Chem. Ber. *106*, 3230 (1973).

[7] We thank Dr. *K. Hildenbrand* for measurement of the ^{13}C-NMR spectra, and Dr. *F. W. Grevels* for valuable discussions.

[8] This appears to be a general property of complexes of type *(2)*.

[9] *M. Herberhold* and *K. Leonhard*, J. Organometal. Chem. 1974. We thank these authors for communicating results prior to publication.

[10] *H. Kisch*, Proc. XVI. Int. Conf. Coord. Chem., Dublin 1974, Abstr. 3.21.

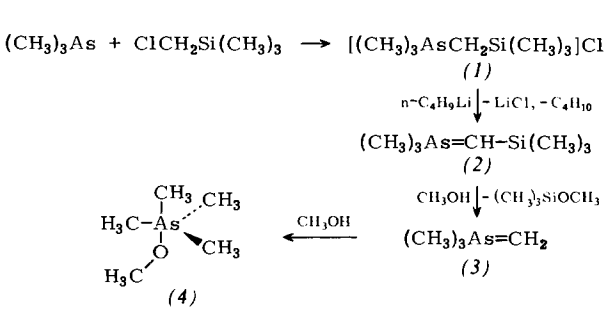
[11] *Note added in proof* (March 11, 1975): In the meantime complexes of type *(3)* have been prepared from diazirines and $Fe_2(CO)_9$; *A. Albini* and *H. Kisch*, J. Organometal. Chem. 1975, in press.

Methoxytetramethylarsorane, $(CH_3)_4AsOCH_3$

By *Hubert Schmidbaur* and *Wolfgang Richter*[*]

Compounds of formula R_4AsX are usually arsonium salts of strictly ionic structure, $R_4As^+X^-$[1]. Methoxytetramethylarsorane *(4)*, however, has now been found to be one of the few compounds of five-coordinate arsenic with covalent bonding, and thus the gap between methoxytetramethyl-phosphorane[2], $(CH_3)_4POCH_3$, and -stiborane[3], $(CH_3)_4SbOCH_3$, is closed.

For the synthesis[10] we used the method of desilylation[4] of the corresponding silyl-substituted arsenic ylide *(2)*[5] with



[*] Prof. Dr. H. Schmidbaur and Dipl.-Chem. W. Richter
Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

subsequent addition of methanol to the free trimethylmethylenearsorane *(3)*[6].

As in the corresponding phosphorus system[2, 4] the reactions *(2)* → *(3)* → *(4)* can be carried out either stepwise or as a "single pot" reaction, in both cases at −20 °C in diethyl ether as a solvent. *(4)* is formed as a colorless distillable liquid (b.p. 38 °C/17 torr) of high chemical reactivity. The compound fumes in air and, when finely divided, is self-inflammable. Its aqueous and alcoholic solutions react strongly alkaline since tetramethylarsonium hydroxide is immediately formed[7].

The ^{1}H- and ^{13}C-NMR spectra of toluene (or benzene) solutions of *(4)* at room temperature show virtual structural equivalence of the four methyl groups bound to arsenic. Only at very low temperatures, however, as with phosphorus analogs, is a splitting of the corresponding lines into two singlet signals (area ratio 3:1) observed. This proves also that *(4)* has a fluctuating trigonal-pyramidal structure[8] (Table 1). Here, for the first time with arsenic, it is possible to distinguish alkyl groups bound axially (a) and equatorially (e) in the same molecule; this has not yet been found for the homologous antimony compound[3].

Table 1. ^{1}H- and ^{13}C-NMR data for $(CH_3)_4AsOCH_3$ *(4)* in [D_8]-toluene, measured against TMS int. [ppm].

	T [°C]	δ(H_3CO)	δ(H_3CAs)
^{1}H	35	3.49	1.27
	−100	3.50	1.45 (e)
			0.00 (a)
^{13}C	0	51.6	20.9
	−105	52.4	17.0 (e)
			26.0 (a)

As with $(CH_3)_4POCH_3$, there is the surprising discovery that the resonance of the axial C atoms lies at lower field than that of the three equatorial C atoms, whereas the H atoms show the reverse relation. This phenomenon is presumably based on the *trans*-influence of the methoxy group.

The ^{13}C resonances of the ylidic C atoms of *(2)* and *(3)* are, however, as expected, recorded at high field and confirm the carbanionic nature of this structural unit[9].

Received: November 4, 1974;
revised: November 29, 1974 [Z 153 IE]
German version: Angew. Chem. *87*, 204 (1975)

[1] *G. O. Doak* and *L. D. Freedman*: Organometallic Compounds of Arsenic, Antimony and Bismuth. Wiley-Interscience, New York 1970.

[2] *H. Schmidbaur, H. Stühler*, and *W. Buchner*, Chem. Ber. *106*, 1238 (1973); *107*, 1420 (1974); Z. Anorg. Allg. Chem. *405*, 202 (1974).

[3] *H. Schmidbaur, J. Weidlein*, and *K. H. Mitschke*, Chem. Ber. *102*, 4136 (1969).

[4] *H. Schmidbaur* and *W. Tronich*, Chem. Ber. *101*, 595 (1968).

[5] *N. E. Miller*, Inorg. Chem. *4*, 1458 (1965).

[6] *H. Schmidbaur* and *W. Tronich*, Inorg. Chem. *7*, 168 (1968).

[7] *K. H. Mitschke* and *H. Schmidbaur*, Chem. Ber. *106*, 3645 (1973).

[8] *H. Schmidbaur, W. Buchner*, and *F. H. Köhler*, J. Amer. Chem. Soc. *96*, 6208 (1974). We thank Dr. *Köhler* also for the ^{13}C-NMR measurements recorded here.

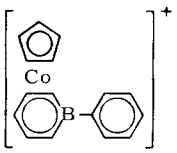
[9] *H. Schmidbaur, W. Buchner*, and *D. Scheutzow*, Chem. Ber. *106*, 1251 (1973); *H. Schmidbaur, W. Richter, W. Wolf*, and *F. H. Köhler*, Chem. Ber., in press.

[10] *Note: (4)* has meanwhile been obtained also from $(CH_3)_5As$ and MeOH: *J. Weidlein*, personal communication.

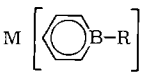
A New Route to Alkali-metal Borinates and to Complex Derivatives of Borabenzene[1]

By *Gerhard E. Herberich* and *Hans Jürgen Becker*[*]

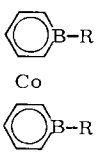
The history of borabenzene derivatives begins with the discovery of the cyclopentadienyl(1-phenylborinato)cobalt cation *(1)*[2] and the independent synthesis of a solution of lithium 1-phenylborinate *(2a)*, M = Li, in tetrahydrofuran[3].



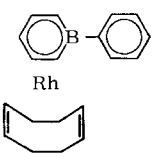
(1)



(2a), R = C_6H_5
(2b), R = CH_3



(3a), R = C_6H_5
(3b), R = CH_3



(4)

Because of their unusual electron configuration, bis(borinato)-cobalt complexes *(3)*, which like the cation *(1)* are accessible from $Co(C_5H_5)_2$ by ring expansion with organylboron dihalides[2b], tend to undergo reactions in which the destabilized metal-ligand bonds are cleaved. We have made use of this tendency previously in ligand-transfer and ligand-substitution reactions[4]. Synthetic possibilities leading much further are now opening up by liberation of alkali-metal borinates from the complexes *(3)*.

When heated with KCN or NaCN in acetonitrile[5], the compounds *(3)* are quantitatively degraded with formation of the corresponding alkali-metal borinates *(2)*, which, after removal of the sparingly soluble cyanides[6], can be used in the solution directly for further reactions or can be isolated as crude powdery products by removal of the solvent.

$$\underset{(3)}{Co(C_5H_5B{-}R)_2} \xrightarrow[(M = Na,\ K)]{MCN} \underset{(2)}{2\ M[C_5H_5B{-}R]}$$

In the case of potassium (1-phenylborinate) *(2a)*, M = K, we obtained, without further purification, ^{1}H-NMR spectra (in [D_8]-THF) that agreed almost completely with the recorded data for the lithium salt[3]; no by-product was recognizable. Thus solutions of alkali-metal borinates *(2)* have now become accessible in only two steps from $Co(C_5H_5)_2$ or in three steps from cyclopentadiene.

The borinates *(2)* can, analogously to the alkali-metal cyclopentadienides[7], be used for a large variety of complexation reactions. For example, from the potassium salt *(2a)*, M = K, and di-μ-chlorodi(1,5-cyclooctadiene)dirhodium[8] we have obtained the first complex borabenzene derivative of rhodium, namely (1-phenylborinato)-(1,5-cyclooctadiene)rhodium *(4)*[9].

$$[Rh(C_8H_{12})Cl]_2 + 2\ K[C_5H_5B{-}C_6H_5] \longrightarrow 2\ Rh(C_8H_{12})(C_5H_5B{-}C_6H_5) + 2\ KCl$$

(4)

Table 1. Data for (1-phenylborinato)-(1,5-cyclooctadiene)rhodium *(4)*.

MS (50 eV): *m/e* (I_{rel} [%]) 364 (100; M^+), 334 (9; $M^+ - C_2H_6 = Rh(C_6H_6)L^+$ with $L = C_5H_5B{-}C_6H_5$), 284 (9; $M^+ - C_4H_6 - C_2H_2$), 256 (35; RhL^+), 254 (30: $RhL^+ - H_2$), 230 (8; $RhL^+ - C_2H_2$), 228 (11; $RhL^+ - C_2H_2 - H_2$), 182 (9; $RhC_6H_7^+$), 180 (11; $RhC_6H_5^+$), 168 (11; $RhC_5H_5^+$); m* = 306.5 (364→334)

^{11}B-NMR (δ[ppm]); measured against external $(C_2H_5)_2O{\cdot}BF_3$ in [D_6]-benzene (100 MHz, room temperature):
-20.9 ± 0.5

^{1}H-NMR (τ[ppm]); measured against internal TMS in $CDCl_3$ [a] (60 MHz, room temperature):

C_6H_5		2.3 m (2H), 2.8 m (3H)	
C_5H_5B:	H^3, H^5	3.68 dd (2H)	$J_{23} = 9.0$ Hz
	H^2, H^6	4.04 d (2H)	$J_{34} = 6.0$ Hz
	H^4	5.02 t (1H)	
C_8H_{12}		6.09 m (4H), 8.05 m (8H)	

[a] In [D_6]-benzene H^2 and H^6 are accidentally isochronous with H^3 and H^5 and appear as a doublet, whereas H^4 is seen as a quintet.

Experimental:

a) *(3a)*[2b] (267 mg, 0.73 mmol) and KCN (1 g, 15 mmol) are heated in acetonitrile (15 ml) for 12 h under reflux with exclusion of air and moisture. After cooling and filtration from the sparingly soluble cyanides removal of the solvent affords $K[C_5H_5B{-}C_6H_5]$ *(2a)*, M = K, as a pale brown, powdery crude product, which is stable under N_2, readily soluble in CH_3CN or THF, but sensitive to water and slowly decomposed in methanol.

b) This crude product is heated with $[Rh(1,5\text{-}C_8H_{12})Cl]_2$[8] (630 mg. 1.28 mmol) in THF (15 ml) for 16 h under reflux. Chromatography on Al_2O_3 (air-free, deactivated by 4% of H_2O) with CH_2Cl_2 gives a pale yellow, rapidly moving first zone. The eluate from this is concentrated to a small volume, covered with pentane and left for crystallization on stepwise cooling to −78 °C. *(3a)* is obtained in 65% yield (347 mg), with m.p. 161—162 °C: it is stable in air; it crystallizes from CH_2Cl_2/pentane in pale yellow, square leaflets, readily soluble in benzene or CH_2Cl_2 but sparingly so in pentane.

Received: September 19, 1974 [Z 149 IE]
German version: Angew. Chem. 87, 196 (1975)

[*] Prof. Dr. G. E. Herberich
Institut für Anorganische Chemie der Technischen Hochschule
51 Aachen, Templergraben 55 (Germany)
Dr. H. J. Becker
Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[1] Derivatives of Borabenzene, Part 6. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and by Farbwerke Hoechst AG.—Part 5: [4b].

[2] a) *G. E. Herberich, G. Greiss,* and *H. F. Heil,* Angew. Chem. *82,* 838 (1970); Angew. Chem. internat. Edit. *9,* 805 (1970); b) *G. E. Herberich* and *G. Greiss,* Chem. Ber. *105,* 3413 (1972).

[3] *A. J. Ashe, III,* and *P. Shu,* J. Amer. Chem. Soc. *93,* 1804 (1971).

[4] Preparation of borinate complexes a) of Mn: *G. E. Herberich* and *H. J. Becker,* Angew. Chem. *85,* 817 (1973); Angew. Chem. internat. Edit. *12,* 764 (1973); b) of Fe: *G. E. Herberich, H. J. Becker,* and *G. Greiss,* Chem. Ber. *107,* 3780 (1974); c) of Co: *G. E. Herberich* and *H. J. Becker,* Z. Naturforsch. *28b,* 828 (1973); *29b,* 439 (1974); d) of Ni: unpublished work.

[5] Other aprotic media can also be used. Even in boiling methanol *(2a)* is the main product, but degradation products are also obtained by methanolysis as is recognizable by ^{11}B-NMR spectroscopy. Thus *(2a)* appears to be less basic than the $[C_5H_5]^\ominus$ ion; cf. $pK_a(C_5H_6) = 15.5$ according to *K. P. Butin, I. P. Beletskaya, A. N. Kashin,* and *O. A. Reutov,* J. Organometal. Chem. *10,* 197 (1967).

[6] Pale brown precipitate, not examined more closely, together with unconsumed MCN.

[7] Cf. *J. M. Birmingham,* Advan. Organometal. Chem. *2,* 365 (1964).

[8] *J. Chatt* and *L. M. Venanzi,* J. Chem. Soc. *1957,* 4735.

[9] Correct C, H analyses are available. The constitution follows from the NMR and MS data. Cf. data for other (1-phenylborinato)-metal groupings: [2b, 4a]; ^{1}H-NMR spectrum of Rh(1,5-C_8H_{12})(C_5H_5): *J. Lewis* and *A. W. Parkins*, J. Chem. Soc. *A 1967*, 1150; MS spectrum of Rh(1,5-C_8H_{12})(C_5H_5): *R. B. King*, J. Organometal. Chem. *14*, P19 (1968); Appl. Spectrosc. *23*, 148 (1969).

The NMR spectra of the complexes *(2)* show equivalence of the cyclopentadienyl protons and of the two terminal CH_2 groups of the allylic ligands. The C_5H_5 signal always appears as a 1:2:1 triplet, showing the symmetrical arrangement of the five-membered ring with respect to the phosphorus atoms.

Table 1. ^{1}H-NMR data for (C_4H_7)(C_5H_5)Pd_2L_2 *(2)* (TMS as internal standard; measurements for *(2b)* at 0°C, for *(2a)* and *(2c)* at room temperature; *J* in Hz).

Complex	Solvent	L		C_5H_5		H^1		H^2	CH_3	
		τ	J_{PH}	τ	J_{PH}	τ	J_{PH}	τ	τ	J_{PH}
(2a)	[D_6]-Benzene	2–3.2	—	4.04 (t)	1.5	7.2 (t)	6.5	8.44 (bs)	8.55 (t)	2.5
(2b)	[D_8]-Toluene	2.5–3.5	—	4.12 (t)	2.7	6.93 (t)	8	9.18 (bs)	9.47 (t)	4
(2c)	[D_8]-Toluene	6.62 (t)	6	3.86 (t)	2.3	6.55		8.64 (bs)	8.7 (t)	4

Preparation and Structure of Novel Binuclear Palladium Complexes Containing a Metal-Metal Bond: μ-(η-C_5H_5)-μ-(η-C_4H_7)Pd_2L_2[1]

By *Helmut Werner*, *David Tune*, *Graham Parker*, *Carl Krüger*, and *David John Brauer*[*]

The sandwich-like complexes (all)PdC_5H_5 react with Lewis bases L (molar ratio 1:4) with loss of the π-bonded ligands and formation of PdL_4[2, 3].

$$(all)PdC_5H_5 + 4\ L \longrightarrow PdL_4 + C_5H_5(all) \qquad (1)$$

all = C_3H_5, 2-$CH_3C_3H_4$, 2-ClC_3H_4, 1,1,2-$(CH_3)_3C_3H_2$, C_6H_9

L = $P(OCH_3)_3$, $P(OC_6H_5)_3$, $P(C_6H_5)_3$

The first step in the ligand replacement consists of attack by L on the metal and simultaneous π-σ rearrangement of the allylic group[4]. The further reaction steps are in general very fast with formation of the products indicated in eq. (1).

Reaction of (2-$CH_3C_3H_4$)PdC_5H_5 *(1)* and L in an *exact 1:1 molar ratio*, instead of 1:4, leads to formation of binuclear complexes (C_4H_7)(C_5H_5)Pd_2L_2 (with palladium formally in oxidation state +1) [eq. (2)]. Analogous compounds (C_3H_5)(C_5H_5)Pd_2L_2 can be detected by NMR spectroscopy in the system $C_3H_5PdC_5H_5$/L.

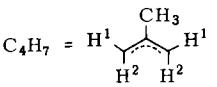
$$2\ (2\text{-}CH_3C_3H_4)PdC_5H_5 + 2\ L \longrightarrow \underset{(1)}{} \qquad (2)$$

$$(C_4H_7)(C_5H_5)Pd_2L_2 + C_5H_5(2\text{-}CH_3C_3H_4)$$

(2a), L = $P(C_6H_5)_3$
(2b), L = $P(OC_6H_5)_3$
(2c), L = $P(OCH_3)_3$

The product *(2a)* forms air-stable orange-yellow crystals, readily soluble in benzene or toluene but insoluble in pentane or hexane. The solutions decompose slowly at room temperature. Compounds *(2b)* and *(2c)* decompose rapidly in the solid state under N_2 at 25°C, but are stable for long periods at −30°C.

[*] Prof. Dr. H. Werner, Dr. D. Tune, and Dr. G. Parker
Anorganisch-chemisches Institut der Universität
CH-8001 Zürich, Rämistrasse 76 (Switzerland)
Dr. C. Krüger and Dr. D. J. Brauer
Max-Planck-Institut für Kohlenforschung
433 Mülheim-Ruhr 1, Kaiser-Wilhelm-Platz 1 (Germany)

C_4H_7 = 

Surprisingly, the coupling constant J_{PH^1} is greater than J_{PH^2} (see Table 1). This result contradicts the order of values for mononuclear π-allylpalladium complexes[5] and is probably due to the unusual position of the $CH_3C_3H_4$ group with respect to the Pd_2L_2 unit. Furthermore, the signal of the 2-methyl protons is a triplet owing to PH coupling; no corresponding splitting was observed for other 2-$CH_3C_3H_4$-palladium-phosphane complexes such as, *e.g.*, $C_4H_7PdCl(PR_3)$.

The crystal structure[6, 7] of *(2a)* is reproduced in Figure 1[8]. The compound contains an almost linear P—Pd—Pd—P group (P—Pd—Pd = 176.6°) with bond lengths Pd—Pd = 2.679 and Pd—P = 2.296 Å[9]. As expected from the NMR data, the cyclopentadienyl and also the methylallyl ligand are coordinated to *both* the palladium atoms. The C_5H_5 and the C_4H_7 planes are parallel to one another and these groups "sandwich" the metal-metal bond. An analogous coordination is probably also present in $(C_6H_6)_2Pd_2(Al_2Cl_7)_2$ (Pd—Pd bond length = 2.58 Å)[11].

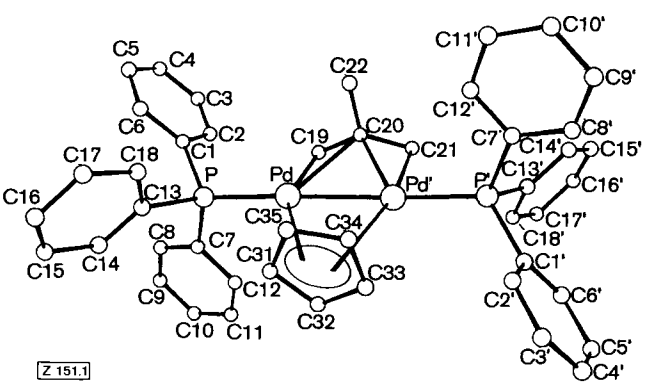


Fig. 1. Structure of the binuclear complex *(2a)* in the crystal; cf. Refs. [6–8].

To the best of our knowledge, *(2a)*—*(2c)* are the first examples of binuclear cyclopentadienyl-metal complexes in which a *five-membered ring spans an M_2 fragment exhibiting a metal-metal bond.* The new compounds react with Lewis acids and with Lewis bases.

μ-(η-Cyclopentadienyl)-μ-[1-3-η-(2-methylallyl)]bis(triphenylphosphanepalladium) (2a)

Triphenylphosphane (141 mg, 0.54 mmol) in toluene (5 ml) was added to a solution of $C_4H_7PdC_5H_5$ (122 mg, 0.54 mmol) in toluene (10 ml) under nitrogen. The mixture was stirred for 3 h at room temperature, the color changing from deep red to orange. After removal of half the solvent and addition of pentane (10 ml) the mixture was kept at −30 °C for 24 h. Orange-yellow crystals were formed; they were filtered, washed with pentane and dried in high vacuum. Yield 85%.

Received: September 30, 1974 [Z 151 IE]
German version: Angew. Chem. 87, 205 (1975)

[1] Part 17 of the series: Studies of the Reactivity of Metal π-Complexes. This work was supported by the Schweizerischer Nationalfonds.—Part 16: Ref. [12].

[2] *E. O. Fischer* and *H. Werner*, Chem. Ber. *95*, 703 (1962).

[3] *V. Harder* and *H. Werner*, Helv. Chim. Acta *56*, 549 (1973).

[4] *G. Parker* and *H. Werner*, Helv. Chim. Acta *56*, 2819 (1973).

[5] *K. Vrieze, A. P. Praat*, and *P. Cossee*, J. Organometal. Chem. *12*, 533 (1968); and literature cited therein.

[6] Crystal data: $a = 9.663(4)$, $b = 9.725(4)$, $c = 10.863(3)$ Å; $\alpha = 84.15(2)$, $\beta = 81.01(2)$, $\gamma = 72.32(3)°$; $Z = 1$; $d_{calc} = 1.49$ g cm^{-3}; $P\bar{1}$; 2206 reflections with $I > 0.5\,\sigma(I)$; $R = 0.089$ (Pd and P anisotropic).

[7] Both the cyclopentadienyl and the methylallyl groups are disordered in the crystal lattice; neither of them was taken into the refinement.

[8] The illustration shows an idealized arrangement of the cyclopentadienyl and methylallyl groups and not the disordered centrosymmetric atom distribution in the crystal lattice.

[9] The compound $(C_3H_5)(I)Pd_2[P(C_6H_5)_3]_2$ described recently has the bond lengths Pd—Pd = 2.686 and Pd—P = 2.278 Å [10].

[10] *Y. Kobayashi, Y. Iitaka*, and *H. Yamazaki*, Acta Crystallogr. *B 28*, 899 (1972).

[11] *G. Allegra, A. Immirzi*, and *L. Porri*, J. Amer. Chem. Soc. *87*, 1394 (1965).

[12] *H. Neukomm* and *H. Werner*, Helv. Chim. Acta *57*, 1067 (1974).

NSF_3 as Ligand in Transition Metal Complexes: (Thiazyl Trifluoride)pentacarbonylrhenium Hexafluoroarsenate[**]

By *Rüdiger Mews* and *Oskar Glemser*[*]

We recently reported the preparation of the first transition metal complexes containing nitrogen-sulfur-fluorine ligands[1, 2].

$$M(CO)_5Br + AgN(SO_2F)_2 \xrightarrow{-AgBr} M(CO)_5N(SO_2F)_2$$

(1), M = Mn, Re

$$M(CO)_5Br + AgNSOF_2 \xrightarrow{-AgBr} M(CO)_5NSOF_2$$

$M(CO)_5NSOF_2$ $\xrightarrow{-CO}$ *(2)*, M = Re

$M(CO)_5Br$ $\xrightarrow{-AgBr,\ -CO}$ $[M(CO)_4NSOF_2]_2$

(3), M = Mn, Re

[*] Prof. Dr. O. Glemser and Dr. R. Mews
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstr. 4 (Germany)

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

Structural investigations[3] on the complexes *(2)* and *(3)* show a great similarity of the sulfur oxide difluoride imide group with the isoelectronic thiazyl trifluoride[4]. It was already known that NSF_3 can function as a base toward very strong Lewis acids[5, 6].

$$NSF_3 + MF_5 \longrightarrow F_5M \cdot NSF_3 \quad (M = As, Sb)$$

$$NSF_3 + BF_3 \longrightarrow F_3B \cdot NSF_3$$

$Ag^+AsF_6^-$ can react quantitatively with $Re(CO)_5Br$ under pressure in NSF_3 as solvent at room temperature in accordance with the following equation:

$$\underset{(4)}{Ag^+AsF_6^-} + \underset{(5)}{Re(CO)_5Br} \xrightarrow[-AgBr]{NSF_3} \underset{(6)}{[Re(CO)_5NSF_3]^+[AsF_6]^-}$$

Reaction of *(4)* and *(5)* gives rise to the coordinatively unsaturated cation $Re(CO)_5^+$ as intermediate; this reacts as acid with the weakly basic solvent to give *(6)*.

The thiazyl trifluoride complex *(6)* is a colorless, crystalline solid which is stable at room temperature (decomposition at 123 °C); it has been characterized by elemental analysis and ^{19}F-NMR and IR spectra. The ^{19}F-NMR spectrum (solution in SO_2, $CFCl_3$ int., room temperature) shows a singlet at −60.8 ppm (NSF_3); the expected 1:1:1:1 quartet ($\delta_F = +59.5$ ppm, $J_{AsF} = 916$ Hz) is found for AsF_6^-. The structure of compound *(6)* follows unequivocally from the IR spectrum. The three absorptions [A_1 2175 (m), E(2084 sh) 2057 (vs), A_1 2010 cm^{-1} (s)] to be expected for C_{4v} symmetry of the central atom are observed in the CO region; these are accompanied by the IR-forbidden B_1 at 2108 cm^{-1} (vw). Because of the positive charge in *(6)* all bands are shifted to higher wave numbers compared to the isoelectronic $Re(CO_5)NSOF_2$[2]. The frequencies of the NSF_3 ligands in transition metal complexes are almost constant (cf. Table 1).

Table 1. IR data [cm^{-1}] of thiazyl trifluoride and a few of its coordination compounds.

	NSF_3	$F_5As \cdot NSF_3$	$F_5Sb \cdot NSF_3$	*(6)*	*(7)* [a]	*(8)* [a]
ν_{SN}	1515 m	1650	1650	1636 m	1637 m	1632 m
ν_{SF}	811 vs	950	955	900 sh	882 s	888 sh
				889 s		876 s
	775 s	889	900	846 s	838 s	830 s

[a] *(7)*: $[Mn(CO)_5NSF_3]^+AsF_6^-$; *(8)*: $[\pi\text{-}CpFe(CO)_2NSF_3]^+AsF_6^-$; preparation, properties, and structure of these compounds will be published in Chem. Ber.

Compared with the free ligands the bands in the transition metal complexes suffer less shift to higher wave numbers than in the adducts with arsenic or antimony pentafluoride—which seems reasonable in view of the acid strength. This

[1] *R. Mews* and *O. Glemser*, Z. Naturforsch. *28b*, 362 (1973); *R. Fröböse, R. Mews*, and *O. Glemser*, to be published in Z. Naturforsch B.

[2] *R. Mews* and *O. Glemser*, J. C. S. Chem. Comm. *1973*, 823.

[3] *B. Buss, D. Altena, R. Mews*, and *O. Glemser*, to be published in J.C.S. Chem. Comm.

[4] *W. H. Kirchhoff* and *E. B. Wilson, Jr.*, J. Amer. Chem. Soc. *84*, 334 (1962).

[5] *O. Glemser* and *W. Koch*, An. Asoc. Quim. Argent. *59*, 143 (1971).

[6] *O. Glemser, H. Richert*, and *H. Haeseler*, Angew. Chem. *71*, 524 (1959); *O. Glemser* and *H. Richert*, Z. Anorg. Allg. Chem. *307*, 318 (1961); *A. Müller, O. Glemser*, and *K. Scherf*, Chem. Ber. *99*, 3568 (1965).

comparison also shows that the ligand is bound to the central atom *via* nitrogen.

Experimental:

Equimolar amounts of *(4)* and *(5)* [2.2 and 3.0 g (7.4 mmol), respectively] in NSF_3 (10 ml) are stirred for 12 h at room temperature in absence of light in a glass bomb furnished with a teflon valve. The solvent is removed and the reaction product *(6)* is dissolved in SO_2 and separated from AgBr by filtration. The yield is quantitative.

Received: December 23, 1974 [Z 170 IE]
German version: Angew. Chem. 87, 208 (1975)

CONFERENCE REPORTS

Systems of Carbohydrate Utilization in Bacteria

By *Kurt Wallenfels*[*]

Utilization of carbohydrates of the nutrient medium as a source of carbon for bacterial growth is subjected to gene-dependent regulation. Control loops exist for autocatalytic enhancement of active transport, *i.e.* enrichment against a concentration gradient, chemotaxis, and primary conversion into metabolizable monosaccharides or their derivatives, depending upon the signal emitted by the nutrient medium. The best studied example is the lac system of *E. coli* which optimizes utilization of natural β-galactosides—lactose or 2-*R*-β-galactosylglycerol.

Galactosylglycerol has a chemotactic action on *E. coli*, and is transported independently of the lac operon into the cell where it induces the lac operon by interaction with the lac repressor, so that synthesis of its dependent proteins is enhanced 10^3 to 10^4-fold.—Lactose must first be converted into allolactose (6-β-galactosylglucose) by the basal activity of β-galactosidase; allolactose forms the inducer. Lactose is then transported by lac permease, which is dependent upon the lac operon.

The control loop can be split up, and the growth behavior of the culture modified, by mutation in one of the genes coding for repressor formation, for lac permease, for β-galactosidase, or for galactosylglycerol permease (studies with *B. Müller-Hill* and *W. Boos*).

With *Aerobacter aerogenes*, utilization of macromolecules such as starch or pullulan is dependent upon an enzyme (pullulanase) which hydrolyzes the 1,6 bonds in these substrates. This enzyme is localized on the exterior of the cell wall and serves for the formation of α-1,4-linked maltosaccharides which migrate into the cell, presumably by active transport. Their conversion into metabolizable monomers is accomplished by phosphorolysis or hydrolysis. Aerobacter phosphorylase has been isolated as a homogeneous protein and its close relationship to the phosphorylases of eucaryotes established by determinations of molecular weight, pH optimum, amino acid composition, and pyridoxal phosphate content. The bacterial phosphorylase also degrades the reserve polysaccharide of the bacteria (aerobacter glycogen) but hardly affects mammalian glycogen. Hydrolysis of the maltooligosaccharides and -polysaccharides and of the 1,6 branching of the limit dextrins of the bacterial glycogen is effected by two amylases and a 1,4- and 1,6-specific glucosidase, which can be separated by the trick of "substrate alienation". The two amylases can be distinguished in that one fraction (230000 dalton) cleaves *o*-nitro-α-phenyl glucoside, while the other (35000 dalton) cleaves *o*-nitrophenyl α-maltoside. The third enzyme (86000 dalton) accepts maltose, isomaltose, saccharose, maltotriose, and presumably other α-glucosyl oligosaccharides resulting from amylopectin and pullulan degradation, as substrates. The regulatory system for the bacterial utilization of starch and similar polysaccharides as a source of carbon from the external medium or from the internal reserves is considerably more complex than the lac system, in keeping with the larger number of enzymes involved (studies with *H. Bender*, *P. Földi*, *G. Kurz*, *D. Linder*).

[*] Prof. Dr. K. Wallenfels
Lehrstuhl-Biochemie, Chemisches Laboratorium der Universität
78 Freiburg, Albertstrasse 21 (Germany)

Lecture at Kiel, December 19, 1974 [VB 380 IE]
German version: Angew. Chem. 87, 139 (1975)

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

Chemotaxis as a model for sensory systems is discussed in an article by *D. E. Koshland Jr.* Bacteria, the simplest objects of study, do not respond to absolute concentrations of stimulating substances, but to changes of concentration with time. A specific receptor protein is responsible for the primary binding of each stimulant; further transmission of the various primary stimuli to a common system is still a subject of hypothesis. The duration of the "memory" for *Salmonella* has been calculated as 1—10 s. [Chemotaxis as a Model for Sensory Systems. FEBS Lett. *40*, S3—S9 (1974); 28 references] [Rd 753 IE—R]

The life cycle of RNA phages is reported on by *C. Weissmann*. Because of their smallness these phages are ideal model systems suitable for the study of fundamental biological processes at a molecular level. The article deals with the process of

infection of the bacterial cell by the phages, insertion of the phage RNA into the ribosomes of the host, synthesis of the virus, and the lysis of the bacterial cell, in which the new phage generation is set free. [The Making of a Phage. FEBS Lett. *40*, S10—S18 (1974); 102 references]

[Rd 754 IE—R]

The control of gene expression at the transcription level is reviewed in an article by *F. Gros*. The validity of the classical operon model could be demonstrated by refined biochemical techniques. Nevertheless, it turned out that many of the original hypotheses contain excessive simplifications. This applies to the complexity of the repressor molecules and their multifarious functions, the expiration of the gene expression with time in developing organisms, and the crucial significance of the conformation of the DNA for its function. [Control of Gene Expression in Prokaryotic Systems. FEBS Lett. *40*, S19—S27 (1974); 168 references]

[Rd 755 IE—R]

Progress in the field of antiviral agents is reviewed by *D. Shugar*. Only a few substances of this type have so far gained a firm foothold in therapy. A particularly interesting aspect is the connection between antiviral activity and antitumor activity which has been observed in some cases. The specificity and mode of action of purine and pyrimidine derivatives and of nucleoside and nucleotide derivatives and their analogs are discussed; the potential dangers in the therapeutic use of these substances and the possible enhancement of the activity on simultaneous utilization of several agents are demonstrated. [Progress with Antiviral Agents. FEBS Lett. *40*, S48—S62 (1974); 144 references]

[Rd 758 IE—R]

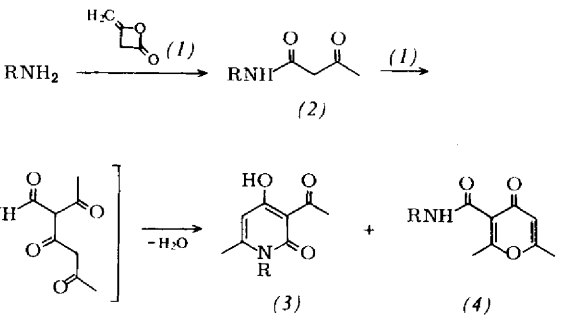
Inhibitors of protein synthesis form the theme of a review article by *D. Vazquez*. The author discusses the results of research over the past ten years regarding the mode of action, selectivity, and specificity of inhibitors. The process of protein biosynthesis is appropriately subdivided into the stage prior to translation, and translation proper. The inhibitors can suppress formation of aminoacyl t-RNA and f-Met t-RNA_F before translation, and the processes of initiation, elongation, and termination during translation. [Inhibitors of Protein Synthesis FEBS Lett. *40*, S63—S84 (1974); 410 references]

[Rd 759 IE—R]

The synthesis of heterocycles with organophosphorus compounds is dealt with in a review by *E. Zbiral*. Tetrahydropyrans, thiacyclohexanes, dibenzo[*b*,*f*]oxepins, coumarins, acridinium betaines, *etc.* are obtained *via* carbonyl-olefination with alkylidenephosphoranes; with 2-oxoalkylidenephosphoranes and a second component, 1,3-dipolar cycloaddition affords 1,2,3-triazoles, pyrazoles, 1,2-oxazoles, and azirines. Iminophosphoranes (P—N ylides) can be used for the synthesis of tetrazoles, pyrazines, 1,2,4,5-tetrazines, 1,2,4-benzotriazines, 1,3-oxazoles, *etc.* Vinylphosphonium salts, *e.g.* triphenylvinylphosphonium bromide, afford pyrrolizines, furan derivatives, chromenes, quinoline derivatives, pyrroles, and pyrazole derivatives; 3-oxo-1-alkenylphosphonium salts (β-acylvinylphosphonium salts) lead to 1,2,3-triazoles, pyrazoles, 1,3-thiazoles, pyrroles, imidazoles, and heterocyclic condensed imidazoles. With vinylphosphane oxides, phosphorus-containing derivatives of dihydro-1,2-oxazoles, dihydropyrazoles, and pyrazoles are formed. [Synthesen von Heterocyclen mit Hilfe von Alkylidenphosphanen, Phosphin-imiden, Vinylphosphonium-salzen und Vinylphosphin-oxiden. Synthesis *1974*, 775—797; 87 references]

[Rd 764 IE—M]

Novel reactions of diketene *(1)* with nitrogen compounds are reported by *T. Kato*. With amines, acetoacetamides *(2)* are formed which in the presence of triethylamine undergo cyclization with elimination of water to give 2-pyridones *(3)* and 4-pyrones *(4)*. Enamines and compounds with C=N double bonds can react with diketene to give 2- and 4-pyridones as well as 1,3-oxazinones. They can annelate further



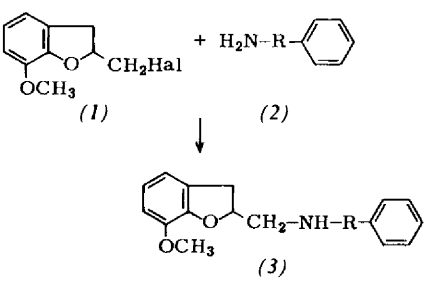
rings to nitrogen heterocycles, *e.g.* pyridine, quinoline, and acridine derivatives, *via* acetoacetamide intermediates. Spiro compounds can be obtained by cycloaddition to the C=C double bond of diketene. [Recent Synthetic Studies Using Diketenes. Accounts Chem. Res. 7, 265—271 (1974); 59 references]

[Rd 767 IE—L]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

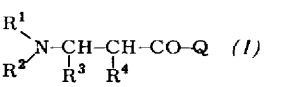
2,3-Dihydro-7-methoxybenzofuran derivatives *(3)* have very good analgetic properties and low toxicity. They are prepared



from the halo compounds *(1)* and the amines *(2)*. R is a bivalent saturated or unsaturated aliphatic group (C_1 to C_4). [DOS 2263093; Eisai Co., Tokyo (Japan)]

[PR 240 IE—K]

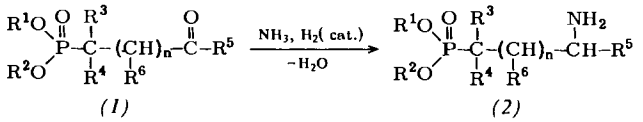
Catalysts with only slight odor for the preparation of polyurethane foam materials, in particular highly elastic soft foam materials, can be selected from among β-amino carbonyl compounds of formula *(1)*, where NR^1R^2 represents a dialkylamino, mor-



pholino, or substituted piperazinyl group, R^3 and R^4 are H or a lower alkyl group, and Q is a C_1 to C_8 alkoxy, *N,N*-dialkylaminoethoxy, or *N,N*-dimethylamino group. [DOS 2358861; Union Carbide Corp., New York (USA)]

[PR 245 IE—D]

Aminoalkylphosphonic esters *(2)* are interesting intermediates for the synthesis of flame-retarding and surface-active materials. They can be prepared from the oxoalkylphosphonic esters



(1) *(2)*

R^1, R^2 = alkyl or R^1—R^2 = alkylene; R^3 = H or alkyl; R^4 = H, alkyl, (subst.) aryl, or furyl; R^5 = H or alkyl or R^4—R^5 = alkylene; R^6 = H or alkyl; n = 0 or 1

(1) by aminating hydrogenation. Compounds *(1)* are accessible by *e.g.*, base-catalyzed addition of vinyl ketones to dialkyl phosphites. [DOS 2358836; Ciba-Geigy AG, Basel (Switzerland)]

[PR 246 IE—D]

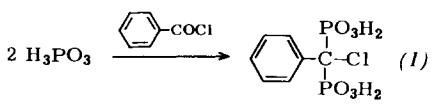
For the preparation of foams from aqueous silicate solution, hydrogen peroxide and a reducing agent, *e.g.* paraformaldehyde or hydrazine, are added. The mixture foams with considerable evolution of heat and becomes hard. [DOS 2227640; Bayer AG, Leverkusen (Germany)]

[PR 256 IE—W]

Copolymerization of ethylene oxide or propylene oxide with carbon dioxide, to give polyethylene carbonates or polypropylene carbonates, can be effected with a catalyst produced from diethylzinc, diethylmagnesium, or triethylaluminum chloride together with water or magnesium sulfate heptahydrate as cocatalyst at 5 to 50 atm and 100 to 200 °C. [DOS 2336854; Nippon Oil Seal Industry Co., Ltd., Fujisawa, Kanagawa (Japan)]

[PR 254 IE—W]

α-Chlorobenzylidenediphosphonic acid (chloro(phenyl)methane-1,1-diphosphonic acid) *(1)*, suitable as a complexing agent, is obtained by heating phosphorous acid with benzoyl chloride at 110—140 °C, preferably in the molar ratio of 1:1.5. *(1)* can be isolated as the sodium salt after separation of the by-products. Because of its good ability to form complexes

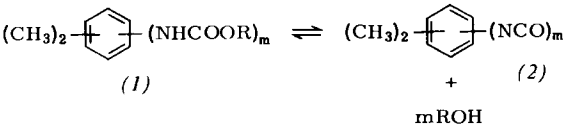


(1)

with multivalent metal ions, its stability against compounds containing active chlorine, and its resistance to hydrolysis at relatively high temperatures, *(1)* and its salts are useful for numerous industrial applications such as industrial cleansers or for water softening processes. [DOS 2310451; Henkel & Cie, Düsseldorf (Germany)]

[PR 247 IE—D]

Thermal dissociation of urethanes *(1)* leads almost quantitatively to the isocyanates *(2)* if conducted as an uncatalyzed process with a short contact time. The urethanes *(1)* are preferably pyrolyzed in the temperature region 350—550 °C at a preferred total pressure within the range 4—105 torr and a residence time of less than 15 s. To avoid the reverse reaction the fission products must be cooled rapidly under



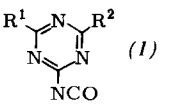
(1) *(2)*

R = CH_3, C_2H_5, *n*-C_3H_7, or *n*-C_4H_9; m = 1, 2, or 3

conditions such that the isocyanate condenses but at least 95 % of the alcohol remains in the vapor form. [DOS 2410505; Air Products and Chemicals, Inc., Allentown, Pa. (USA)]

[PR 248 IE—D]

For the preparation of mono- or diisocyanato-*s*-triazines *(1)* the corresponding *s*-triazinylamines are treated in solution at 150 °C (minimum) with phosgene, if necessary in the presence of a catalyst such as dimethylformamide. 3-Alkoxypropioni-



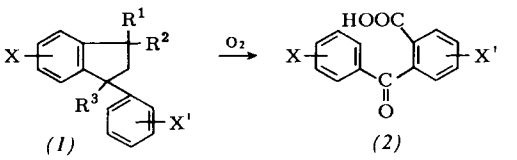
(1)

R^1 = —NCO, halogen, OR', SR', or NR'R"; R^2 = halogen, C_6H_5, R', OR', or NR'R"; R' and R" = alkyl

triles with 1—4 C atoms in the alkoxy group, nitrobenzene, tetrahydrothiophene 1,1-dioxide, and *o*-dichlorobenzene are suitable solvents. [DOS 2409084; Ciba-Geigy AG, Basel (Switzerland)]

[PR 249 IE—D]

Halogenated *o*-benzoylbenzoic acids *(2)* are obtained by liquid-phase oxidation (25—30 atm, 160 °C, 3—4 h) of halogenated indans *(1)* by oxygen in the presence of heavy-metal salts



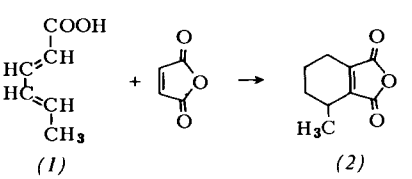
(1) *(2)*

R^1, R^2, R^3 = H or alkyl; X, X' = halogen

and a compound that affords bromide ions. Cobalt and manganese salts are suitable heavy-metal compounds. [DOS 2259681; BASF AG, Ludwigshafen (Germany)]

[PR 242 IE—G]

Isomer-free 3,4,5,6-tetrahydro-3-methylphthalic anhydride *(2)*, a hardener for epoxy resins, is obtained by the addition of sorbic acid *(1)* to maleic anhydride at 80—200 °C, decarboxy-

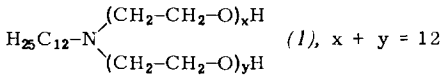


(1) *(2)*

lation occurring simultaneously. [DOS 2315040; Ciba-Geigy AG, Basel (Switzerland)]

[PR 252 IE—W]

For the preparation of flowing powder, filler-containing rubber mixes, a rubber solution is emulsified in water in the presence



(1), x + y = 12

of compounds *(1)*. A solid filler, *e.g.* carbon black, is introduced and the mixture is precipitated in aqueous sodium silicate (water glass) at 90—95 °C and a pH of preferably 1.0 to 3.5. The solvent, *e.g.* hexane, is distilled off continuously. [DOS 2214121; Chemische Werke Hüls AG, Marl (Germany)]

[PR 250 IE—W]

BOOK REVIEWS

Buffers for pH and Metal Ion Control. By *D. D. Perrin* and *B. Dempsey*. Chapman and Hall, London 1974. 1st Edit., vii, 176 pp., numerous tables, bound £3.50

Many chemical and biological systems are governed by acid-base equilibria and are therefore critically dependent on the pH of the solution. The pH conditions can be altered by addition of a buffer, a pair consisting of a Lowry-Brönsted acid and its conjugate base. In practice the question arises again and again as to the buffer system most suitable for the individual case, and in this respect the present laboratory primer will be welcomed by all biologists and chemists who have to deal with pH and metal ion buffers in aqueous and nonaqueous media. The theoretical fundamentals are first discussed, briefly and strictly from the standpoint of practical use, this being followed by collections of data about buffers scattered throughout the literature: zwitterion buffers, particularly those for biochemical work and separations, for biological and medical applications, and for physicochemical measurements, as well as metal ion buffers and standards for ion-selective electrodes are tabulated in complete detail, partly in appendices. The limitations and pitfalls in working with buffers are discussed, as are the disturbances to be borne in mind on a particular choice of buffer, but here unfortunately without always referring to the literature. The competition of structurally similar sugars with Tris buffers could have been added. The construction of pH-buffer tables from the thermodynamic p*K* values is explained: the appended programs are in FOCAL instead of the BASIC that is understood by the usual desk-top computers, but transposition is not difficult. The experimentalist will also welcome the description of the purification of buffers and the introduction to the preparation of standard solutions. The book thus constitutes both a useful and a reliable and convenient aid in every chemical, biochemical, or biological laboratory.

L. Jaenicke [NB 246 IE]

Mathematik für Naturwissenschaftler und Ingenieure (Mathematics for Scientists and Engineers). Vol. 1. Vector, differential and integral calculus. By *A. Jeffrey*. Translated by *R. Janoschek*. Verlag Chemie GmbH, Weinheim 1973. 1st Edit, viii, 385 pp., 86 figures, 18 tables, paperback, DM 39.—.

This book is based on an introductory course in mathematics for engineering students, corresponding roughly to the material of Analysis I and II used at German universities. The original English edition, comprising one volume, has been divided into two volumes in the translation. The eight chapters of Volume 1 deal with the material of Analysis I, *i.e.* with differential and integral calculus. Chapter 1 begins with a short introduction to the elementary theory of sets and describes the basic properties of the real number system; the modern notation is used. After this concession to modern trends in current mathematics the author remains for the rest of the book within the usual "classical" framework of analysis.

The following three chapters deal with the concept of a function, numerical series, and complex numbers, and then lead on to elementary vector calculus. Chapter 5 is concerned with differentiation, including partial derivatives. A special chapter on exponential functions, hyperbolic functions, and logarithms is followed by the two final chapters on integral calculus with a detailed description of integration procedures.

A remarkable feature of this book is that it is an attempt—otherwise rarely undertaken—to combine rigorous mathematical methods of proof with opportunity to practice the calculation techniques. The author has certainly succeeded in attaining this aim, by apt selection of the material.

The mathematical proofs provided with every important statement are simple and clear and are thus easily understood. Moreover, the text contains many examples with detailed descriptions of the approach to the solution, which makes it easy for the reader to learn how to handle formulas and relationships. Numerous practice exercises at the end of each chapter contribute to this aim; hints on how to arrive at the solution are given in the Appendix. The examples and practice problems are taken from scientific and technical fields wherever possible, in order to demonstrate the range of application of the mathematical apparatus. The systematic division into text, definitions, propositions, and examples increases the clarity of the work.

The book may be highly recommended to all students of scientific and technical disciplines in the first few terms and also for private study.

Theo Ankel NB 245 IE]

Comprehensive Biochemistry. Vol. 29 A. Comparative Biochemistry, Molecular Evolution. Edited by *M. Florkin* and *E. H. Stotz*. Elsevier Scientific Publ. Comp., Amsterdam 1974. 1st Edit., xii, 328 pp., 67 figures, 20 tables, bound Dfl. 90.—.

The present volume in this still continuing series of texts[*] contains two chapters, both dealing with evolution: "Concepts of Molecular Biosemiotics and of Molecular Evolution" by *M. Florkin* and "Biochemical Evolution in Plants" by *T. Swain*. The first of these titles will convey little even to a fairly sophisticated reader. A glossary provides help, in which he finds, *e.g.* "Bioseme. Minimal configuration aspect, carrier

[*] Cf. Angew. Chem. internat. Edit. *13*, 825 (1974).

(significator) of the molecular signification (signified) either sequential, structural, *etc.*"—but also: "Allomones. Coactones (q.v.), ...; Coactones. Ecomones (q.v.), ...; Ecomones ...."; etc. All 110 pages are loaded with this kind of freight, which makes severe demands on the reader. The intention is to bring systematic order into the presentation of phylogenetic development, in which the evolution of life is assumed to be from simple biomolecules by asymmetric, autocatalytic, and aggregating forces. The molecular processes occurring during phylogenesis of organisms ("diachronic molecular epigenesis") are mostly considered on the basis of cellular chain molecules ("metabolic catenary biosyntagmas") which become better suited to their structure, function, or regulation, and more versatile, by lengthening or shortening, branching and ramification. The causes are point mutations, feedback, selection, gene duplication, *etc.* Useable biomolecules thus function after self-aggregation into structures of higher order on the physiological and ecological plane. The author's phenomenal knowledge of the facts and historical perspectives and his intellectual insight into his material can only be marvelled at—only the preparation of the dish makes it hard to digest.

The subsequent vegetarian fare is simpler and more heart-warming, the more so since it is spiced with anecdotal asides. Plants and animals are of the same age on the evolutionary time-scale, but the former have adapted themselves much more intelligently—being bound to one place—in order to come to grips with their living space. While animals differ little in their fundamental biochemical capacities—but all the more so in their controlled types of behavior—plants produce a highly diverse range of materials that make their survival possible. The development and the distribution of cellular macromolecules, the primary and secondary constituents of the plant kingdom, are discussed and it is brought out how the various secondary biosynthetic routes determine which niche the given plant will adopt in the ecosystem. Change is the mother of evolution and woe betide him who attempts to confine biochemical evolution in a procrustean bed! In this volume the promised standard of content and production is maintained; it is announced that the second sub-volume will deal with the molecular evolution of bacteria and animals; after that there will still be seven further volumes before the whole series is complete.

L. Jaenicke [NB 247 IE]

Absorption Spectroscopy of Organic Molecules. By *V. M. Parikh*. Addison-Wesley Publishing Co., Reading, Mass 1974. 1st Edit., x, 325 pp., paperback $ 10.75.

Since the intrusion of modern spectroscopic methods into all subdisciplines of chemistry, and thus into general training programs for chemists, there has been no lack of attempts to write books presenting these techniques in a simple manner. We have noted a total of about 20 titles intended as an introduction to these methods for students.

V. M. Parikh has now written a further book of this kind. Following upon a general introduction to spectroscopy he deals with UV, IR, and NMR spectroscopy, and mass spectrometry in four sections, dividing the material into general/-theory, instrumental and evaluation of spectra. Then come a section on the identification of organic compounds with examples and an appendix of tabular surveys (IR and NMR assignment tables *etc.*). Each chapter closes with test questions and a bibliography which is quite extensive in some cases.

Unfortunately, the book which is clearly intended for students, contains a number of failings likely to confuse the beginner but unlikely to distract the expert. Thus some of the IR spectra exhibit precisely those mistakes which are symptomatic of the beginner and whose elimination can be regarded as the primary task of such introductory books ("negative absorptions", excessive amounts of sample, *etc.*). Moreover, the NMR spectra are poorly reproduced (very dark background, poor plotting). In some of the spectra the integration can only be recognized with difficulty. In addition, references to journals unlikely to be found in college libraries (*e.g.* Phil. Mag., Sov. Phys. Tech. Phys., Vacuum, J. Sci. Instrum.) will be of little to help to students. Hence the book has to be pigeon-holed somewhere between an introduction and a monograph and can only really be recommended to those concerned with the teaching of instrumental analysis. Such readers may indeed profit from a variety of ideas found in the book.

Egon Fahr [NB 242 IE]

Orbitale organischer Moleküle (Orbitals of organic molecules). By *W. L. Jørgensen* and *L. Salem*. Translated by *E. König*. Verlag Chemie GmbH, Weinheim 1974. 1st Edit., x, 294 pp., 1180 figures, bound DM 32.—.

The authors intend this book (original edition: The Organic Chemist's Book of Orbitals, 1973) for "a new generation of chemists eager to understand molecular structure at the electronic level". They begin with an introduction (44 pages) to the qualitative construction of σ- and π-type molecular orbitals from group and bond orbitals, while assuming their "reality" and practical "utility", ask for chemical applications, and cite references for further reading (76 titles) including such topics as the frontier orbital and the relaxability methods.

The comparison of qualitative orbitals with the perspective computer plots of contours of eigenfunctions obtained by extended Hückel or open-shell MINDO/2 calculations presented on 226 pages is impressive. Clarity is enhanced by suitable normalization, avoidance of changes of perspective, and the use of solid and dashed contours. Skillful arrangement of the very complicated drawings permits combination of the sets of orbitals to give projectable pictures and supplementation by the tabulated occupations. Details concerning the calculation are given for all examples of 104 conformers of 95 molecules (14 containing no carbon atom) with 2 (hydrogen) to 36 (cyclohexane, norbornadiene) valence electrons, and new molecular geometries are cited. In all except four cases, all occupied and several unoccupied (2.4 on average) orbitals are depicted, with group-theoretical and, wherever sensible, orbital type designations, and assignments to known *ab initio* orbital energies. It is accepted that the various methods of calculation may also differ with regard to the geometric parameters. This fact alone should induce one to compare the orbital sequences thus defined with results or interpretations of photoelectron spectroscopy.

Notwithstanding a number of unclear points in the translation and the occasional rather unfortunate choice of terms (*e.g.* "Äthyl-Radical, halbiert" or "Benzol, Dewar-Form") the book is eminently suitable for the illustration of semi-empirical wave functions in the teaching of quantum chemistry.

Gerd Kaupp [NB 244 IE]

Lehrbuch der Organischen Chemie. (Textbook of organic chemistry). By *R. T. Morrison* and *R. N. Boyd*. Translated by *I. Mayer-Ruthardt*. Verlag Chemie GmbH, Weinheim 1974. 1st Edit., xxxiii, 1392 pp., 225 figures, 46 tables, bound DM 78.—.

The present German translation of the third edition of "Organic Chemistry" will be of great value to chemistry stu-

dents, and to those requiring a source of readily accessible information, in German speaking countries.

The work is divided into three main sections. Part 1 deals with fundamentals (881 pages), and part 2 treats specialist fields (251 pages). Biomolecules is the collective term for the material presented in part 3. (139 pages). From the entire field of organic chemistry and a number of bordering areas an excellent choice of material has been made, and the subject matter is presented in a didactically skilled manner.

Apart from the most important classes of substances, part 1 contains individual chapters on structure and properties, stereochemistry (subdivided into stereochemistry and structure and stereochemistry and reactions), spectroscopy, and carbanions. In keeping with the material part 2 has a more heterogeneous structure. A chapter on aryl halides and nucleophilic aromatic substitution is followed by chapters on reactions of carbonyl compounds, rearrangements and neighboring group effects, the Woodward-Hoffmann rules (explained with the aid of HOMO-LUMO relationships), polycyclic aromatic compounds, heterocyclic compounds, and macromolecules. In part 3 the main emphasis is placed on fats, carbohydrates, amino acids, and proteins, and an introduction to biochemical processes is also given. Recent trends receive mention in all parts of the book.

The optical presentation of the subject matter is clear; preparations and reactions of compounds are collected in tabular form.

Exercises and problems included in the various chapters help the student to check his progress, and also provide ideas for conducting lectures and seminars. Some of the problems serve to take the reader beyond the actual text of the book. Solutions are given at the end of the volume. References for further reading intended to extend and deepen the students knowledge cover 7 pages.

In the reviewer's opinion, the present work is a welcome alternative to existing German-language textbooks and should find a wide readership.

Jörg Daub [NB 243 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Lehrprogramm Orbitalsymmetrie. By *A. J. Bellamy*. Vol. 28 of the series "taschentext". Verlag Chemie/Physik-Verlag, Weinheim 1974. VI, 107 pp., stitched, DM 17.80.

Handbook of Moisture Determination and Control. Principles, Techniques, Applications. Vol. 1. By *A. Pande*. Marcel Dekker, New York 1974. XI, 266 pp., bound, $ 28.50.

Elektroorganische Chemie. Grundlagen und Anwendungen. By *F. Beck*. Verlag Chemie, Weinheim 1974. XVI, 391 pp., bound DM 88.—.

Kinetics & Mechanisms of Polymerization Reactions. Applications of Physico-chemical Principles. By *P. E. M. Allen* and *C. R. Patrick*. From the series "Ellis Horwood Series in Physical Chemistry". Edited by *T. M. Sugden*. Ellis Horwood, Chichester/John Wiley & Sons, New York 1974. XV, 596 pp., bound, £ 18.00.

The Chemistry of Synthetic Dyes, Vol. VII. Edited by *K. Venkataraman*. Academic Press, New York 1974. XVII, 372 pp., bound, $ 45.00.

Vom Wasser, Band 43. Issued by the Fachgruppe Wasserchemie der Gesellschaft Deutscher Chemiker. Responsible for text: *W. Husmann*. Verlag Chemie, Weinheim 1974. VIII, 584, 120 pp., bound, DM 108.—.

Spouted Beds. By *K. B. Mathur* and *N. Epstein*. Academic Press, New York 1974. XV, 304 pp., bound, $ 24.50.

Transport Phenomena in Aqueous Solutions. By *T. Erdey-Grúz*. Akadémiai Kiadó, Budapest/Adam Hilger, London 1974. 512 pp., bound, £ 15.00.

Natural Products Chemistry, Vol. 1. Edited by *K. Nakanishi, T. Goto, S. Itô, S. Natori*, and *S. Nozoe*. Kodansha, Tokyo/Academic Press, New York 1974. X, 562 pp., bound, $ 32.50.

Organic Semiconductors. Dark- and Photo-conductivity of Organic Solids. By *H. Meier*. From the series "Monographs in Modern Chemistry". Edited by *H. F. Ebel*. Verlag Chemie, Weinheim 1974. XV, 661 pp, bound, DM 138.—.

Chemical Analysis of Organometallic Compounds. By *T. R. Crompton*. Vol. 4 of the series "Analysis of Organic Materials". Edited by *R. Belcher* and *D. M. W. Anderson*. Academic Press, London 1974. Vol. 2 (Elements of groups IV A–B): IX, 163 pp., bound, £ 5.00; Vol. 3 (Elements of group IV B): X, 211 pp., bound, £ 6.50.

Verbrennung und Feuerungen. By *R. Günther*. Springer-Verlag, Berlin 1974. xv, 432 pp., bound, DM 108.—.

Formale Kinetik. Experimentelle Methoden der Physik und der Chemie. By *H. Mauser*. Bertelsmann Universitätsverlag, Düsseldorf 1974. 368 pp., stitched, DM 78.—.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 4036, 4037, Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N. Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim, Pappelallee 3. P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 4031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 4
April 1975
Pages 193–272

Relationships between the Chemistry of Dispersed Metals and Chemical Syntheses with Metal Atoms[**]

By Hans Wolfgang Kohlschütter[*]

An interesting and topical question in modern inorganic chemistry is: To what extent are the well-known chemistry of dispersed metals and the new technique of chemical synthesis with free metal atoms interrelated? Or in other words: Where, do these two facets of metal chemistry meet? In an attempt to glean an answer to this question three important aspects are considered: metal sols, activated metals as powders, and deposits in vacuum processes (evaporation and cathodic sputtering of metals).

1. Metal Sols

The classic example is the well-known red gold sol obtained by reduction of gold chloride ($HAuCl_4$)[1]. Between 1925 and 1972 the following observations were made[2]: The first step of the gold precipitation involved formation of elementary nuclei with a small number of gold atoms (30—300). These then form simple or complicated twins; *i.e.* in the second stage complex nuclei are formed by crystallographic interactions between elementary nuclei. In the third step, growth of complex nuclei to particles containing large numbers of gold atoms (≈ 5000, ≈ 70000, ≈ 124000) takes place. The number of atoms in the particles depends on the reduction processes used. In 1925 *R. Zsigmondy* received a Nobel prize for his work on gold nuclei and their growth. In 1972, crystallographic twinning in complex nuclei was discovered by means of high resolution electron microscopy[3].

The particles of red gold sols are negatively charged[4]. A theoretical and experimental interpretation of the reasons for these charges is sought for by investigations on the formation of ionic gold compounds at the surface of gold particles as well as on the physical chemistry of gold (metal)/electrolyte (solution) interfaces[5]. The charges contribute to the stabilization of the gold sols in a dynamic equilibrium according to[7]

$$V = V_R + V_A$$

where V_R = repulsion potential between neighboring particles
V_A = attraction potential
V = resulting potential

Because of these electric charges gold particles can be fixed to the surfaces of solids, as has been shown in an elegant experiment by *Thiessen*[6]. On thin leaf-shaped crystals of kaolin adsorption of negatively charged gold particles occurred

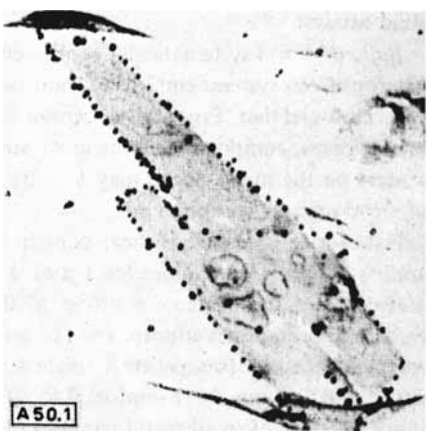


Fig. 1. Adsorption of gold particles on kaolin [6].

[*] Prof. Dr. H. W. Kohlschütter
Eduard-Zintl-Institut für Anorganische und Physikalische Chemie der Technischen Hochschule
61 Darmstadt, Hochschulstrasse 4 (Germany)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

only at the edges where the crystal lattice of the kaolin is broken. Here the positive potential of its cations in the interior of the lattice can overlap the negative potential of the gold particles. The large basal faces of the kaolin crystal, on the other hand, remain empty since these faces are the sites of negative OH ions in the lattice of kaolin.

Particles in gold- and silver sols exhibit special physical properties due not only to processes taking place at the interface between metal and solution but also to the slight extension of the metallic phase in the interior of the particle. Thus, the free path of the electrons can play an important role in measurements of dielectric constants[8].

2. Activated Metals in Powder Form

Activated metals are frequently the products of topochemical reactions. They are prepared by reduction of finely divided metal oxides with hydrogen at the lowest possible temperatures[9]. Grains of metal are formed from the grains of metal oxides. These contain aggregates of primary particles. Such a primary particle is a small section of the crystal lattice which coherently diffracts X rays, and which has been found to contain 10^4—10^5 atoms in the case of *e.g.* Au, Cu, Fe, Ni[10]. The heat content of such highly dispersed metals has been found to be only 1 to 3 kcal/mol higher than that of compact metals. This difference is small compared to the evaporation enthalpy of free atoms, which in the case of Au, Cu, Fe, Ni is *ca.* 100 kcal/mol. These small calorimetric effects are due to enlargement of the specific surface area and, in part, to lattice defects. Activated metals of this type are used as starting materials for syntheses and as catalysts, as for example in

1) The Mond-process[11]

$$NiO \xrightarrow[400\,^{\circ}C]{CO} Ni_{active}$$

$$Ni_{active} \xrightarrow[80\,^{\circ}C]{CO} Ni(CO)_4$$

2) Hydroformulation

$$2\ RCH{=}CH_2 \xrightarrow{CO + H_2} RCH_2{-}CH_2{-}CHO + RCH(CHO)CH_3$$

in *homogeneous* systems with the soluble catalyst $(CO)_3CoH$[12], in *heterogeneous* systems with metallic cobalt as solid catalyst.

Ballard[13] has systematically compared homogeneous and heterogeneous systems employing transition elements as catalysts. He found that "Probably we cannot expect stoichiometric metal organic compounds on the metal surface. But the active centers on the metal phase may already have the character of metal organic compounds."

Data for the increase in heat content of activated metals are merely lump sum values for 1 mol. They were originally derived from the heats of solution of the metals in acids. Further information is afforded by: 1) calculation of the energy which is necessary to separate a single atom from the crystal lattice (carried out for cadmium)[14]; 2) calculation of the vapor pressure of small metal particles (carried out for silver spherocolloids)[15].

3. Deposits in Metal Evaporation and Cathodic Sputtering in Vacuum

The deposition of metals by evaporation processes and by cathodic sputtering also involves formation and growth of nuclei. Not only physicists but also chemists have already carried out a great deal of experimental work in this field. At first, however, dispersed metals produced in this way were not pure owing to the presence of residual gases in inefficiently evacuated systems. The progress made in physical technology and the improved equipment that is now available have opened the way to a more detailed understanding of the elementary processes in nucleus formation and nuclear growth, and consequently to the development of methods for the production of high grade purity metals. The production of high-purity substances is of fundamental significance[16].

4. Conclusion

that the chemistry of dispersed metals falls between that of compact metal phases and that of free metal atoms. Indeed the production of free metal atoms and the aggregation of a few metal atoms can be seen as partial problems in chemical syntheses with metal atoms. Looking at it this way we immediately recognize the striking interrelationship between two facets of metal chemistry. Even with the small number of examples selected here we recognize that between the chemistry of dispersed metals and syntheses with metal atoms there is some kind of demarcation line with bridgeheads on both sides. This is readily demonstrated by comparing chemical synthesis with *free* metal atoms (produced by evaporation or cathodic sputtering processes) and chemical synthesis with *partially* free metal atoms (in the active centers of metal surfaces).

Special features in chemical syntheses with metal atoms are: 1) free metal atoms approach the reaction centers with high kinetic energy or in excited states; 2) substances which are present during the evaporation or sputtering of metals in closed systems are no longer "impurities", they are "reaction partners"—chosen on the basis of modern theories of chemical bonding.

Our rough survey illustrates that chemists from *quite different scientific backrounds* are turning their attention to the study of relationships between the chemistry of dispersed metals and metal atom synthesis. Progress in this sector is based on results of *experimental* work in chemistry and physics[17].

Received: June 28, 1974 [A 50 IE]
German version: Angew. Chem. 87, 213 (1975)

[1] *R. Zsigmondy* and *P. A. Thiessen:* Das kolloide Gold. Akademische Verlagsgesellschaft, Leipzig 1925.
[2] Number of atoms calculated from data on the linear diameter of particles.
[3] *N. Uyeda, M. Nishino,* and *E. Suito,* J. Colloid Interface Sci. *43,* 264 (1973).
[4] *M. Faraday,* Phil. Trans. Roy. Soc. London *147,* 145 (1875).
[5] *E. Matijevic,* J. Colloid Interface Sci. *43,* 217 (1973).
[6] *P. A. Thiessen,* Z. Elektrochem. Angew. Phys. Chem. *48,* 675 (1942).
[7] *S. Okamoto* and *S. Hachisu,* J. Colloid Interface Sci. *43,* 30 (1973).
[8] *U. Kreibig* and *C. v. Fragstein,* Z. Phys. *224,* 307 (1969).
[9] *R. Fricke* in: Handbuch der Katalyse, Vol. IV. Springer-Verlag, Berlin 1942.

[10] Gold: Z. Phys. Chem. *A 181*, 409 (1938); copper: Z. Phys. Chem. *A 183*, 177 (1938); iron: Z. Phys. Chem. *B 37*, 60 (1937); nickel: Z. Elektrochem. Angew. Phys. Chem. *46*, 90 (1940).

[11] Cf. Ullmanns Encyklopädie der technischen Chemie, 3rd Edit. Urban and Schwarzenberg, München 1960, Vol. 12, p. 700.

[12] *R. F. Heck* and *D. S. Breslow*, J. Amer. Chem. Soc. *83*, 4023 (1961).

[13] *D. G. H. Ballard*, Chem. Brit. *10*, 20 (1974).

[14] *I. N. Stranski*, Z. Phys. Chem. *B 38*, 451 (1938).

[15] *G. I. Zinsmeister* in *M. Auwärter*: Ergebnisse der Hochvakuumtechnik und der Physik dünner Schichten. Wissenschaftliche Verlagsgesellschaft Stuttgart 1971, p. 205.

[16] *G. Möllenstedt, C. Jönsson*, and *K. Wittmann* in *M. Auwärter*: Ergebnisse der Hochvakuumtechnik und der Physik dünner Schichten. Wissenschaftliche Verlagsgesellschaft, Stuttgart 1971, p. 131.

[17] See also: *K. J. Klabunde*, J. Organometal. Chem. *71*, 309 (1974).

Reactions of Transition Metal Atoms with Organic Substrates[***]

By Philip S. Skell and Michael J. McGlinchey[*]

1. Introduction

The foundations of atom chemistry were laid five or six decades ago with the investigation of hydrogen, oxygen, and nitrogen atoms using methods such as discharges through gases, and continued with the researches into the alkali metal atoms by pioneers such as *Michael Polanyi* in the 1920's. Free radical chemistry was gradually evolving and chain reaction processes involving halogen atoms were eventually elucidated. However, by the 1950's the chemistry of probably less than a dozen atomic species was well documented and the higher boiling (and potentially more interesting) elements were virtually ignored, presumably due to the lack of a convenient experimental method.

The development of atomic carbon chemistry in the 1960's was a natural consequence of our own interests in carbenes and other short-lived species. A major contributor was *Lyle Wescott* who solved the problem of producing and reacting carbon atoms[1]. Carbon was vaporized either by use of an arc or by resistive heating, and the hot species was then transferred to a cold zone across a vacuum which insulated the hot source from the site of reaction. The residual pressure (10^{-5} torr) and the dimensions of the container were chosen such that the mean free path was much greater than the distance from the hot source to the cold reaction zone, thus avoiding gas phase reactions; it was anticipated that exothermic reactions occurring at low pressure in the gas phase would result in formation of "hot" molecules which would fragment faster than they could be cooled. Since then many modifications have been introduced, such as laser evaporation of metals and rotating cryostats, but the basic principles are the same although the scope of the experiments has been greatly extended. Mention should also be made of the early advances accomplished by *Margrave, Timms, et al.* with the most interesting high temperature species SiF_2 which has a remarkably long lifetime[2].

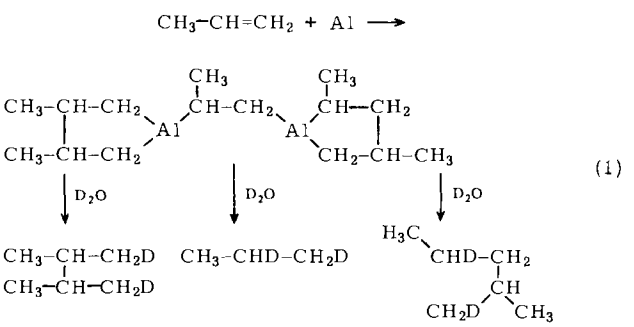
One might dispel initially the illusion that the high temperature origin of the atoms would result in "hot atom" chemistry as a consequence of high kinetic energy. The kinetic energy of a species derived from a 3000 °C source is approximately 6 kcal/mol (≈0.25 eV) which is a trivial contribution to the overall energy of reaction. However, these atoms are of course more reactive than the atoms in the usual condensed phase form of the element since their binding to other like atoms has been overcome.

After several years surveying the field of metal atom chemistry we now feel that it is possible to describe a reasonable number of reactions of a wide variety of atomic species. These range from main group elements such as Mg, B, Al, C, and Si through typical transition elements, *viz.*, Cr, Mn, Fe, Co, and Ni, to the very high boiling elements such as Mo, W, Re, and Pt.

The broadest survey of metal atom reactions was carried out by cocondensing the atoms with propene. With few exceptions propene reacts with metal atoms to form organometallic compounds. No two elements behave identically but there was a noticeable trend from σ to π character for the organometallic products on progressing from left to right across the Periodic Table.

2. Aluminum Atoms and Alkenes

Aluminum, for instance, gave no simple isolable compounds directly and the yellow viscous residue was analyzed by hydrolysis with D_2O to mark each carbon aluminum bond with a deuterium atom[3]. The major products upon hydrolysis were deuterated propane, 2,3-dimethylbutane, 2-methylpentane, and traces of *n*-hexane. A reasonable organoaluminum intermediate, which accounts not only for the products but also for the deuterium distribution observed, is shown in Scheme 1.



(1)

A question which immediately arises is the mechanism of the dimerization of the olefin, *i.e.*, is an aluminacyclopropane initially formed which then opens to a diradical and adds to a second molecule of propene to produce the aluminacyclopentane system? A preliminary indication was provided by

[*] Prof. Dr. P. S. Skell[**] and Dr. M. J. McGlinchey
The Pennsylvania State University
College of Science, Department of Chemistry
University Park, Pa. 16802 (USA)
[**] Present address: Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[***] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e.V. at Darmstadt (May 12–15, 1974).

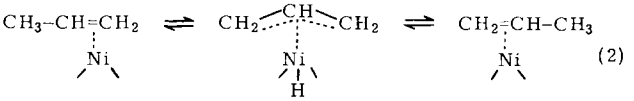
the reaction of 1,3-butadiene with aluminum atoms followed by hydrolysis with D_2O to produce almost exclusively 1-butene and very little 2-butene. The magnesium butadiene adduct hydrolyzes to a 1:1 mixture of 1-butene and *cis*-2-butene[3a]. The preference for 1,2- rather than 1,4-addition might imply an aluminacyclopropane intermediate but it is not a necessary conclusion.

The reaction with *cis*- or *trans*-2-butene to produce the *meso*- and *d,l*-2,3-dideuteriobutanes shows that the reaction is not stereospecific; there is almost no memory of the configuration of the original olefin. However, introduction of a Lewis base such as dimethyl ether or trimethylamine either to the cold matrix or even as a cocondensate with the aluminum and 2-butene yields, after D_2O treatment, 95% of the *cis* addition product; that is *trans*-2-butene yields *d,l*-2,3-dideuteriobutane and *cis*-2-butene produces the *meso*-compound[4]. This provides much more compelling evidence for initial production of an aluminacyclopropane whose rate of ring opening is greatly reduced by the presence of the complexing ligand. It is difficult to rationalize such a retention of stereochemistry on the basis of two aluminum atoms per double bond. Furthermore, at the vaporization temperature, aluminum is predominantly in the ^2P electronic ground state and thus bears some resemblance to singlet carbenes which are known to add stereospecifically to olefins.

In the aluminum-propene reaction the number of deuterium atoms incorporated in solvolysis products per mole of metal reacted accounts for about 2.7 of the 3 valences of aluminum. However, in the aluminum-2-butene reaction the stoichiometry is very different. A ratio of Al : H_2 : butane = 2 : 1 : 2 is found in the hydrolysis products. Furthermore, hydrolysis with D_2O affords D_2 instead instead of H_2; thus no Al-H bonds were originally present since they would have given rise to HD. A probable explanation is the presence of aluminum-aluminum bonds, a previously unreported phenomenon in organoaluminum chemistry. As yet, a molecule such as bis(2,3-dimethylaluminacyclopropane) has not been isolated; such a purification would be fraught with experimental difficulties. Nevertheless, it is possible to titrate out with iodine (1 mole of I_2) that portion of the aluminum-butene system which is responsible for D_2 formation on deuterolysis, while leaving the aluminum to butane ratio unchanged[4a].

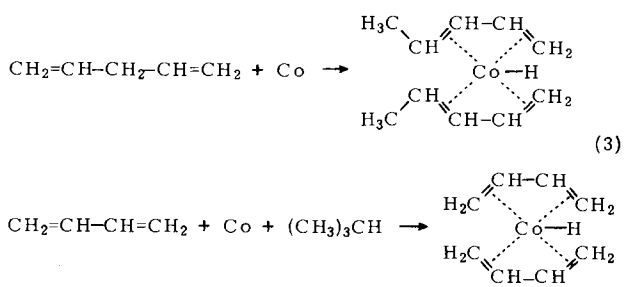
3. Cobalt or Nickel Atoms and Alkenes

It is clear from Section 2 that aluminum forms σ-bonded organometallics. In complete contrast, cobalt and nickel liberate unlabeled propene when the residue from the metal-propene reaction is treated with D_2O[5]. However, the products are not just simple π-complexes, because the cocondensate of nickel (or cobalt) and 1-butene, when allowed to warm up, catalytically isomerizes the substrate to a mixture of *cis*- and *trans*-2-butenes. This process might occur *via* a π-allylmetal hydride intermediate such as has been elegantly demonstrated by *Bönnemann* in the case of propene(trifluorophosphane)nickel[6] or by addition of a Ni-H compound to the alkene to give alkylnickel intermediates and subsequent elimination. The former could be shown to apply. Nickel vapor was cocondensed in separate experiments with 2-deuteriopropene and 3-deuteriopropene. The latter gave a mixture which also contained 1-deuteriopropene, whereas 2-deuteriopropene apparently remained unscrambled. Furthermore, 3-deuteriopropene led to both undeuterated and dideuterated propenes demonstrating that both inter- and intramolecular exchange occurs[7]. This evidence is consistent with a π-allylmetal hydride intermediate which permits a 1,3-hydrogen shift (Scheme 2).



(2)

The successful isomerization of terminal olefins to nonterminal olefins suggested the possibility of isomerizing nonconjugated to conjugated dienes. However, such reactions, *e.g.*, with 1,4-pentadiene and Co atoms are exceedingly complex. Among the early reaction products are linear pentenes and C_5H_6 compounds which polymerize. These disproportionation reactions are not the only problem, however, since the conjugated dienes which eventually appear form stable complexes with the metal (*e.g.*, cobalt) and stop the catalytic process. This is, nevertheless, a route to the novel bis(diene)cobalt hydride complexes (Scheme 3) which can also be synthesized by cocondensing the appropriate conjugated diene with cobalt vapor and a molecule possessing a readily abstractable hydrogen atom[8].



(3)

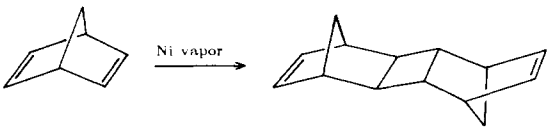
The ^1H-NMR data for these complexes are similar to those reported by *Pettit* for the reaction product of dienes and carbonyliron compounds[9].

The reaction of 1,3-butadiene with nickel vapor gives as the major product a gray residue, which may contain bridging butadiene ligands[5]. This gray residue reacts with more butadiene to produce the blood-red 2,6,10-dodecatrienylenenickel which *Wilke et al.*[10] had previously obtained by other routes in their masterful elucidation of the nickel-catalyzed cyclotrimerization of butadiene. It is also possible to isolate from the reaction of nickel vapor and 1,3-butadiene traces of a volatile yellow material which has been tentatively claimed to contain bis(butadiene)nickel but which certainly contains bis(crotyl)nickel.

4. Metal Atoms and Arenes or Cyclic Dienes

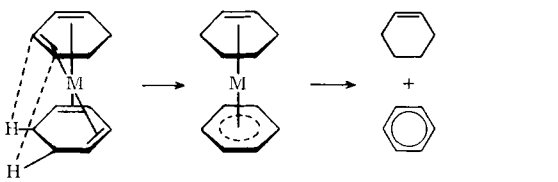
A variety of reactions of metal vapors with cyclic dienes have been observed. Foe example, nickel vapor and 1,5-cyclooctadiene react to yield bis(1,5-cyclooctadiene)nickel directly[5]. However, this route is unlikely to oust the more conventional method which utilizes ethoxydiethylaluminum to reduce bis(pentanedionato)nickel in the presence of 1,5-cyclooctadiene and which is more amenable to relatively large

scale work[11]. In contrast, nickel vapor and norbornadiene yielded no isolable organometallic product but gave predominantly the *exo-trans-exo* dimer of norbornadiene (Scheme 4)[5].



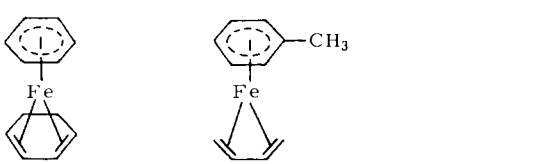
(4)

In yet another type of reaction with cyclic dienes, metal vapors such as Cr, Fe, Co, and Ni bring about rapid, catalytic disproportionation of 1,3- or 1,4-cyclohexadiene to cyclohexene and benzene when the whole cocondensate is allowed to warm to 0 °C. It is tempting to postulate initial formation of a bis(diene)metal complex which then undergoes hydrogen transfer possibly *via* a metal hydride intermediate (Scheme 5).



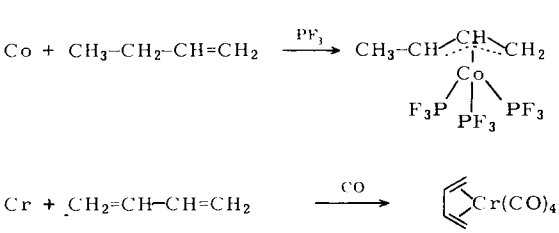
(5)

Although we have not isolated such a diene complex in this case it is possible when using iron vapor to obtain (η-benzene)[1—4-η-(1,4-cyclohexadiene)]iron(0). This type of arene-(diene)metal complex is also synthesizable by cocondensing iron vapor with an arene and then adding a suitable diene to the cold matrix. Thus, one can readily prepare (η-butadiene)-(η-toluene)iron(0) and other analogous species (Scheme 6)[12].



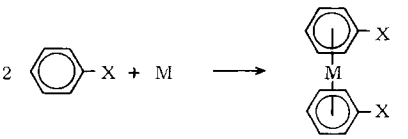
(6)

Another synthetic use of this technique of adding a stabilizing ligand to a reaction matrix is the addition of PF_3[13a] or CO to metal-olefin cocondensates (Scheme 7)[13].



(7)

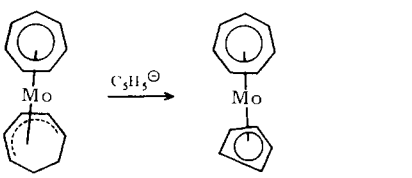
It was first shown by *Timms* in 1969 that the cocondensation method is a viable route to the bis(cyclopentadienyl)metal sandwich compounds, and also that bis(benzene)chromium is synthesizable directly[14]. This provides the cue to the realization that bis(arene) compounds of chromium, molybdenum, and tungsten should be capable of being synthesized even when the arene contains functional groups possessing lone pairs of electrons. Such compounds had previously defied attempts at synthesis because the conventional Fischer-Hafner technique[15] required the use of $AlCl_3$ and this Lewis acid complexed with the substituted arenes and stopped the reaction sequence. Now, however, using the direct synthesis, it has proven possible to make bis(arene)metal compounds of Cr, Mo, and W with the arenes substituted by fluoro, chloro, amino, methoxy, methoxycarbonyl and other functional groups (Scheme 8)[16, 17].



(8)

This has clearly opened up new areas of interest to the organometallic chemist since bis(arene)chromium chemistry was formerly limited to metalation and hydrogen exchange reactions.

An interesting extension of this is the reaction of molybdenum atoms with cycloheptatriene to produce the cycloheptatrienyl(cycloheptadienyl)molybdenum sandwich. The cycloheptadienyl unit is labile and easily replaced by cyclopentadienyl anion (Scheme 9)[17a].



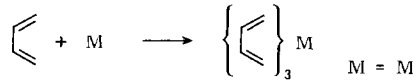
(9)

In contrast to the reaction with nickel atoms[5], norbornadiene is not just dimerized by molybdenum and tungsten atoms but instead a catalytic polymerization occurs in which one ring is opened[20b]. It has been suggested that this process might occur *via* a series of olefin dismutation processes which are so prevalent in molybdenum chemistry[21].

An amusing corollary to this reaction promises to be that of Mo with azulene; however, the product has not yet been unambiguously identified.

5. Tris(butadiene)molybdenum

Yet another novel reaction has been discovered using Mo or W vapors to produce tris(butadiene)molybdenum (or -tungsten) by direct reaction with 1,3-butadiene in the condensed phase (Scheme 10)[18]. The only comparable previously known system is tris(methyl vinyl ketone)tungsten[19] which adopts the relatively unusual trigonal prismatic structure[20].

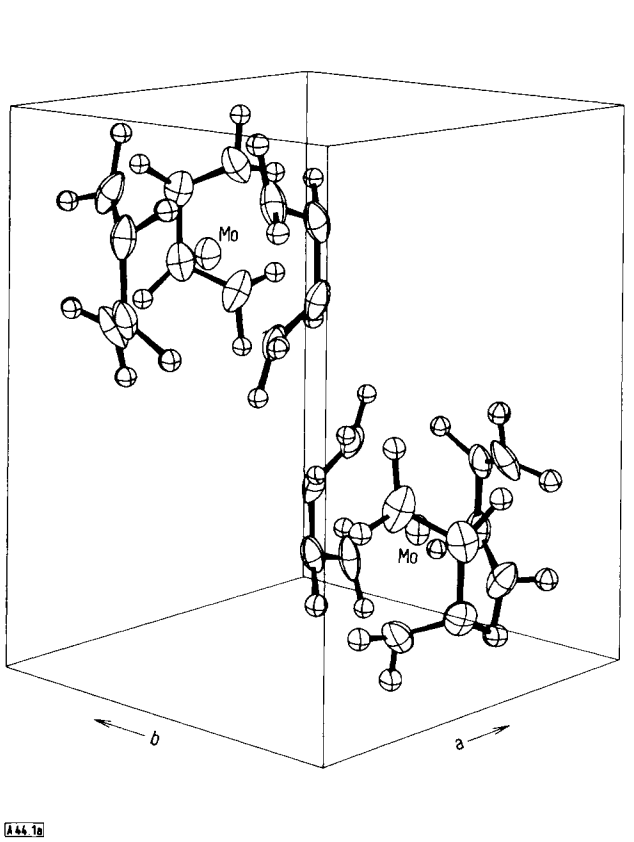


(10)

The new tris(butadiene)molybdenum is sublimable and air-stable, and its X-ray structure shows that the central molybdenum is equidistant from all the carbon atoms[20a]. The butadienes are all *cisoid* and in a trigonal prismatic arrangement in a girdle around the Mo such that they are aligned in the same direction. There is a small distortion in the planarity

of the butadiene system and the C_2—C_3 bond is longer than in free 1,3-butadiene.

of some of the types of reaction possible is presented in Table 1.



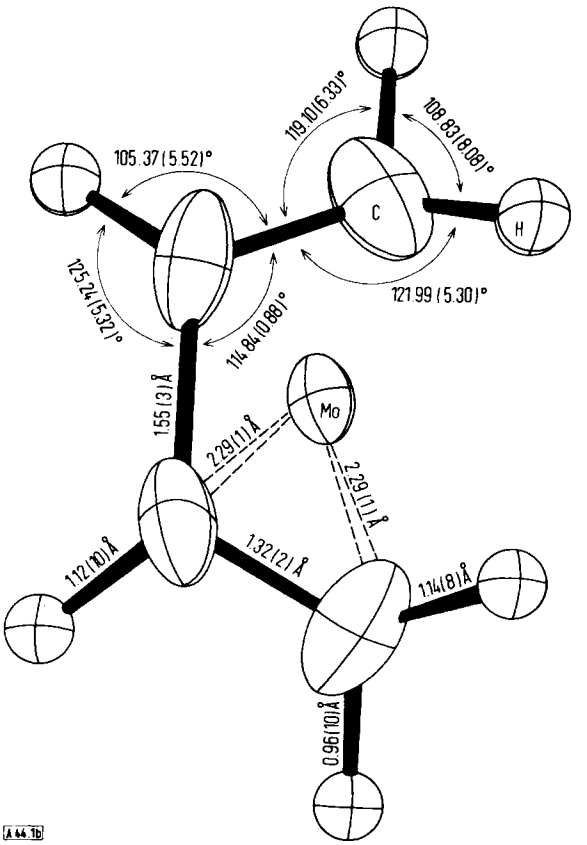


Fig. 1. Crystal structure of tris(butadiene)molybdenum. Space group $P6_3/m$, C_{6h}^2; $a=b=7.208(11)$, $c=11.829(24)$ Å; $Z=2$; $\rho_{calc.}=1.61$ g/cm³ [20a].

6. Metal Atoms and Water

A surprisingly interesting substrate is water, which shows some unexpected reactions with metal vapors. Thus, although chromium and hydrogen chloride react at −196 °C to release one mole of hydrogen per mole of chromium, reaction with water yields half a mole of hydrogen at −196 °C and the other half a mole on warming up. Methanol behaves in a similar manner to water, finally producing dimethoxychromium(II)[21a]. The two hydrogen-producing processes occurring at liquid nitrogen temperature and on warming up show remarkably different isotope effects, as revealed using mixtures of H_2O and D_2O; some of these processes look like free electron reactions while others do not, and these systems obviously merit further investigation. Mo and W show no reaction with H_2O at −196 °C, yet do so on warming up.

Table 1. Possible reactions of metal atoms with organic compounds.

Reaction types	Examples
a) Synthesis of sandwich compounds	$(C_6H_5-OCH_3)_2Cr$ $(C_7H_7)Mo(C_5H_5)$
b) Synthesis of olefin complexes	(1,5-cyclooctadiene)$_2$Pt (1,5-cyclooctadiene)$_2$Ni (1,3-butadiene)$_3$W
c) Indirect synthesis by addition of a stabilizing ligand	$(C_6H_5-CH_3)Fe(PF_3)_2$ (C_5H_5)Co(isoprene)
d) Synthesis of involatile products; analyzed by hydrolysis	$R_2Al-AlR_2$
e) Catalytic isomerizations	1-butene → 2-butene 1,4-pentadiene → 1,3-pentadiene
f) Catalytic hydrogenations	olefin/Pd + H_2 → alkane
g) Acetylene trimerizations	propyne → 1,2,4- and 1,3,5-trimethylbenzenes
h) Catalytic disproportionations	1,3-cyclohexadiene → benzene and cyclohexene

7. Reactions of Metal Atoms in Excited States

We have so far discussed some reactions of metal atoms with organic substrates in an attempt to go some way towards bridging the gap between the conventional electronic picture of an atom and the reactions of a conglomeration of these atoms such as is usually presented in chemical texts. Clearly the reactions of elements in a monoatomic form differ dramatically from the reactions of the bulk metal and a classification

One final point to consider is that not only ground state atom chemistry can be studied by this technique but also atoms in electronically excited states. This is nicely exemplified by our earlier work with carbon atoms which are produced in a ^3P ground state by resistive heating but which contain a sizeable percentage of ^1S and ^1D excited states when produced in an arc[22]. Of course a large number of excited states may be populated by arcing but the time required for the flight of the high temperature species to the walls ($\approx 10^{-5}$ s) allows sufficient time for optically allowed transitions to occur so that only a limited number of metastable

states are going to survive the trip and be able to exhibit some chemistry. The chemistry of the electronically excited state(s) can differ dramatically from that of the ground state, and one such system which nicely demonstrates this is the reaction of magnesium which alkyl halides (Scheme 11).

$$CH_3-CH_2-CH_2-Cl + Mg(^1S) \xrightarrow{-196\,^\circ C} CH_3-CH_2-CH_2-Cl/Mg$$

deeply colored

$$\xrightarrow{-120\,^\circ C} CH_3-CH_2-CH_2-Mg-Cl \quad (75\%) \qquad (11)$$

colorless

$$CH_3-CH_2-CH_2-Cl + Mg(^3P) \longrightarrow CH_3-CH_2-CH_2^{\bullet} + \overset{\bullet}{M}gCl \longrightarrow$$

$$CH_3-CH{=}CH_2 + CH_3-CH_2-CH_3 + n\text{-hexane}$$

(35%) (34%) (traces)

Magnesium vapor produced thermally (by resistive heating of a crucible) is essentially ^1S ground state magnesium which reacts with alkyl halides to give good yields of non-solvated Grignard reagents. Magnesium vapor produced by arcing contains 65–70% of the electronically excited ^3P state which reacts with alkyl halides to yield radicals[23].

The apparent triviality of these excited state reactions should not obscure the underlying principle that by techniques such as arcing it should be possible to elucidate the chemistry of the electronically excited states of many atoms, and this is one direction in which the field of atomic reactions will be heading in the not too distant future.

Received: August 2, 1974 [A 44 IE]
German version: Angew. Chem. 87, 215 (1975)

[1] *P. S. Skell, L. D. Wescott, Jr., J.-P. Golstein,* and *R. R. Engel,* J. Amer. Chem. Soc. *87,* 2829 (1965).
[2] *P. L. Timms, R. A. Kent, T. C. Ehlert,* and *J. L. Margrave,* J. Amer. Chem. Soc. *87,* 2824 (1965).
[3] *P. S. Skell* and *L. R. Wolf,* J. Amer. Chem. Soc. *94,* 7919 (1972).
[3a] *T. Terasawa* and *P. S. Skell,* unpublished results.
[4] *L. R. Wolf,* Ph. D. Thesis, The Pennsylvania State University, University Park, Pa., 1974.
[4a] *J. E. Dobson* and *P. S. Skell,* unpublished results.
[5] *P. S. Skell, J. J. Havel, D. L. Williams-Smith,* and *M. J. McGlinchey,* J. C. S. Chem. Comm. *1972,* 1098.
[6] *H. Bönnemann,* Angew. Chem. *82,* 699 (1970); Angew. Chem. internat. Edit. *9,* 736 (1970).
[7] *P. S. Skell* and *M. J. McGlinchey,* unpublished results.
[8] *J. J. Havel,* Ph. D. Thesis, The Pennsylvania State University, University Park, Pa., 1972.
[9] *G. F. Emerson, J. E. Mahler, R. Kochar,* and *R. Pettit,* J. Org. Chem. *29,* 3620 (1964).
[10] *G. Wilke, M. Kröner,* and *B. Bogdanović,* Angew. Chem. *73,* 755 (1961).
[11] *B. Bogdanović, M. Kröner,* and *G. Wilke,* Liebigs Ann. Chem. *699,* 1 (1966).
[12] *D. L. Williams-Smith, L. R. Wolf,* and *P. S. Skell,* J. Amer. Chem. Soc. *94,* 4042 (1972).
[13] *E. Koerner von Gustorf, J. Buchkremer, Z. Pfajfer,* and *F.-W. Grevels,* Angew. Chem. *83,* 249 (1971); Angew. Chem. internat. Edit. *10,* 260 (1971).
[13a] *P. S. Skell* and *D. L. Williams-Smith,* unpublished work.
[14] *P. L. Timms,* Chem. Commun. *1969,* 1033.
[15] *E. O. Fischer* and *W. Hafner,* Z. Naturforsch. *10B,* 665 (1955).
[16] *P. S. Skell, D. L. Williams-Smith,* and *M. J. McGlinchey,* J. Amer. Chem. Soc. *95,* 3337 (1973).
[17] *M. P. Silvon, E. M. Van Dam,* and *P. S. Skell,* J. Amer. Chem. Soc. *96,* 1945 (1974).
[17a] *M. P. Silvon* and *P. S. Skell,* unpublished results.
[18] *P. S. Skell, E. M. Van Dam,* and *M. P. Silvon,* J. Amer. Chem. Soc. *96,* 626 (1974).
[19] *R. B. King* and *A. Fronzaglia,* Inorg. Chem. *5,* 1837 (1966).
[20] *R. E. Moriarty, R. D. Ernst,* and *R. Bau,* J. C. S. Chem. Comm. *1972,* 1242.
[20a] *M. M. Yevitz* and *P. S. Skell,* unpublished results.
[20b] *E. M. Van Dam,* and *P. S. Skell,* unpublished results.
[21] Prof. *G. Wilke,* personal communication.
[21a] *D. Howl* and *P. S. Skell,* unpublished results.
[22] *P. S. Skell, J. J. Havel,* and *M. J. McGlinchey,* Accounts Chem. Res. *6,* 97 (1973).
[23] *J. E. Girard,* Ph. D. Thesis, The Pennsylvania State University, University Park, Pa., 1971.

Isolation and Reactions of Metal Atoms in Matrices[**]

By George C. Pimentel[*]

1. Introduction

The matrix isolation technique was devised to permit the leisurely spectroscopic study of extremely reactive molecular species[1–4]. In this method, normally transient molecular species are embedded (trapped) at high dilution and at very low temperature in an inert solid environment. Anyone involved today in metal atom synthesis will see the similarity of this diagnostic process to the low temperature reaction conditions that have proven so successful in metal atom synthetic chemistry. Hence, it is not surprising that the matrix isolation technique has already contributed significantly to the study of chemical synthesis with metal atoms. The course of metal atom reactions can be interrupted so that the reaction mechanisms can be examined. Not only the chemical identity, but also the molecular structure of reaction intermediates can often be obtained. Sometimes undesired side reactions can be eliminated and kinetic barriers can be revealed. These valuable potentialities imply that workers in metal atom chemistry will wish to become familiar with matrix isolation, first, to be able to evaluate the interesting work of this sort now appearing in the literature and, second, to be able to put the method to use when applicable.

In this review, experimental methods will be described and then the potentialities of matrix isolation will be illustrated by specific examples.

Fortunately, the matrix isolation technique has been the subject of several books and numerous recent and authoritative reviews[5–11]. The book by *Meyer*[6] takes a comprehensive and coherent look at the spectroscopy of low temperature samples, including electronic spectroscopy. It has a valuable

[*] Prof. Dr. G. C. Pimentel
University of California
Berkeley, Calif. 94720 (USA)
Present address: Max-Planck-Institut für Plasmaphysik
8046 Garching bei München

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12–15, 1974).

chapter on experiment details, and a tabular survey of over 800 substances that had been studied by matrix methods through 1969. The book edited by *Hallam*[7] focuses on vibrational spectroscopy and its chapters are authoritatively written by active workers in the field. Of particular interest here are the chapters by *Andrews* (Ch. 5) and by *Ozin* (Ch. 9) because these two authors have themselves made important contributions to metal atom chemistry.

2. Spectroscopic Techniques

Each of the spectroscopic fields, visible-ultraviolet, electron spin resonance (ESR), infrared, and Raman spectroscopy has its place in matrix isolation work. In each spectral region, commercial spectrometers can be and are usually used. Because low temperature matrix samples display rather sharp spectral features (infrared line widths are usually about $1\,cm^{-1}$ and sometimes as narrow as a few tenths of a wave number), spectral resolution of 0.3—0.5 cm^{-1} is adequate, a performance readily available in commercial instruments. It is important to note, however, that this level of spectral resolution is usually *needed* to derive full benefit from the matrix method. Through isotopic substitution, the number of equivalent atoms of the type substituted can often be determined, provided the isotopic shifts are resolved. Since the limit of this diagnostic information is fixed by the line widths, valuable information can be lost if spectral slit widths exceed the natural line widths.

detectable Raman signals without excessive matrix heating by the light source. The concentrated beam provided by a laser source circumvents these difficulties provided proper attention is paid to the fact that only momentary excessive heating of a matrix sample can cause diffusion and abort the entire experiment.

In this early stage of experience with matrix Raman spectroscopy, it is probably too early to define the optimum experimental parameters. Instead, it may be more informative to list the conditions that have been successfully used by some of the pioneers, with attention to the laser power, the wavelengths used, and to the sample support and optical geometry.

Table 1 shows that matrix isolation Raman spectra were first successfully recorded and reported in the literature almost simultaneously in four different laboratories. *Shirk* and *Claassen*[12] first reported matrix-isolated Raman spectra of SF_6 and of $CHCl_3$. Their laser beam was dispersed to a 4 mm long line focus with a cylindrical lens to reduce local heating. They deposited the sample on a platinum mirror surface and illuminated at an angle of about 30° from grazing incidence. They were able to observe all three Raman active frequencies of SF_6 and seven of chloroform with spectral resolution near $10\,cm^{-1}$.

Nibler and *Coe*[13] described in detail the technique they developed and the important parameters for successful matrix spectroscopy. They deposited onto a polished aluminum surface and illuminated at 10 to 30° from grazing incidence, this

Table 1. Pioneering work on matrix isolation Raman spectroscopy.

Date	Laser source	Wavelength [Å]	Power [W]	Matrix/Sample (*M/R*)	Spectrometer/slit width	Geometry *etc.*	Ref.
April 1971	Ar ions	4880 5145	1 1	$Ar/SF_6 = 500:1$ $Ar/CHCl_3 =$ 100—200:1	Spex, double monochromator $\approx 10\ cm^{-1}$	line focus $\approx 30°$ [a] Pt mirror	[12]
	Kr ions	6471	0.5				
Nov. 1971	Ar ions	4880 5145	0.05—0.75	$CO_2/CS_2 = 10^4:1$ $N_2/CH_4 = 100:1$ $N_2/CCl_4 = 100:1$	Cary 82 $4\ cm^{-1}$	focused beam 10–30° [a] polished Al depolarization 3 °C temperature rise at 0.75 W	[13]
June 1971	Ar ions	4880	?	$CO_2/SeO_2 = 100:1$	Spex 1401 (?)	?	[14]
Aug. 1971	?	?	?	$N_2/PbCl_2 = ?$	?	depolarization	[15]
Oct. 1971	?	5682	>0.01	Kr, $Xe/Br_3 = ?$	?	?	[16]
May 1972	Ar	?	0.01—0.125	Ar, $N_2/MX_2 = ?$ M = Ge, Sn, Pb X = Cl, Br	Spex 1401	polished Cu, Ag, Pt, Al depolarization	[17]
	Kr	?					
April 1972	Coherent Radiation Model 52 GA	4880 5145	1.6 1.9	$Ar/LiO_2 = ?$	Spex Ramalog $5\ cm^{-1}$	Cu wedge 0.3 °C temperature rise at 1 W	[18]
July 1972				Ar/OF_2, OF = 100:1			[19]

[a] Angle of incidence measured from surface.

The recent advent of laser Raman spectroscopy warrants somewhat more attention to this type of instrumentation. Raman spectra were conspicuously absent in the first decade of matrix isolation because it was not possible to record Raman spectra of matrix samples with conventional Raman light sources. The extremely high matrix scattering that always accompanies good isolation made it impossible to obtain

angle being optimized for maximum signal. The N_2 matrix Raman signal was found to be proportional to laser power up to 750 mW, using a focused beam. The temperature rise in the mirror sample support was also proportional to power and gave a 3 °C temperature rise at 750 mW. These authors verified the equivalence of support temperature and sample temperature by observing the $\alpha \rightarrow \beta$ phase transition of pure,

solid PD_3. While Rayleigh scattering was not a problem (*Nibler* and *Coe* used a Cary triple monochromator), fluorescence was found to be troublesome. A tiny bit of stopcock grease or pump oil condensed on the metal tip could cause excessive interference from fluorescence. They were able to detect the Raman spectrum of CS_2 in a CO_2 matrix at a dilution of $1:10^4$, though matrix ratios between 100 to 500 are more usually required. Finally, they demonstrated the feasibility of measuring depolarization ratios and showed that the results are somewhat but not strongly dependent on the excitation geometry and the glassy or frosty character of the sample.

Ozin et al. published three brief reports[14–16] in the period encompassed by references [12] and [13]. These concise papers displayed the first matrix-isolation spectra of transient species (SeO_2, $PbCl_2$, $SnBr_2$, Br_3), but they were relatively devoid of description of the special experimental techniques and problems involved in the excitation and recording of matrix Raman spectra. However, the following year, *Ozin* and *VanderVoet*[17] reported some of their experimental procedures. They found that highly polished mirror support surfaces made of Cu, Ag, Pt, and Al give lowest background scattering and are particularly suited for depolarization measurements. They maximized signal intensities by optimizing the N_2-shifted Raman line provided by the matrix, using a three-axis universal stage for movement of the cryostat. Because of matrix warming (it is not indicated whether their laser beam was focused), they emphasize the importance of recording spectra first at the lowest possible laser energy. These spectra aid in recognizing diffusion from local heating at higher powers. They found that 10 to 125 mW laser powers were adequate for obtaining spectra without local heating and diffusion effects.

Hatzenbühler and *Andrews*[18, 19] were also early pioneers in the matrix Raman technique and perhaps the first to apply it to transient species generated through metal atom reactions. They deposited their samples on an oxygen-free hard copper wedge (8:1 slope) to obtain the highest possible thermal conductivity in their sample support. They found only 0.3 °C temperature rise in the support wedge using 1 watt of laser power at 4880 Å. They obtained 5 cm^{-1} resolution while scanning at 10—20 cm^{-1}/min.

3. Cells and Cryostats

The matrix method was developed with the use of liquid refrigerants—liquid hydrogen and helium being needed for most of the truly inert matrix materials. This inhibited to some extent the entry of new workers to the field, because of the difficulties in handling these cryogenic liquids, the expense, the sometimes limited availability of helium and because of safety considerations. *Meyer*[6] devotes eight well-deserved pages to safety precautions, enough to cause a novice to think twice about his interest in the hoped-for results.

All of these obstacles have been essentially removed within the last four or five years because of commercial instrumental developments. Reliable and compact cryogenic optical cells are now sold and even more important, closed cycle cryostats that provide temperatures in the range of 10 to 30 °K without the need to handle either liquid helium, liquid hydrogen, or ultrapure, high pressure gases. With an investment of only about $ 10000 (plus spectrometer) a novice can readily undertake matrix isolation experiments like those to be described. Both *Meyer*[6] and *Hallam*[7] include whole chapters devoted to the design of optical cells and to cryogenic systems, so it is considered unnecessary to repeat them here. It is worth noting however, that among the excellent closed cycle cryostats now available, the "Displex" unit by Air Products Ltd. and the "Cryodyne" unit by Cryogenic Technology Inc. are well suited to matrix isolation studies. Their performance characteristics are similar to those of other devices: Cool-down times between 30 and 60 min are routine to temperatures in the range 16 to 20 °K and these operating temperatures can be maintained with total heat loads of one watt. Larger capacity and somewhat more expensive units will reach temperatures of 11—12 °K with heat load capacities of 1.5 watts. For argon and the heavier inert gases, a temperature of 20 °K or lower is needed and during sample deposition, the heat load requires one watt capacity or greater to prevent local warming of the sample. For neon matrices, 4 °K, hence liquid helium coolant, is needed.

4. Deposition Temperature

The incubation period that was required for the fruition of the matrix isolation technique was connected with the development of low temperature cryostats (see Section 3) and with the discovery of the important parameters involved in successful sample preparation. In the earliest systematic studies of isolation efficiency[3], it was found that diffusion of the reactive constituent, R, (whose isolation is desired) was far more difficult to avoid than had been anticipated. Ultimately, a rule of thumb evolved: diffusion would be too rapid to permit isolation of a triatomic molecule if the matrix temperature even momentarily rose to a temperature above about half the melting point[20]. For the important matrices of N_2 and Ar, diffusion of water is liable to occur if the temperature reaches 35 °K and isolation will be lost if it exceeds 40 °K. Diatomic molecules diffuse more readily; for example, NO diffuses in N_2 in the range 12 to 18 °K[21] while single atoms are even more mobile. All of these remarks refer, of course, to the temperature of the matrix itself, which can be several degrees higher than the supporting substrate during periods of high heat load (*e.g.*, during deposition, during photolysis of a deposited sample, and, especially during operation of a high temperature Knudsen cell or hot wire near the substrate). These observations led to the early recognition of the importance of monitoring the sample substrate temperature in addition to that of the cold metal block to which it is thermally connected. During periods of high heat load, the substrate temperature may rise a few degrees above that of the surrounding copper block—CsI and CsBr are two popular substrates and they have poor thermal conductivities at very low temperatures. It can be added that the temperature *difference* between the copper block temperature and the CsI "window" temperature helpfully indicates the maintenance of thermal contact between the two. This is a crucial property of the cold cell that occasionally changes capriciously from experiment to experiment. A convenient habit is to measure during "cool-down" the lag between the time the copper block temperature passes, say, 30 °K and the time that the window reaches that same temperature. This time lag is an individual characteristic of each cold cell, but if it noticeably exceeds its norm (which should be less than 5 to 10 minutes), then

thermal contact is suspect. Experience proves that time is lost if depositions are carried on with fluctuating thermal behavior in the cold cell.

The window temperature can be measured with a thermocouple pushed into a hole drilled in the salt window; indium sheet wrapped around the thermocouple or Wood's metal poured into the hole provides adequate thermal connection. A suitable thermocouple composition is gold/gold-cobalt alloy (2.1% Co), which retains a useful temperature coefficient even down to 4°K. By comparison, copper/constantan has a lower dE/dT by a factor of 2.5 at 20°K and by a factor of 4 at 4°K, making it almost useless at the lower temperatures.

A highly reflecting metallic substrate can be used in laser Raman studies[12, 13, 17, 18] which eliminates the thermal contact problem and brings the sample significantly closer to coolant temperature[13]. The same advantage can be gained in infrared absorption work by focusing the spectrometer beam onto the sample deposited on a reflecting surface. The reflected beam passes through the sample twice, and the necessary extra spectrometer optics are not an expensive addition, nor are they troublesome to focus.

5. Sample Preparation

A matrix suspension of a reactive species may be prepared by slow deposition of a gas mixture of the matrix and a suitable photosensitive precursor. Then photolysis, either after or during deposition, gives the desired species *in situ* in the matrix environment. If vacuum ultraviolet photolysis is needed, it is almost essential to photolyze during deposition because matrix scattering is so severe at the shorter wavelengths that it will not penetrate the matrix. Of course, photolysis during deposition increases the heat load at this crucial time and it prevents recording the matrix spectrum before photolysis and then again at various photolysis times.

More important to the study of metal atom chemistry are depositions involving high temperature atom sources. *Linevsky* was an early pioneer in the use of a Knudsen cell in his classic matrix study of molecular lithium fluoride[22]. Simultaneous deposition of argon (or other inert gas) in excess from another jet provided the matrix environment. The Knudsen cell temperature was varied to change the matrix/-LiF = M/R ratio so that monomers and dimers could be distinguished.

For evaporation temperatures up to 500°K, a small Knudsen cell no more than one centimeter in diameter can be incorporated in the base of the cold cell. A simple design is described by *Andrews* and *Pimentel*[23] which they used to evaporate atomic lithium in a matrix study of its reaction with nitric oxide. The stainless steel Knudsen cell was wound with heating wires, and slipped into a Pt-mirrored quartz sleeve. A chrome-plated copper radiation shield with a suitable orifice minimized radiation heating of the cold window placed only 4 cm away.

A comparably simple Knudsen cell was described by *Weltner et al.*[24] for evaporation temperatures as high as 2700°K. A cell one inch long and 1/8 inch in outside diameter was made of 0.010 inch tungsten sheet and heated resistively. The sample effused through a 0.050 inch hole in the cell wall. *Weltner* and *McLeod*[25] designed another resistance-heated furnace made to evaporate expensive or rare samples. A cylinder 1/2 inch long and 3/16 inch diameter was made from .005—.010 inch tantalum sheet. After the sample was placed inside, the cylinder was closed with tantalum caps crimped in place, and heated through water-cooled copper electrodes with an AC current of 150 amps at 6 volts. Temperatures of 2700°C were accessible. This cell was used, for example, to evaporate carbon atoms (C_2, C_3, *etc.*) from a 50 mg sample of ^{13}C-enriched graphite. The design is potentially an important one for evaporating expensive, isotopically enriched metal samples or for rare and specially pure metals.

Induction heating can also be used to advantage as again can be typified by the work of *Weltner*[26]. To evaporate carbon vapor at 2300—2600°K, a small sample (5/8 by 1/2 inch) of graphite was supported by tungsten rods at the center of an induction coil of 3/16 inch diameter.

For some purposes, much more complicated double oven evaporation cells are needed. Metals often evaporate as a mixture of monomeric, dimeric and polymeric species. The relative amount of these species can be varied by changing the temperature, a significant aid in the identification of spectral signatures. Unfortunately, in most matrix work, the rate of deposition must be controlled by the oven temperature. Hence, a double oven, with separate temperature control, is needed. The rate of deposition is determined by the first oven temperature. The gas effuses into a second oven chamber at a higher and variable temperature to alter the degree of aggregation prior to entrapment in the matrix material. A recent example of such a double oven Knudsen cell has been reported by *Frey et al.*[27] for use up to 800°K.

A simpler but effective evaporation technique for metal atoms is to use a heated filament of the desired metal instead of the Knudsen cell. The efficacy has been demonstrated by *Kündig et al.*[28a]. Typical filament dimensions were $1.75 \times 0.375 \times 0.008$ inches through which would be passed 80—150 amps at 1—1.5 volts. Of course, suitable baffles must be provided to avoid excessive heating, but high evaporation temperatures are much more readily obtained than with a Knudsen cell. Unfortunately, the hot filament loses two useful features of the Knudsen cell approach. First, from a Knudsen cell, the amount of metal deposited per unit time can be at least roughly calculated by assuming that the inside vapor pressure remains near equilibrium. This estimate, coupled with the argon deposition rate, provides at least a crude estimate of the concentration of the evaporated species. Second, the equilibrium assumption also permits deliberate variation of the monomer to dimer ratio through temperature control.

Two methods for direct determination of the deposition rate can be mentioned. *Andrews* and *Pimentel* calibrated their Knudsen cell evaporation rate *versus* temperature by evaporating onto the cold window for a measured time followed by chemical analysis of the deposited metal[23]. *Ozin et al.* have adopted an elegant method commonly used in monitoring evaporation rates in thin film preparation[28b]. A quartz crystal that serves to tune an RF oscillator is placed near the evaporating filament in geometry equivalent to that of the deposition surface. As evaporation coats the surface of the quartz crystal, the mechanical loading alters the RF oscillator frequency. A deposit of 10^{-8} g can be detected. Continuous monitoring with a frequency counter measures the deposition rate (once the device is calibrated) during each experiment. This does not, of course, provide any information at all about the

monomer to polymer ratio which is determined by little-understood kinetic processes rather than by equilibrium.

This uncertainty about the various metallic species (monomers, dimers, trimers, *etc.*) that are directed to the matrix surface is even further aggravated in electron-beam evaporative techniques. This method has the advantage that very high temperatures can be reached easily, facilitating evaporation of even the more refractory metals. *Shirk* and *Bass* have also shown that metal atoms can be "evaporated" by bombarding a metal surface with positive ions (*e.g.* Ar^+, Kr^+, Xe^+) produced by passing a gas through a glow discharge[29]. They refer to the technique as "sputtering", and for good reason—electron and ion bombardment are known to eject aggregates as well as single atoms.

6. Isolation Efficiency: M/R and Deposition Rate

The last experimental parameters that deserve discussion are those that determine isolation efficiency. Of course, if diffusion occurs during sample preparation, the experimenter will not be confident that he is studying the reactions of single metal atoms. Hence, when diffusion occurs, the matrix isolation technique has been compromised.

The variables at the experimenter's disposal are the "window" temperature, the choice of matrix material, the concentration ratio (M/R), and the deposition rate. These variables can be explored by reference to the paper by *Andrews* and *Pimentel*[30] on the isolation of lithium atoms in inert gas matrices. Lithium atom is undoubtedly the most difficult atom to isolate except for H atom and since both monomeric Li and dimeric Li_2 were measured by these authors[30], quantitative statements about isolation efficiency can be made. The example displays the effects and it can be taken as a "worst case" (except for H).

As mentioned in Section 4, the window temperature must be *well below* half the melting point of the matrix or there is no possibility of isolation. For nitrogen and argon, temperatures between 15 to 20°K (0.2 to 0.3 of the melting point) are quite satisfactory for diatomic and triatomic molecules, but lower temperatures are needed for atoms. This effect is displayed for Li by the first four lines of Table 2. The data taken from *Andrews* and *Pimentel*, show more than a ten-fold improvement in isolation efficiency for argon under the rather poor isolation conditions used and a two-fold improvement for krypton when T_W was lowered from 15°K to 4°K. Obviously, the lower the deposition temperature, the better, but, unfortunately, experimental difficulties of other sorts limit the use of this advantage. Liquid helium is expensive, liquid hydrogen does not conveniently offer a temperature below its triple point, 15°K, and commercial, closed cycle coolers usually furnish temperatures no lower than about 10 to 15°K. Furthermore, scattering by the matrix becomes more and more serious as the deposition temperature is lowered below the "diffusion temperature" (about 1/2 T_M). A good compromise between isolation efficiency and scattering is to place the window temperature in the range (0.2—0.3) T_M (where T_M is the matrix melting point).

Table 2. Effect of experimental parameters on the isolation efficiency of lithium atoms [a] (data from [30]). T_W = window temperature, M/R = ratio matrix/sample.

Parameter	Matrix	M/R	T_W[°K]	[Li]/[Li_2]
T_W	Ar	3300:1	15	0.0006:1
	Ar	3300:1	4	0.0096:1
	Kr	3300:1	15	0.0069:1
	Kr	3300:1	4	0.019:1
Matrix material	Kr [b]	18000:1	4	0.037:1
	Xe [b]	18000:1	4	0.30:1
M/R	Ar	3300:1	4	0.0096:1
	Ar	18000:1	4	0.035:1
	Kr	3300:1	4	0.019:1
	Kr	18000:1	4	0.037:1
	Xe	18000:1	4	0.30:1
	Xe	170000:1	4	[c]

[a] Deposition rate 4.5 mmol/h unless otherwise specified.
[b] Deposition rate 1—1.6 mmol/h.
[c] No Li_2 detected.

The above discussion implies that isolation can be improved at fixed deposition temperature by choosing a matrix with a higher melting point. Table 2 shows the magnitude of the improvement for lithium isolation for the matrix materials Kr and Xe under otherwise identical experimental conditions. Unfortunately, this considerable improvement can be lost because of "frosty", highly scattering matrices formed by the matrix of higher T_M and better isolation efficiency.

Concentration, or M/R, is the third parameter at the experimenter's disposal. Table 2 displays the effectiveness of M/R in this respect for each of the inert gases, Ar, Kr, and Xe. Of course, lower values of M/R suffice for isolating diatomics and larger molecules, which diffuse less readily. In general, M/R must exceed 100 and, for N_2 or Ar matrices at 15°K, ratios exceeding 500 will isolate triatomic molecules very effectively. Of course, if reaction between two deposited species if desired, then concentration ratios may desirably be lower. For example, if reaction between a metal atom and a reaction partner is intended, M/R must be low enough to give a reasonable likelihood of encounter in the matrix but high enough to prevent secondary reactions. *Pimentel et al.*[31-33] usually fix the more concentrated reactant concentration near $M/R = 300$. In some applications, the ease of diffusion of metal atoms relative to the reaction partner might be used to advantage.

Finally, the deposition rate is extremely important in determining isolation. Inert gas and nitrogen matrices have very poor thermal conductivity, so they warm significantly during deposition. Of course, the room temperature matrix gas carries a significant heat capacity and it releases, as well, its heat of sublimation during solidification. As the deposit thickness increases, this heat release at the surface can produce a significant thermal gradient through the sample. If this thermal gradient becomes too large, diffusion occurs, and the isolation function of the matrix is subverted. Under any circumstances, at a given M/R and deposition rate, isolation efficiency is found to decrease as the sample thickness increases. These effects were quantitatively displayed by *Leroi et al.*[34] in their study of the infrared spectrum of CO in argon.

The obvious reply to this difficulty is to control the heat input by lowering the deposition rate as far as practical. To ensure optimum isolation, very slow deposition rates are used by most experienced users of the matrix technique. For example, in the Berkeley laboratories, the matrix sample might be deposited at a rate of 2—3 mmol/h for a deposition time as long as 10 to 48 h.

Apparently in contradiction to this dictum are experiments recently published concerning "pulsed deposition". This deposition technique was pioneered by *Rochkind*[35] with specific application to quantitative analytical use where isolation was not important. *Perutz* and *Turner*[36] then found that under some conditions, effective isolation could also be achieved with pulsed deposition, which offers the hope that deposition times can be shortened significantly. Here in the Berkeley laboratories, *Louis Allamandola*[37] has made a systematic study of pulsed deposition and, indeed, there are advantages to be gained. A sample of CH_3OH in $N_2(M/R=100)$ was deposited at a rate of 3 mmol/h, first in continuous flow and then at the same *average* rate, but in pulses of 30 ms duration at two pulses/min. There was a slight loss of isolation efficiency; perhaps 25% less monomer was obtained. However, there was a significant sharpening of the absorption features of the monomer that made the pulsed sample spectra more readily interpretable. *Rochkind*[35] first noticed this spectral improvement and we join him in attributing it to a local annealing of the matrix cage due to the pulse. Thus our experience is that pulsed deposition is desireable and that judicious choice of pulse size and spacing might decrease deposition times but not by more than a factor of two or three.

7. Metal Atom Reactions by Matrix Isolation

The study of metal atom reactions through matrix isolation spectroscopy can be said to be founded in the matrix study of metal atoms themselves. This implies electronic spectroscopy, of course, and it reaches back to the early work by *McCarty* and *Robinson* (Hg, Na in Ar, Kr, Xe[38]), *Schnepp* (Mg, Mn in Ar, Kr, Xe[39]), *Roncin* and *Damany* (Hg in Ar[40]), and *Brewer*, *Meyer et al.* (Hg in Ar, Kr, Xe[41], Na, K in Ar, Kr, Xe[42]). Today, spectra of atoms in inert gas matrices have been reported for almost half of the elements, as well summarized by *Meyer*[6]. Typical of recent work is the spectrum of tantalum atoms isolated in argon by *Graham* and *Weltner*[43]. The evaporation and isolation of this refractory element suggests that any desired element in the Periodic Table is accessible for this type of study. Furthermore, the spectroscopy furnishes an elegant model: more than 40 sharp absorptions were resolved between 2200 and 5100 Å and, with few exceptions, these features were connected with gas phase counterparts, a significant aid in the interpretation of the latter.

The more direct interest of the present review is, of course, matrix study of reactions of metal atoms with other molecules. A number of laboratories are now beginning work of this sort, mainly using infrared and/or Raman spectroscopy, but also using ESR. This current work will be surveyed briefly, considering first reactions of metal atoms with inorganic molecules and then their reactions with organic molecules.

7.1. Inorganic Substances

Andrews and *Pimentel*[23] may have been the first to attempt deliberate use of the matrix technique to study the reaction of a metal atom with another molecule. They wished to compare the structure and bonding of the then-unknown triatomic molecule LiNO to the counterpart molecules HNO and FNO. Their infrared spectra display the power of isotopic substitution in matrix spectroscopy; absorption frequencies from six different isotopic molecules involving ^6Li and ^7Li, ^{14}N and ^{15}N, and ^{16}O and ^{18}O provided enough information to show that the lithium atom cannot be bonded to the nitrogen atom in the bent triatomic structure known for HNO.

This pioneering study has been fruitfully and productively pursued by *Andrews et al.*, as exemplified by their detailed study of lithium (and the other alkali metals) with O_2[44, 18, 45]. These infrared and Raman spectra again exploit the full potentialities of isotopic substitution and they show unequivocally that the molecule LiO_2 is a symmetric isosceles triangular molecule which *Andrews* finds to be interpretable in terms of ionic bonding between Li^+ and O_2^-.

Table 3 lists other studies of this type now appearing from *Andrews'* laboratory which already include alkali metal atom reactions with F_2O, N_2O and O_3.

Table 3. Some matrix isolation studies of metal atom reactions with inorganic compounds. IR and R = investigation by IR-Raman spectroscopy, respectively.

Metal atom	Reaction partner	Product	Method	Ref.
Li	NO	LiON	IR	[23]
Li	O_2	LiO_2	IR/R	[18, 44, 45]; cf. [46]
K, Rb	O_2	KO_2, RbO_2	IR	[47]
Na, K	O_2	NaO_2, KO_2	R	[48]
Cs	O_2	CsO_2, CsO_4	IR	[49, 50]
Li	F_2O	LiOF, OF	IR/R	[51, 19]
M = Li to Cs	N_2O	MO, M_2O	IR	[52]
M = Li to Cs	O_3	MO_3	IR/R	[53]
Ni	N_2	$Ni(N_2)$, $Ni(N_2)_2$	IR	[54—56]
Pd	N_2	$Pd(N_2)_3$	IR/R	[57]
Pt, Pd	CO	$M(CO)_n$ $n=1,2,3,4$	IR/R	[58—60]
Ni	O_2	$Ni(O_2)$, $Ni(O_2)_2$	IR	[61]

In 1971, *Burdett* and *Turner*[54] carried out codepositions of nickel atoms and nitrogen in argon matrices. They identified certain spectral features with $Ni(N_2)$ and $Ni(N_2)_2$ complexes. This work, while later repeated and reinterpreted[55], forecast and perhaps stimulated a significant series of studies by *Ozin et al.* As shown in Table 3, in *Ozin's* laboratory a number of transition metal complexes have now been studied with N_2, CO and O_2. Current work, by both *Turner*[54] and *Ozin*[57–61] extends studies to other transition metals and to mixed com-

plexes of these molecules. Again, isotopic substitutions are used to elucidate the molecular geometries ("end-on" or "sideways").

Obviously, much is to be learned about the early reaction steps in metal atom reactions and about the bonding in reaction intermediates. Indeed, there is already much information available from these pioneering studies, some of it not yet assessed. For example, the mere finding that alkali metals react with O_2, N_2O and F_2O under matrix deposition conditions implies that there cannot be large activation energy barriers to reaction. While the temperature at which reaction occurs is ill-defined, the time required for cooling from room temperature to below 20°K is surely a small fraction of a second. As a guess, an activation energy of 2 or 3 kcal might be sufficient to prevent reaction. Such arguments have been broached by *Pimentel*[62] but much remains to be considered.

Turning to bonding, the reactions of alkali metals with oxygen forecast enlightening developments concerning transient species. The unequivocal determination of a symmetrical triangular geometry and the change of the oxygen-oxygen stretching frequency from 1600 cm^{-1} to 1100 cm^{-1} surely denotes electron transfer, as concluded by *Andrews et al.*[45, 49]. The Li-O_2 result probably explains why *Andrews* and *Pimentel*[23] had difficulty in their normal coordinate analyses—the only geometries explored were linear or bent but oblique angled MNO and MON structures. No doubt the lithium atom is placed beside and between the nitrogen and oxygen atoms and bonded to both, undoubtedly with substantial charge transfer.

These conclusions contrast with the findings of *Ozin et al.* on the simplest transition metal complexes with N_2 and O_2. Accepting *Ozin*'s assignments, Table 4 shows the O—O or the N—N stretching frequencies and their shifts from that of the uncomplexed diatomic parent. Approximate bond orders can be assigned[63] on the assumption that transfer of a full electron charge to any of these diatomics places an electron in an antibonding orbital and reduces the bond order by 1/2. Clearly both the geometries and the bond orders of the transition metal "complexes" with O_2 are similar to those of the molecules formed by the alkali metal atoms with O_2. In contrast, the transition metal complexes with N_2 are of "end-on" geometry, they are much more weakly bound, and they apparently involve much lower charge transfer. It is noteworthy that the implied charge transfers in the metal-oxygen molecules do not anticorrelate (as might be expected) with the metal atom ionization energies, which range from 90 kcal/mol for cesium to 207 kcal/mol for platinum.

Table 4. Frequencies, bond orders, and charge transfers in metal atom complexes with O_2 and N_2. Matrix material: Ar.

Complex [a]	Frequency ν_c [cm^{-1}]	Shift $\nu_0 - \nu_c$ [b]	Bond order	Charge transfer	Geometry	Ref.
CsO_2	1114	435	1.52	0.96	"side-on"	[49]
LiO_2	1097	452	1.51	0.99	"side-on"	[45]
PdO_2	1024	525	1.44	1.12	"side-on"	
NiO_2	966.6	583	1.40	1.21	"side-on"	
PtO_2	926.6	622	1.36	1.27	"side-on"	
PdN_2	2212	118	2.88	0.24	"end-on"	
PtN_2	2170	160	2.84	0.32	"end-on"	
NiN_2	2088	242	2.76	0.48	"end-on"	

[a] Unless otherwise stated, the frequencies are taken from Ch. 9 of Ref. [7].
[b] ν_0 is the frequency of the pure compound in the matrix: 2330 cm^{-1} for N_2 [54] and 1549 cm^{-1} for O_2 [64].

7.2. Organic Substances

Again, *Andrews* and *Pimentel*[65] were probably the first to attempt a deliberate matrix reaction between a metal atom and an organic molecule. They were trying to produce the methyl radical, CH_3, by codepositing lithium atoms and methyl iodide. Indeed, the desired abstraction reaction occurred, producing CH_3 in the same matrix cage with LiI. An absorption at 730 cm^{-1} was definitively shown to be due to a CH_3 group.

Subsequent matrix studies by *Milligan* and *Jacox*[66] based on *in situ* vacuum ultraviolet photolysis of methane provided another spectrum equally well attributable to the methyl radical, but now absorbing at 611 cm^{-1}. *Tan* and *Pimentel*[67] were able to clarify the discrepancy and show that the absorption at 730 cm^{-1} was due to a methyl group strongly perturbed by or, more likely, bonded to the adjacent lithium halide molecule. This conclusion was bolstered by the spectra of reaction products between sodium atoms and potassium atoms with methyl iodide and methyl bromide. Regarding the CH_3MX cluster as a molecule, it has some possible relationship to a Grignard reagent, although the alkali metal atom does not find itself in a conventional bonding situation.

Once more, *Andrews* went on to exploit these leads. With interest focused on the vibrational frequencies of the halogen-substituted methyl counterpart, *Andrews et al.* have reacted lithium atoms with CCl_4[68], CBr_4[69], CHX_3(X=Cl, Br)[70], $CHBrF_2$[71], $CH_2X^1X^2$(X^1 = Cl, Br, X^2 = F, Cl, Br, I)[72], and CH_2I_2[73]. These authors interpret their spectra as those of essentially free halogen-substituted methyl radicals, in contrast to the findings for CH_3 when prepared by matrix reaction between alkali metal atoms and a methyl halide.

Whatever the significance of the spectra, there is no question that *Andrews et al.* were able to obtain reaction and new, normally transient species when alkali metal atoms and substituted methanes are codeposited under matrix conditions. The work of *Andrews* eloquently demonstrates a rich future for the matrix isolation study of metal atom reactions with organic molecules.

8. Conclusions

The ever increasing use of metal atoms in the synthesis of new metal-organic compounds enhances the significance

of the matrix isolation studies described here. While matrix experiments are relatively tedious, they can be extremely informative about bonding, molecular geometry and reaction pathway. There seems no doubt that metal atom synthetic chemistry will benefit from careful matrix study of prototype reactions. Fortunately, these results can be confidently expected, as attested by the productivity of the laboratories of *L. Andrews* (University of Virginia), *G. A. Ozin* (Toronto University), *J.J. Turner* (University of Newcastle upon Tyne), and others.

Received: July 30, 1974 [A 45 IE]
German version: Angew. Chem. *87*, 220 (1975)

[1] *E. Whittle, D. A. Dows*, and *G. C. Pimentel*, J. Chem. Phys. *22*, 1943 (1954).
[2] *I. Norman* and *G. Porter*, Nature *174*, 508 (1954).
[3] *E. D. Becker* and *G. C. Pimentel*, J. Chem. Phys. *25*, 224 (1956).
[4] *G. C. Pimentel*, Spectrochim. Acta *12*, 94 (1958); Pure Appl. Chem. *4*, 61 (1962).
[5] *A. M. Bass* and *H. P. Broida*: Formation and Trapping of Free Radicals. Academic Press, New York 1960.
[6] *B. Meyer*: Low Temperature Spectroscopy. Elsevier, New York 1971.
[7] *H. Hallam*: Vibrational Spectroscopy of Trapped Species. Wiley, New York 1972.
[8] *D. E. Milligan* and *M. E. Jacox*: Spectra of Radicals. Physical Chemistry, Academic Press, New York 1970, Ch. 5.
[9] *J. S. Ogden* and *J. J. Turner*: Matrix Isolation. Chem. Brit. *7*, 186 (1971).
[10] *L. Andrews*: Infrared Spectra of Free Radicals and Chemical Intermediates in Inert Matrices. Ann. and Rev. Phys. Chem. *22*, 109 (1971).
[11] *A. J. Barnes*: Applications of Matrix Isolation Infrared Spectroscopy. Rev. Anal. Chem. *1*, 193 (1972).
[12] *J. S. Shirk* and *H. H. Claassen*, J. Chem. Phys. *54*, 3237 (1971).
[13] *J. Nibler* and *D. Coe*, J. Chem. Phys. *55*, 5133 (1971).
[14] *D. Boal, G. Briggs, H. Hübner, G. A. Ozin, E. A. Robinson*, and *A. VanderVoet*, Nature *231*, 173 (1971); *G. A. Ozin* and *A. VanderVoet*, J. Mol. Struct. *10*, 173 (1971).
[15] *H. Hübner, G. A. Ozin*, and *A. VanderVoet*, Nature *232*, 166 (1971).
[16] *D. H. Boal* and *G. A. Ozin*, J. Chem. Phys. *55*, 3598 (1971).
[17] *G. A. Ozin* and *A. VanderVoet*, J. Chem. Phys. *56*, 4768 (1972).
[18] *D. A. Hatzenbühler* and *L. Andrews*, J. Chem. Phys. *56*, 3398 (1972).
[19] *L. Andrews*, J. Chem. Phys. *57*, 51 (1972).
[20] See *G. C. Pimentel*: Radical Formation and Trapping in the Solid Phase. Ch. 4 in Ref. [5].
[21] *I. Haller*, Dissertation, University of California, Berkeley 1961.
[22] *M. J. Linevsky*, J. Chem. Phys. *38*, 658 (1963).
[23] *W. L. S. Andrews* and *G. C. Pimentel*, J. Chem. Phys. *44*, 2361 (1966).
[24] *W. Weltner, Jr., D. McLeod, Jr.*, and *P. H. Kasai*, J. Chem. Phys. *46*, 3172 (1967).
[25] *W. Weltner, Jr.* and *D. McLeod*, J. Chem. Phys. *40*, 1305 (1964).
[26] *W. Weltner, Jr., P. N. Walsh*, and *C. L. Angell*, J. Chem. Phys. *40*, 1299 (1964).
[27] *R. A. Frey, R. D. Werder*, and *H. H. Gunthard*, J. Mol. Spectrosc. *35*, 260 (1970).
[28a] *P. Kündig, M. Moskovits*, and *G. A. Ozin*, J. Mol. Spectrosc. *14*, 137 (1972).
[28b] *M. Moskovits* and *G. A. Ozin*, J. Appl. Spectrosc. *26*, 481 (1972).
[29] *J. S. Shirk* and *A. M. Bass*, J. Chem. Phys. *49*, 5156 (1968).
[30] *L. Andrews* and *G. C. Pimentel*, J. Chem. Phys. *47*, 2905 (1967).
[31] *W. L. S. Andrews* and *G. C. Pimentel*, J. Chem. Phys. *44*, 2527 (1966).
[32] *L. Y. Tan* and *G. C. Pimentel*, J. Chem. Phys. *48*, 5202 (1968).
[33] *B. S. Ault* and *G. C. Pimentel*, J. Phys. Chem. *77*, 1649 (1973).
[34] *G. E. Leroi, G. E. Ewing*, and *G. C. Pimentel*, J. Chem. Phys. *40*, 2298 (1964).
[35] *M. M. Rochkind*, Anal. Chem. *39*, 567 (1967); *40*, 762 (1968).
[36] *R. N. Perutz* and *J. J. Turner*, J. C. S. Faraday II, *69*, 452 (1973).
[37] *L. J. Allamandola*, Ph. D. Dissertation, University of California, Berkeley 1974.
[38] *M. McCarty, Jr.*, and *G. W. Robinson*, J. Mol. Phys. *2*, 415 (1959).
[39] *O. Schnepp*, J. Phys. Chem. Solids *17*, 188 (1961).
[40] *J.-Y. Roncin* and *N. Damany-Astoin*, C. R. Acad. Sci. *253*, 835 (1961).
[41] *L. Brewer, B. Meyer*, and *G. D. Brabson*, J. Chem. Phys. *43*, 3973 (1965).
[42] *B. Meyer*, J. Chem. Phys. *43*, 2986 (1965).
[43] *W. R. M. Graham* and *W. Weltner, Jr.*, J. Chem. Phys. *56*, 4400 (1972).
[44] *L. Andrews*, J. Chem. Phys. *50*, 4288 (1969).
[45] *L. Andrews* and *R. R. Smardzewski*, J. Chem. Phys. *58*, 2258 (1973).
[46] *H. Huber* and *G. A. Ozin*, J. Mol. Spectrosc. *41*, 595 (1972).
[47] *L. Andrews*, J. Chem. Phys. *54*, 4935 (1971).
[48] *R. R. Smardzewski* and *L. Andrews*, J. Chem. Phys. *57*, 1327 (1972).
[49] *L. Andrews, J.-T. Hwang*, and *C. Trindle*, J. Phys. Chem. *77*, 1065 (1973).
[50] *M. E. Jacox* and *D. E. Milligan*, Chem. Phys. Lett. *14*, 518 (1972).
[51] *L. Andrews* and *J. I. Raymond*, J. Chem. Phys. *55*, 3078 (1971).
[52] *R. C. Spiker, Jr.*, and *L. Andrews*, J. Chem. Phys. *58*, 702, 713 (1973).
[53] *R. C. Spiker, Jr.*, and *L. Andrews*, J. Chem. Phys. *59*, 1851, 1863 (1973).
[54] *J. K. Burdett* and *J. J. Turner*, J. Chem. Soc. *D 1971*, 885.
[55] *H. Huber, E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, J. Amer. Chem. Soc. *95*, 332 (1973).
[56] *M. Moskovits* and *G. A. Ozin*, J. Chem. Phys. *58*, 1251 (1973).
[57] *G. A. Ozin, M. Moskovits, P. Kündig*, and *H. Huber*, Can. J. Chem. *50*, 2385 (1972).
[58] *H. Huber, E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, Nature *235*, 98 (1972).
[59] *P. Kündig, M. Moskovits*, and *G. A. Ozin*, J. Mol. Struct. *14*, 137 (1972).
[60] *E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, Can. J. Chem. *50*, 3587 (1972).
[61] *H. Huber* and *G. A. Ozin*, Can. J. Chem. *50*, 3746 (1972).
[62] *G. C. Pimentel*, J. Amer. Chem. Soc. *80*, 62 (1958).
[63] *G. C. Pimentel* and *R. D. Spratley*: Understanding Chemistry. Holden-Day, San Francisco, Ch. 15, 1971.
[64] *B. R. Cairns* and *G. C. Pimentel*, J. Chem. Phys. *43*, 3432 (1965).
[65] *W. L. S. Andrews* and *G. C. Pimentel*, J. Chem. Phys. *44*, 2527 (1966); *47*, 3637 (1967).
[66] *D. E. Milligan* and *M. E. Jacox*, J. Chem. Phys. *47*, 5146 (1967).
[67] *L. Y. Tan* and G. C. *Pimentel*, J. Chem. Phys. *48*, 5202 (1968).
[68] *L. Andrews*, J. Chem. Phys. *48*, 979 (1968).
[69] *L. Andrews* and *T. G. Carver*, J. Chem. Phys. *49*, 896 (1968).
[70] *T. G. Carver* and *L. Andrews*, J. Chem. Phys. *50*, 4223, 4235 (1969).
[71] *T. G. Carver* and *L. Andrews*, J. Chem. Phys. *50*, 5100 (1969).
[72] *L. Andrews* and *D. W. Smith*, J. Chem. Phys. *53*, 2956 (1970); *55*, 5295 (1971).
[73] *D. W. Smith* and *L. Andrews*, J. Chem. Phys. *58*, 5222 (1973).

Reactions between Metal Atoms and Gases during the Production of Thin Films in High Vacuum[**]

By Max Auwärter[*]

1. Introduction

Production of thin films by reaction of one element with another or with several partners can be achieved in many ways.

In the case of aluminum, oxidation in air at room temperature will lead to a layer of 20 Å Al_2O_3 after 20 minutes; this is sufficient for passivation of the metal. Anodic oxidation is considerably faster and therefore more suitable for obtaining thicker layers. In appropriate electrolytes aluminum can be oxidized at a rate of 11 Å/s, resulting in layers of some 1000 Å of Al_2O_3; this is almost 1000 times faster than natural oxidation. Technical exploitation of this process is of great significance.

The production of thin films from the gaseous phase is a shape forming process which has found little attention so far in industrial chemistry. In the most recent edition of Ullmanns Encyklopädie der technischen Chemie 1973[1a] only flame spraying and pebble bed sintering are mentioned as coating methods from the gaseous phase. In both cases the coating material is in a fine-to-rough dispersed state, mainly in the form of an aerosol.

Although chemical vapor deposition has long been used as a method for the production of thin films, it was not until recent years that it gained increasing commercial importance. Typical reactions are:

$$\underset{(g)}{SiCl_4} + \underset{(g)}{2H_2} \rightarrow \underset{(s)}{Si} + \underset{(g)}{4HCl}$$

$$\underset{(g)}{2GeI_2} \rightarrow \underset{(s)}{Ge} + \underset{(g)}{GeI_4}$$

These reactions are used for the production of pure germanium and silicon.

Very interesting are gas decomposition processes at high substrate temperature:

$$\underset{(g)}{TiCl_4} + \underset{(g)}{2H_2O} \rightarrow \underset{(s)}{TiO_2} + \underset{(g)}{4HCl}$$

$AlCl_3$, $TaCl_5$, and $SnCl_4$ react analogously.

Chemical vapor deposition reactions, for instance pyrolytic reactions, take place mainly at atmospheric pressure or at best in slight vacuum, that is between 1 bar and 1 mbar; very often a carrier gas (hydrogen) is used. In this case only those variables controlling the reaction are of decisive importance for the process; hence even geometrically complex objects, for instance carbon fibers, can be coated uniformly at a growth rate of 100 Å/s at 1000 °C.

Coating processes based on condensation, that is transition from the gaseous to the solid state, take place mainly in high vacuum (10^{-3} to 10^{-7} mbar). (This process is determined by those variables controlling the mass transport.) In this range the film growth and the sequence of reaction can be controlled quite precisely. On geometrically simple objects a film thickness of some 1000 Å can be kept within tolerances of a few Å. The microroughness lies, depending on the material, between 10 to 100 Å; the film growth ranges, in the case of reactive evaporation, between 1 and 5 Å/s.

We can see that the growth rate is slower by almost one order of magnitude compared to that in the previously mentioned methods. In contrast to pyrolytic methods, of particular importance is the possibility of maintaining the temperature of the substrates and thus of the growing film as low as desired. For this reason, and because of the excellent controllability, this process is of particular importance for coating of temperature sensitive and high quality substrates in optics and electronics. Since a number of physical and chemical effects are strongly dependent on the state of the boundary layer and the surface layer of a solid, the application of reactive evaporation may become of growing importance in the next few years.

2. Processes in High Vacuum

According to the kinetic theory of gases, the number of collisions, Z_{volume}, of gas atoms in volume V assuming two-body collisions is

$$Z_{volume} = \bar{v} n V/2l$$

where V = volume in cm^3, $\bar{v}$ = mean molecular velocity in cm/sec, n = number of molecules in one cm^3, l = mean free path in cm.

The impingement rate on the wall Z_{wall} is

$$Z_{wall} = \bar{v} n F/4$$

where F = surface area in cm^2.

Thus we obtain for the ratio of the impingement rate and number of collisions in unit volume, the impact ratio

$$Z_{wall}/Z_{volume} = lF/2V$$

Examples are given in Table 1.

Table 1. Impact ratio Z_{wall}/Z_{volume} for oxygen in a cubic reaction space with 10 cm sides. l = mean free path.

Pressure [mbar]	l [cm]	Z_{wall}/Z_{volume}
1	6.5×10^{-3}	0.3×10^{-3}
10^{-3}	6.5	0.3
10^{-6}	6.5×10^{3}	0.3×10^{3}

At 10^{-3} mbar the impingement rate is almost equal to the number of collisions in unit volume, whereas at 10^{-6} mbar the number of collisions can be neglected as compared

[*] Prof. Dr. M. Auwärter
Balzers Aktiengesellschaft für Hochvakuumtechnik und Dünne Schichten
FL-9496 Balzers (Liechtenstein)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

to the number of impingements on the wall. At 10^{-6} mbar the impingement rate (Z_{wall}) on one square centimeter is 10^{14}. Since in the case of monomolecular coverage 1 cm^2 is covered by approximately 10^{15} molecules, a clean surface will be covered with one monolayer of the residual gas within a few seconds, if the condensation coefficient equals 1. Its value is dependent on the gas, the type and state of the substrate, and also on the temperature. This example shows that the inclusions of residual gas in a thin film which condenses at a rate of 2 Å/s are quite substantial and that one would have to use considerably lower pressures in order to eliminate them.

In the high-vacuum range the dominant residual gas is water vapor. This results in the presence of relatively strong van der Waals bonds with most substrates. In order to break these and subsequently remove the water molecules with a vacuum pump, the reaction vessel has to be heated for many hours at 400 °C.

Figure 1 shows the mass spectrum of the surface of a carefully cleaned stainless steel target before and after heating[14]. Figure 2 is another example for the almost always undefined chemical state of the surface of a solid; it shows the positive secondary ions measured on the surface of a supposedly clean Si-surface with a secondary ion mass spectrometer[15].

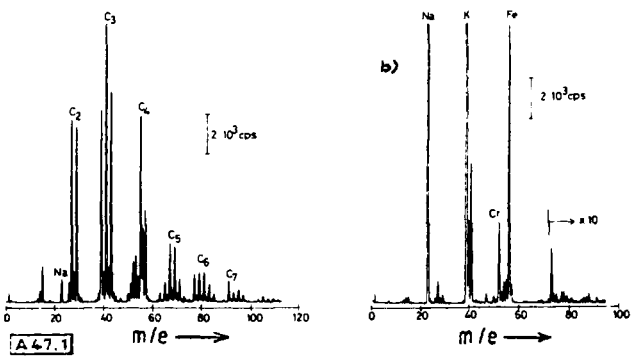


Fig. 1. Mass spectrum of the surface of stainless steel a) before and b) after bakeout [14].

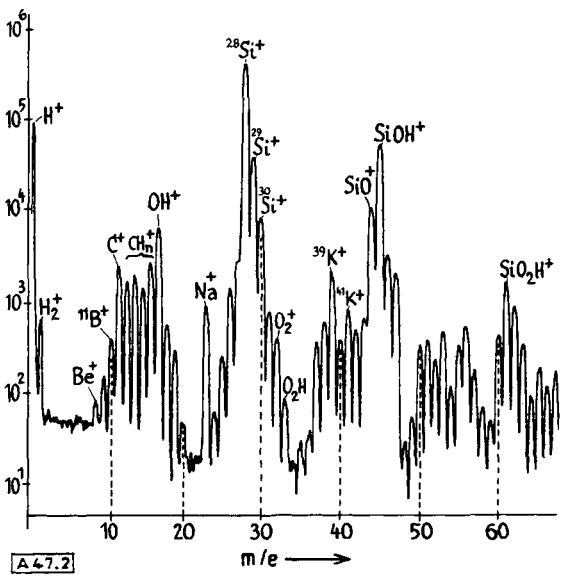


Fig. 2. Mass spectrum of positive secondary ions of the surface of a silicon disk [15].

We may assume that condensation of atoms of metals and insulators on a substrate surface will be substantially influenced by adsorbed gases. Many properties of substrates, as for example the adhesion of the condensed layer, will be changed in a way which is in most cases not easily predictable.

Of prime importance is the bonding of the adsorptive to the adsorbent. In the case of pure physisorption, desorption can be obtained rather easily. Atomic adsorption, however, very often involves several different adsorption states. Besides water, oxygen is also particularly strongly bound. Its heat of adsorption corresponds to the heat of formation of oxides, so that chemisorption approximates to chemical bonding. When coating substrates, as for instance glass, oxygen generally plays a less important role. This is quite different, however, in the case of transition metals, where an oxide-boundary layer is formed because of the incompletely filled d-shell due to diffusion of oxygen.

The bonds with hydrogen are considerably weaker; consequently desorption can be achieved relatively easily.

Nitrogen is almost always adsorbed molecularly and therefore exhibits the bonding character of a physisorption. There are however substrates at which the molecule dissociates, resulting in chemisorption due to atomic adsorption. This happens in the case of refractory metals like Zr, Ti, Mo, Ta, and W.

Hydrocarbons, which are frequently present in vacuum systems, are cracked, particularly at metallic substrates.

In order to remove adsorbed layers, the substrate is exposed to a glow discharge. In this process sputtering also occurs so that atoms from the electrode condense on the substrate and form nucleation centers. In contrast to the rather short mean residence time of a physisorbed gas molecule, the residence time of a condensed atom or molecule at the surface of a substrate is considerably longer; this means however that during this residence time of the single molecule other condensing molecules must interact with it. Nuclei are particularly suited for this interaction. *Hass*[1b] has investigated this interaction on silver and observed the formation of droplets by means of electron micrographs. *Zinsmeister*[2] recently made a significant contribution to the nucleation theory. *Zehnder*[3] has found that condensation of Zn—Cd atoms on paper becomes possible only after prenucleation, for instance with silver atoms.

Originally, thin films produced by evaporation of suitable materials in high vacuum were mainly applied in optics. The substrate material was therefore generally glass. Other substrate materials, for instance metals, first came into use after the development of microelectronics.

3. Reactive Evaporation

The equipment for manufacturing of thin films is simple. A crucible is heated electrically in a chamber evacuated to high vacuum. Preferred materials are refractories, such as molybdenum, tantalum and tungsten; others are pyrolytic graphite and ceramic materials of high thermal stability, such as ThO_2, BeO, ZrO_2, Al_2O_3 and MgO. For evaporation of aluminum, boron nitride/titanium boride crucibles have been used successfully. Electrically nonconducting crucibles have to be heated indirectly. Fig. 3 shows several types of evaporation sources.

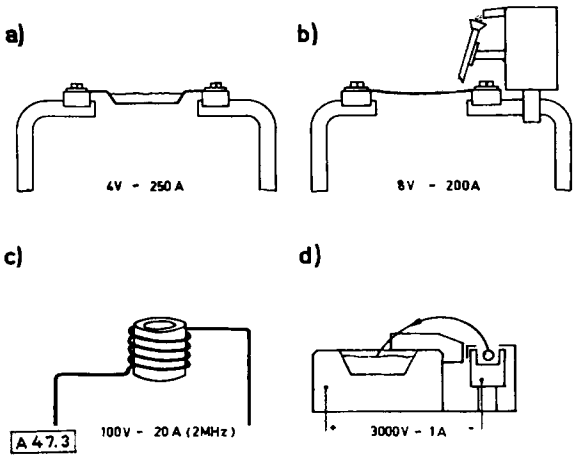


Fig. 3. Examples of evaporation sources: a) Boat evaporation, b) Flash evaporation, c) Inductive heating, d) Electron beam evaporation.

When SiO_2 is heated at 1500 K in a crucible made of material that has reducing properties, sublimation of the reaction product SiO will occur according to

$$M + SiO_2 \rightarrow MO + SiO.$$

The physical properties of SiO are quite different from those of SiO_2. The suboxide SiO has a higher index of refraction n, and higher optical absorption, which is disturbing for most applications in the visible and ultraviolet range; but it is easier to evaporate. If reaction with the crucible material is avoided, then evaporation of SiO_2 as such is possible without dissociation. Highly energetic electron beams are particularly suitable in this case. On penetrating the quartz glass, the beam is retarded and dissipates its energy.

TiO_2 is not only reduced to TiO by reactive crucible materials, but may also dissociate thermally at the high evaporation temperatures. The free oxygen will be removed by the pumping system. The oxygen deficiency can be compensated for by maintaining a partial pressure of oxygen. If at least a partial back reaction, in this case reoxidation, can be maintained in this way, we speak of *reactive evaporation.*

Atoms and molecules evaporating from the crucible are allowed to condense onto a substrate which is mounted at a suitable distance from the crucible.

In reactive evaporation the total pressure of permanent gases and water vapor, which is always present in high vacuum, is so chosen as to avoid collisions occurring between evaporated particles and the residual gas.

Hence, the mean free path l must be at least equal to the distance between crucible and substrate:

$$l = \frac{kT}{\sqrt{2}[\pi(r_1+r_2)^2 P]}$$

where P = total pressure, r_1 and r_2 = radii of gas molecules and evaporating substance, respectively, k = Boltzmann constant, T = absolute temperature.

The total pressure P has to be adjusted to the geometry of the system. The distance between crucible and substrate will range between 20 cm and 2 m, depending on the equipment.

The molecular beam leaving the crucible has a cosine distribution. Its particle density (per volume unit) decreases with the distance R from the crucible approximately according to Lambert's law with $1/R^2$.

For simplification let us call the molecules of the condensing substance A and those of the residual gas B. Because of collisions with the wall, B molecules will impinge on the substrate with arbitrary angle distribution in contrast to A molecules, which impinge with directed angle distribution. Since we exclude collisions between the A molecules, the B molecules, and between A and B molecules, the maximum pressure of B molecules is given. Thus the impingement rate of B molecules (*e.g.* oxygen) on the substrate as a function of the geometry can be calculated from $Z_{wall} = n\bar{v}F/4$. For a crucible-substrate distance of 64 cm and an equal mean free path, the partial pressure of oxygen, which equals the total pressure by displacing the other gases, may be 10^{-4} mbar at most. The corresponding impingement rate Z_{wall} on the substrate is $\approx 10^{16}$ cm^{-2} s^{-1} for $\bar{v} = 4 \cdot 10^4$ cm/s.

Ritter[4] as well as *Kerner* and *Mutschler*[5] have determined the condensation coefficient for B molecules, by investigating the reaction between A and B molecules. Whereas A particles have a condensation coefficient of 1, that of the B particles is ≈ 0.1. To initiate the reaction approximately 10^{15} particles cm^{-2} s^{-1} of A molecules must impinge on the substrate. The kinetic energy $m\bar{v}^2/2 = 3kT/2$ of an A molecule is considerably greater than that of a B molecule. Collisions of A with B molecules would reduce the kinetic energy through interaction: this would lead to soft layers on condensation. We now understand why the required mean free path of the B molecules must be maintained. The allowed margin in choosing the oxygen pressure of the B molecules is very narrow. For a chosen crucible—substrate distance of 64 cm, it will range between 3×10^{-4} and 7×10^{-5} mbar. Control of pressure, for example to 1×10^{-4} mbar, has to be done automatically, because manual control would not be precise enough. Fig. 4 illustrates the above mentioned example of TiO evaporation; it shows the refractive index n of TiO_2 films—prepared by reactive evaporation of TiO—as a function of oxygen pressure. Very similar results are obtained with Ti.

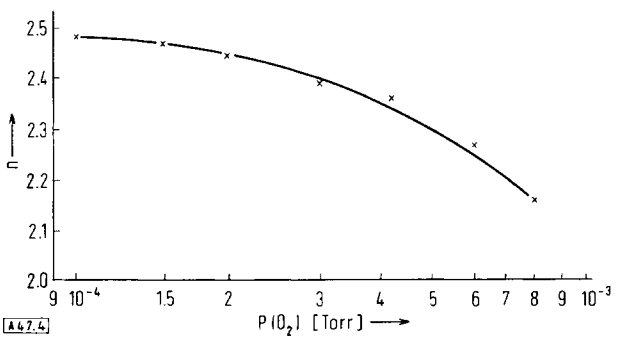


Fig. 4. Refractive index n ($\lambda = 550$ nm) of TiO_2 films as a function of the oxygen pressure during reactive evaporation. $P(O_2)$ = oxygen pressure [4].

Let us briefly study the phenomena of condensation of the A particles and adsorption of B particles on the substrate. The A molecules have a longer mean residence time on the surface of the substrate than the B molecules. In addition, similarly to B molecules in a way, they form a two-dimensional gas with a surface mobility that will depend on the nature of the substrate and the A and B molecules respectively. Thus there is the possibility that small A-aggregates are formed as droplets.

According to *Thomson* the following expression holds for the vapor pressure of a droplet:

$$P_r = P_\infty \exp. \frac{2\sigma V_A}{rkT}$$

where P_r = vapor pressure of the droplet, r = radius of droplet, V_A = volume of an A molecule, P_∞ = equilibrium pressure at the temperature T[K], σ = surface tension.

The smaller r is, the greater will be the vapor pressure P_r of the A molecules in the droplet. Therefore extremely small droplets disappear through desorption of the A molecules or combine with larger already existing droplets. To obtain a stable nucleus, that is a sufficiently large droplet, a critical nucleus size must be exceeded. For nucleation, there must be an oversaturation of A molecules on the surface of the substrate. In order that an A particle condenses, it must impart its excess kinetic energy to the substrate during the mean residence time, which happens after a few lattice vibrations. A measure of the energy exchange is the accommodation coefficient

$$\gamma = (T_g - T_g')/(T_g - T_0)$$

where T_0 = temperature of the surface, T_g and T_g' = the temperature of the A molecule before and after reflection.

After condensation is completed $T_g' = T_0$, *i. e.* $\gamma = 1$.

If, due to surface migration, one adsorbed atom starts interacting with another, the strength of bonding is increased. Upon further growth, the stable nuclei expand parallel to the surface. Thus at first a two-dimensional colloid-dispersed state is generated, which proceeds until the droplets growing by coalescence combine. In many substances the thickness follows the growth structure at the surface; thus, for instance, MgF_2, ZnS and other compounds, on glass substrates exhibit a columnar growth. Fig. 6 shows the columnar growth of a 1800 Å thick ZnS film[6].

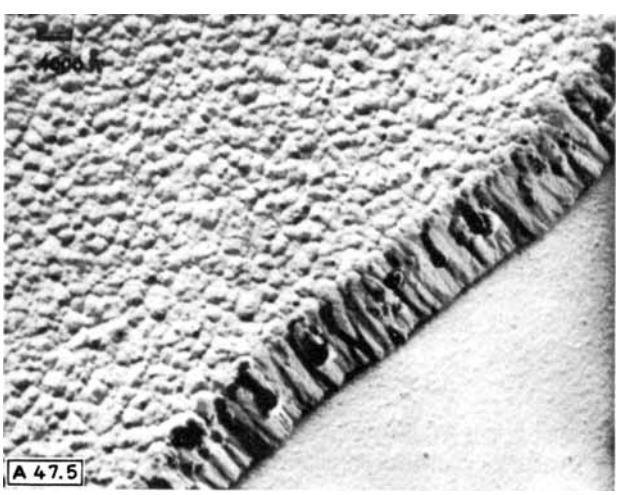


Fig. 5. Electron micrographic cross-section of a 1800 Å thick ZnS film [6].

The competition between cluster formation and the desired reaction

$$2SiO + O_2 \rightarrow 2SiO_2$$

leads to an inhibited reaction in which in addition to Si—O—Si bonds, Si—Si bonds are also formed. The latter are not oxidized completely in the course of film growth, especially at higher substrate temperatures.

Oxidation is also not complete at lower temperatures, even though no Si—Si bonds seem to be formed[7]. Indeed, in a reactive evaporation experiment with non-excited O_2 molecules, *Cremer*, *Kraus*, and *Ritter* found layers of composition Si_2O_3[8]. Reaction of SiO with oxygen requires practically no activation energy. The same is true for the reactive evaporation of Al_2O_3.

In the case of the more reactive Ti, TiO_2 is formed from TiO with O_2 as reactive gas; the TiO_2 is present in the form of a mixture of anatase and rutile.

Fig. 6 shows the growth of reactively deposited TiO_2 films as a function of substrate temperature[9].

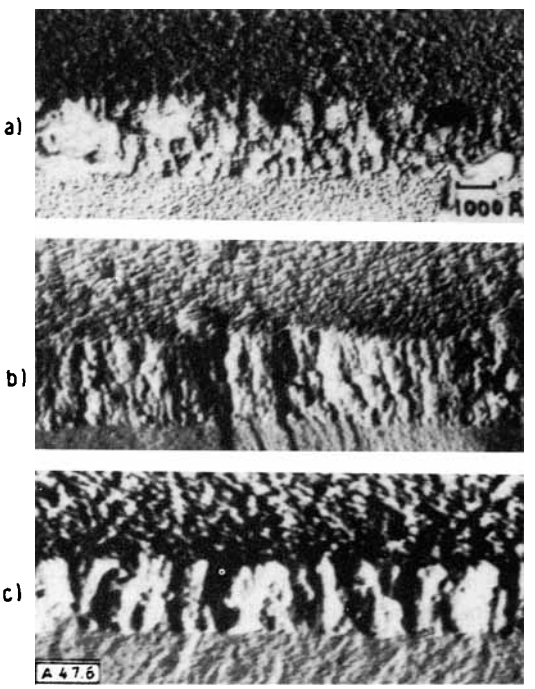


Fig. 6. Electron micrographic cross-section of TiO_2 films, deposited at different substrate temperatures: a) 30 °C, b) 150 °C, c) 400 °C [9].

An interesting reaction is shown by ZnS and other II—VI compounds when evaporated in high vacuum:

$$\underset{(s)}{ZnS} \rightarrow \underset{(g)}{Zn} + \underset{(g)}{{}^1/_2 S_2}$$

i. e., in the gaseous phase, there exist only Zn atoms and S_2 molecules due to dissociation. No condensation of Zn and only a partial condensation of S_2 takes place on the substrate. Only after interaction of Zn and S_2 at the surface is ZnS formed again, *i. e.* ZnS with a small surplus of sulfur.

The temperature dependence of this process and of the oxidation of SiO and TiO is negative, *i. e.* less oxide or sulfide is formed at higher substrate temperatures, since the chemisorption of oxygen or sulfur decreases with increasing substrate temperature[10].

The author first introduced reactive evaporation in 1952 and proposed the activation of B molecules with a gas dis-

charge in order to obtain increased interaction between A and B particles during condensation[11]. Recently, similar experiments have been performed on a laboratory scale by *Heitmann*[12], using a plasma discharge, and by *Zollinger*, with an arrangement that allows the process to be carried out on an industrial scale[13]. The ions, which are generated in small concentrations only, and the excited states result in accelerated reaction between A particles and B particles; an example is

$$2SiO + O_{2\,excited} \rightarrow 2SiO_2$$

With this method the less reactive nitrogen leads to formation of nitride. Furthermore, the generation of carbides is possible. Using reactive evaporation with activated gas, higher condensation rates can be obtained, thus increasing the economics of the method somewhat compared to classic "reactive evaporation".

Among the methods of film production at low pressures, cathode sputtering is the oldest. The underlying physical principles of sputtering using gas discharges will not be dealt with in detail here. Two electrically insulated electrodes are mounted opposite each other in a vacuum chamber, which is evacuated to 1×10^{-2}—5×10^{-2} mbar. On applying a direct voltage of 1—5 kV a self-sustained gas discharge is initiated. Because of the electrical field the positive ions of the sputter gas formed in this way strike the cathode with high energy, most of them penetrating it and imparting their energy, *e.g.*, to dislocations in the lattice. Thus focused collision cascades are generated in atomic arrangements that favor such generation; subsequently atoms of the very last surface layer of the cathode are ejected into the gas phase. If the sputter gas possesses a chemical affinity for the cathode material, they react with each other.

If the cathode consists of two or more components, then, in contrast to thermal evaporation, fractional distillation does not occur, even if the vapor pressures of the components differ. The thin film deposited on the substrate will have the same composition as the starting material.

Oxides, carbides, nitrides and sulfides can be produced with reactive sputtering. The growth rates are somewhat smaller than in the case of reactive evaporation. Nevertheless this process has found broad application in electronics due to many advantages it offers.

The question whether the processes described are suitable for the production of materials in large quantities can only be answered when the mass transport of the reaction partners is compared with that of other processes. Since vacuum equipment can be manufactured with dimensions of only a few meters without being too expensive, the quantity of material that can be deposited by condensation is limited because of the limited size of the substrate. Obviously the condensation area may be increased by suitable attachments, for instance by an unrolling band. Thin films possess great internal stresses because of the extremely high disorder; this may cause peeling off from the substrate at film thicknesses of a few thousand nanometers. This would not cause any limitation to the production of material, since, in this way, a new substrate surface is always being regenerated for condensation. For comparison purposes the determining factor is always the growth rate.

The output of distillates of a molecular evaporator is, on the average, 1.5×10^{-4}—4×10^{-4} g/cm^2 s. For a density of $\rho = 1$ (g/cm^3) the resulting growth rate is 1.5×10^{-4}—4×10^{-4} cm/s.

We have quoted the growth rate in reactive evaporation as being 1—5 Å/s, or 1×10^{-8}—5×10^{-8} cm/s. In reactive sputtering, the mass transport is even smaller. Thus the possible output of molecular evaporators per cm^2 and second is 10^4 times greater. The evaporator surface is almost the same size as the condenser surface, and the vapors escape from a very thin liquid film. In this way it is possible to preserve sensitive products to the greatest extent by using the shortest possible residence time and the lowest possible temperature.

In comparison to the condensation surface, we have in reactive evaporation a point-shaped vapor source, the output of which is therefore considerably limited. The vacuum processes described are obviously used in those cases, where one aims at obtaining an increased value of the product by refining the substrate or by utilizing physical effects. They therefore also differ from processes in which materials are evaporated under high vacuum without chemical reaction.

The method of reactive evaporation is therefore limited to those applications in which one wishes to modify properties of solids in some particular way by extremely thin films. Surface-dependent effects are: corrosion, friction, electrical properties such as *e.g.* electron emission, reflection and absorption. For those interested in reaction kinetics, the vital question is whether thin films of this type can be employed to advantage in the area of heterogeneous catalysis. It is conceivable that thin films may be useful at least for test purposes. Thus, for example, a bolometer strip of minimal heat capacity, which is protected by an inactive thin film and whose electrical resistance is temperature-sensitive, could be coated with an additional thin and catalytically effective film. A reaction will always be exothermic or endothermic, *i.e.* the temperature will change, and this will be indicated by a change in the resistance of the bolometer.

It is difficult to predict to what extent thin films may become of importance in chemical processes. One thing is sure, however: neither reactive evaporation nor reactive sputtering is suitable for the production of large quantities of materials.

Received: July 5, 1974 [A 47 IE]
German version: Angew. Chem. *87*, 227 (1975)

[1] a) Ullmanns Encyklopädie der technischen Chemie, 3rd Edit. Verlag Chemie, Weinheim 1973, Vol. 3; b) *G. Hass*, Naturwissenschaften *25*, 232 (1937).
[2] *G. Zinsmeister*, Krist. Techn. *5*, 207 (1970).
[3] *E. Zehnder*, Optik (Stuttgart) *10*, 156 (1953).
[4] *E. Ritter*, J. Vac. Sci. Technol. *3*, 225 (1966).
[5] *K. Kerner* and *G. Mutschler*, Bosch Techn. Ber. *3*, Heft 3, p. 3 (1970).
[6] *H. K. Pulker* and *E. Jung*, Thin Solid Films *9*, 57 (1972).
[7] *A. Faessler* and *H. Krämer*, Ann. Phys. [7] *4*, 263 (1959).
[8] *E. Cremer*, *Th. Kraus*, and *E. Ritter*, Z. Elektrochem. *62*, 939 (1958).
[9] *H. K. Pulker* and *K. H. Günther*, lecture at the meeting of the Oesterreichische Physikalische Gesellschaft, Oct. 1973, Innsbruck.
[10] *E. Ritter* and *R. Hoffmann*, J. Vac. Sci. Technol. *6*, 733 (1969).
[11] *M. Auwärter*, Austrian Pat. 192650 (1952), Gerätebauanstalt Balzers.
[12] *W. Heitmann*, Appl. Opt. *10*, 2414 (1971).
[13] *E. Zollinger*, DOS 2305359 (1973), Balzers Aktiengesellschaft für Hochvakuumtechnik und Dünne Schichten.
[14] *W. K. Huber* and *E. Loebach*, Verh. Deut. Phys. Ges. 5, 470, 0-28 (1972).
[15] *R. Buhl*, lecture at the meeting of the Deutsche Glastechnische Gesellschaft, April 1974, Frankfurt a. M.

Formation of Ad-Layers and Clusters on Condensation of Metal Vapors on Solid Surfaces[**]

By Rolf Niedermayer[*]

Synthesis of organometallic materials can be accomplished in many cases by cocondensation of metal atoms and organic molecules at low temperatures. The reaction kinetics is determined by the competition between metal cluster growth and formation of the organometallic compound. Interesting compounds may contain one or more metal atoms; the latter type could be obtained by reaction between a cluster containing the desired number of metal atoms and an organic molecule. A precise knowledge of the events occurring on condensation of metal atoms and cluster formation can therefore be of value in the control of chemical synthesis. These phenomena have been investigated in connection with the study of the growth of thin metallic films, both experimentally and theoretically. Direct observation of the formation of very small clusters is difficult. The good agreement between experimental results and recent calculations for the development of large clusters, however, allows reliable theoretical conclusions for the first stages of adsorption and cluster formation. The present contribution describes experimental work on film growth and relevant theoretical concepts, and an attempt is made to develop applications to organometallic synthesis.

1. Introduction

The common point of interest between the physics of thin films and low temperature condensation as a synthetic method[1] is the fate of a single atom on a solid surface. Only one method provides a direct answer to this question: field ion microscopy. It can conveniently be used for the direct observation of condensation, as well as subsequent diffusion, desorption, or possible cluster formation. However, the conditions of observation are severely restricted and the utility of the method consequently restricted. We therefore have to rely on more indirect methods if we wish to vary the experimental conditions over a wide range.

Those stages of condensation, in which coherent layers or extended clusters have already been formed, can easily be observed by electron microscopy or electron diffraction under a great variety of conditions[2-4], and it has become possible to analyze these experiments quantitatively[4, 5]. Examples of the experimental and theoretical results cited in this report will give an impression of the state of the art. The quality of these results for later growth stages permits conclusions to be drawn for the early stages, and thus provides an insight into the history of the individual condensed atom. This insight can be summarized by a number of simple mathematical expressions which conclude the present discussion.

2. Two-Dimensional Growth

An understanding of condensation phenomena requires that a distinction be made between a number of binding energies: Λ_0 the evaporation energy of the adsorbate, for example of the adsorbed metal, characterizes the binding of the metal atoms to one another. The energy required to separate a metal atom from a surface is known as the desorption energy (E_{des}). Finally, a certain activation energy has to be expended to move an adsorbed atom from one binding site to another, *i.e.* the migration or diffusion energy (E_{diff}).

Metal atoms condensed onto other metal atoms or onto semiconductors are often bound with a high desorption energy of the order of magnitude existing between the metal atoms. The desorption energy on ionic crystals, *e.g.* alkali halides, is somewhat lower, approximately 20 kcal/mol, while the binding of metal atoms to graphite or similar substrates, and probably to noble gases, is weaker, the desorption energy being about $\leqslant 10$ kcal/mol[6-9].

These differences in binding energy essentially determine the mode of film growth. It can in fact be shown that three-dimensional cluster formation is preferred if the binding between the metal atoms themselves is much stronger than their binding to substrate. Theoretical considerations[3, 10] lead to the following condition for three-dimensional cluster formation:

$$\Lambda_0 \geqslant 3 \cdot E_{des} \tag{1}$$

while two-dimensional clusters form if

$$\Lambda_0 \leqslant 3 \cdot (E_{des} - E_{diff}) \tag{2}$$

In intermediate cases the growth will be two-dimensional or three-dimensional, depending on the geometry of the lattices of substrate and film.

These general rules predict that metals on metals or semiconductors have an initial tendency to grow in two dimensions. In some instances this two-dimensional growth continues to form thicker films, but in most cases growth changes to the three-dimensional mode after completion of the first few monolayers.

An example of purely two-dimensional growth up to 80 ML (monolayers) currently being investigated by *Mlynczak*[6] will now be discussed. Ultrahigh vacuum and cleanliness of the substrate are absolutely essential if reliable conclusions are to result from investigations of this kind. In this experiment sodium is evaporated slowly onto a tungsten (100) surface.

[*] Prof. Dr. R. Niedermayer
Institut für Experimentalphysik IV der Universität
463 Bochum, Postfach 2148 (Germany)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices onf the Merck'sche Gesellschaft für Kunst und Wissenschaft e.V. at Darmstadt (May 12—15, 1974).

The number of condensed atoms, the structure of the film, the desorption energy, and the frequency constant of desorption can be determined independently in each individual experiment. Under certain conditions the diffusion energy can also been measured. All these data are necessary for analysis of a growth experiment, but in most cases they are not available at the same time.

Condensation of sodium at a rate of 10^{12} atoms/cm^{2}s onto tungsten at 370°K leads to saturation after deposition of 5×10^{14} atoms/cm^2 (Fig. 1). The structure of this film has been investigated *in situ* by grazing incidence high energy

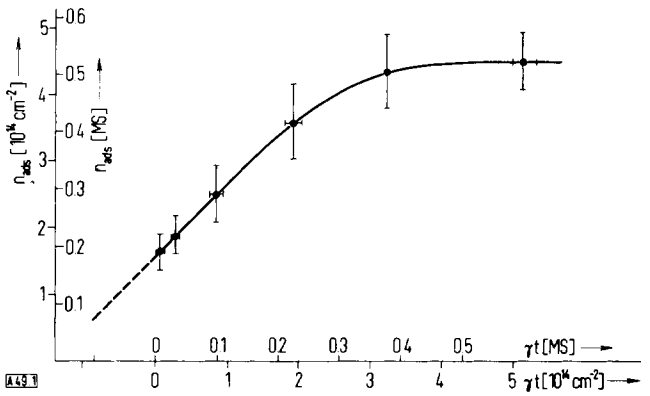


Fig. 1. Dependence of the number of sodium atoms n_{ads} adsorbed on a W(100) surface upon the number $\gamma \cdot t$ of atoms presented to the substrate. Impingement rate $\gamma = 9 \times 10^{11}$ atoms cm^{-2}s^{-1} (0.06 ML min^{-1}); substrate temperature, 370°K.

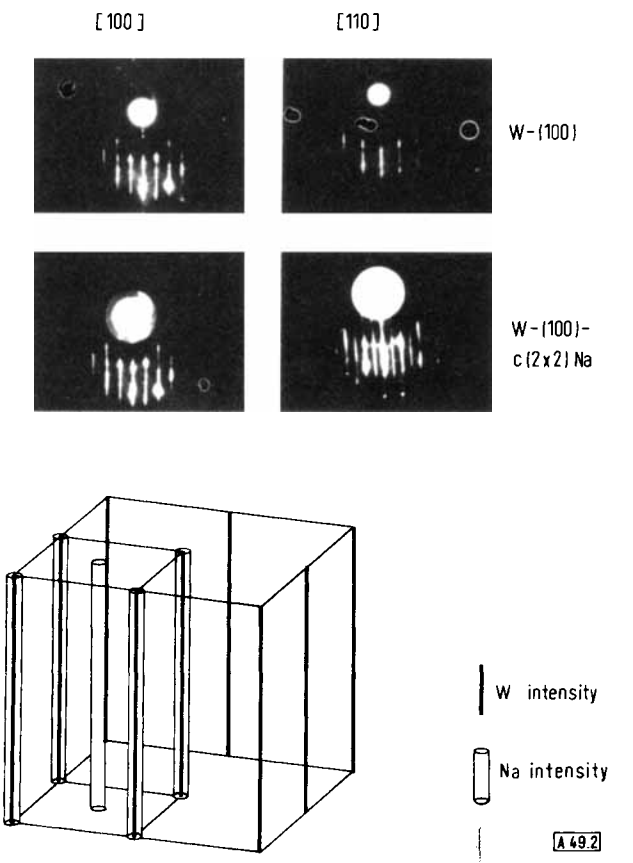


Fig. 2. Diffraction pictures of a clean W(100) surface in the [100] and the [110] azimuths, and of a W surface covered by 5×10^{14} Na atoms cm^{-2}. The lower part of the figure shows a drawing of the reciprocal mesh of the sodium-covered surface.

electron diffraction (RHEED) which affords diffraction patterns like that in Figure 2.

Both the diffraction pictures of the substrate and those of the film show elongated streaks perpendicular to the substrate and are characteristic of diffraction by two-dimensional structures. The Na-covered surfaces show additional streaks in the [110] azimuth. This provides an indication of the positions of the Na atoms, as shown in Figure 3.

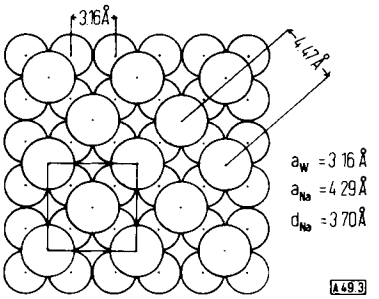


Fig. 3. Model of the sodium-covered tungsten surface as derived from the diffraction pictures.

The sodium atoms are seen to form a superlattice on W(100), which consists of a centered square mesh whose edge is exactly twice as long as that of the underlying tungsten surface. This means that the distance between the sodium atoms is about 4% greater than in the lattice of the compact material. The number of atoms per cm^2 in this configuration is precisely 5×10^{14} atoms. Comparison with the deposition experiment of Figure 1 shows that saturation occurs after completion of the above structure, *i.e.* that the desorption energy then falls. Similar observations are made in many other cases of metal film growth[2]. The energy of desorption is $E_{des} = 2.5 \pm 0.2$ eV, while the heat of evaporation of sodium is only 1.09 eV. According to eq. (2), this ratio of binding energies must lead to two-dimensional growth. At lower temperatures, *e.g.* 310°K, further growth proceeds linearly with time and remains two dimensional. The diffraction pictures still show streaks and remarkably, indicate no relaxation of the lattice constant to its bulk value up to 80 ML. Corresponding diffraction patterns are shown for 20 and 80 ML in Figure 4. The distortion of the lattice of the film up to relatively large thicknesses, *i.e.* real pseudomorphic growth, is a rather singular result of this investigation. It can be understood from the plot of the desorption energy as a function of thickness, shown in Figure 5. We have already stated that the first monolayer

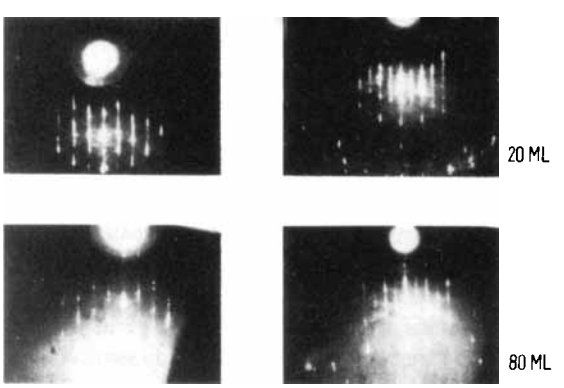


Fig. 4. Diffraction pictures of a W(100) surface covered by 2×10^{16} and 8×10^{16} Na atoms cm^{-2} ($T = 310$°K).

is adsorbed with a binding energy of 2.5 eV. The next layer is bound with 1.27 eV—as is apparent from Figure 5—and then the binding energy decreases monotonously to 1.06 eV, which is attained after 4 monolayers and corresponds approximately to the bulk evaporation energy of sodium. A layer of minimum binding energy would permit lattice relaxation *via* two-dimensional dislocations. However, no such layer is present in our example, and so relaxation must be severely impeded[11, 12]. The Na layer therefore remains strained, like a sheet of rubber stuck under tension to a piece of wood.

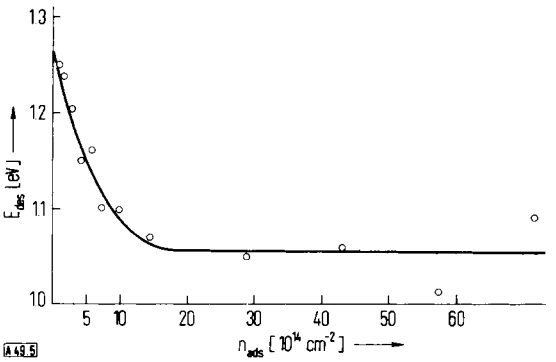


Fig. 5. Dependence of the desorption energy of sodium from tungsten on the number of deposited sodium atoms.

3. Three-Dimensional Growth

To our knowledge the example of extreme two-dimensional growth in Section 2 is the only known case of extended pseudomorphism, and should be considered as a limiting case of film growth. Incorporation of two-dimensional dislocations in an intermediate layer usually ensures early relaxation of the layer lattice. However, early transition to three-dimensional growth is more common, and can be particularly well demonstrated for an example studied by *Steinhage*[7]. *Steinhage* also investigated growth of an alkali metal, *i.e.* potassium, on W(100), using the same equipment but somewhat less refined. The potassium films start to grow two dimensionally in exactly the same way as Na films. The binding energy of the first monolayer is higher than that of the second. The structure of both layers corresponds to Figure 3. However, the third monolayer has a different structure and is much more weakly bound. The desorption energy falls to about 10% of the bulk evaporation energy of potassium after completion of the third monolayer, and further growth proceeds *via* three-dimensional clusters. The lattice parameters of these clusters agree with the bulk lattice constants. The diffraction pictures of the final structure are shown in Figure 6; the appearance of spots instead of streaks indicates three-dimensional diffraction, *i.e.* clusters. Compensation between the first two strained layers and the unstrained clusters must take place *via* an arrangement of two-dimensional dislocations in the interface. It appears significant that the change in the mode of growth occurs precisely when the binding energy has a minimum value.

Very similar results can be obtained in experiments on the growth of many metals on other metals or on semiconductors. However, these systems do not permit accurate determination of the number of clusters, and recourse is generally taken to the growth of metals on alkali halides for

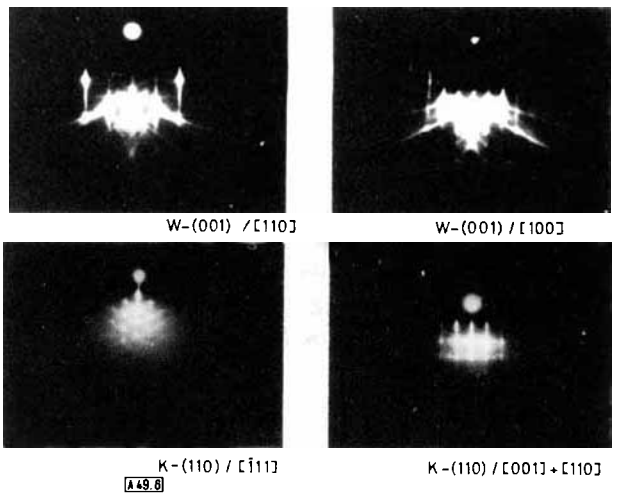


Fig. 6. Diffraction pictures of a clean W(100) surface and of three-dimensional potassium clusters grown on this surface.

investigations on cluster formation and nucleation. In these experiments the cluster layer is fixed in a thin amorphous carbon film and the substrate then dissolved. The carbon films are subsequently investigated by transmission electron microscopy to measure of the number and size of nuclei. Typical examples are the growth experiments for Au on NaCl conducted by *Robins et al.*[13, 14]. Figure 7 shows a series of electron micrographs of the nucleation and coalescence of gold clusters on a (100) rock salt face at a condensation rate of 10^{13} cm^{-2}s^{-1} and a substrate temperature of 250 °C. Nucleation is homogeneous, apart from a few steps of the substrate. The nuclei are partly oriented in preferential directions; their number passes through a maximum and then decreases slowly owing to coalescence. The particles are approximately 150 Å in diameter at the time of maximum nucleus density. Evaluation of such micrographs reveals the dependence of the number of nuclei upon time (Fig. 8). The

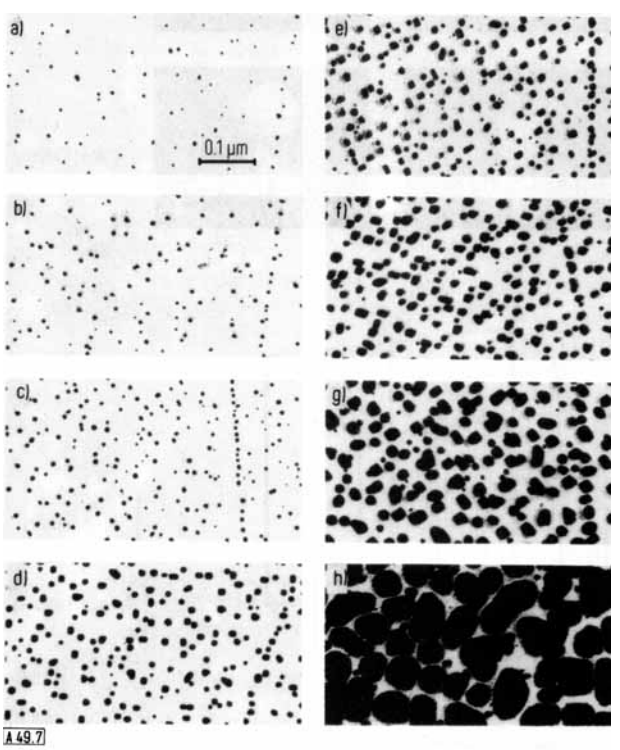


Fig. 7. Electron micrographs of clusters in various growth phases (Au on NaCl (100) surface).

increasing curve (short time scale) corresponds to the end of the nucleation stage while the decreasing curve (long time scale) represents the coalescence stage.

Thus the nucleation rate $\dot{N}_c$, the saturation concentration $N_{c(sat)}$, and the cluster size can be measured as a function of time t, substrate temperature T, and impingement rate J_{imp}. These results can be understood quite well in terms of a kinetic theory of cluster growth, and lead to conclusions about the initial stages of growth.

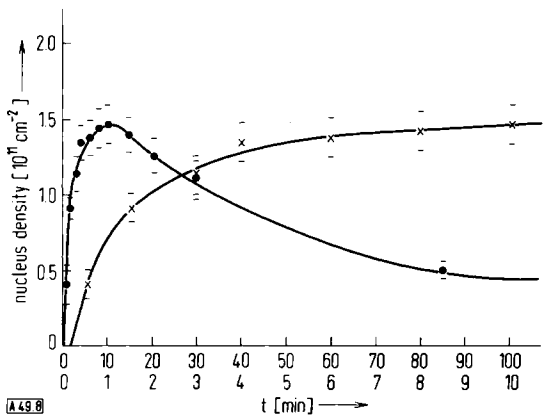


Fig. 8. Evaluation of the growth experiment of Fig. 7. Dependence of nucleus density upon deposition time (×, short time scale; , long time scale). Impingement rate $\gamma = 10^{13}$ atoms $cm^{-2} s^{-1}$; substrate temperature, $T = 523$°K.

4. Kinetic Theory of Cluster Growth

Cluster growth can be analyzed with the aid of a fundamentally simple kinetic theory. A brief account of this theory will be followed by a discussion of the results obtained for the growth of gold on rock salt, which permits a comparison with experiment (Section 3).

Cluster growth has attracted much theoretical attention during the last decade[4, 5], most of the work being based on a model of a sequence of molecular reactions. Monomers B_1 react with i-atomic polymers B_i.

$$B_i + B_1 \underset{J_i}{\overset{\alpha_{i+1}}{\rightleftharpoons}} B_{i+1} \tag{3}$$

The decay probabilities α_{i+1} can be calculated from thermodynamics, and the growth probabilities J_i by solution of the diffusion problem[15, 16]. The complete polymerization process can be described by a set of differential equations:

$$\dot{n}_i = J_{i-1} n_{i-1} - (J_i + \alpha_i) n_i + \alpha_{i+1} n_{i+1} \tag{4}$$

The growth probabilities depend on all polymer concentrations and the size of the growing polymer, while the decay probabilities depend on the properties of the decaying polymer and on temperature only. In connection with this theory a polymer will be called a "cluster". If the set of equations (4) can be solved then all experimentally important quantities can be easily derived. These quantities are: the total number of stable clusters

$$N_c = \sum_{i=i^*+1}^{\infty} n_i \tag{5}$$

where B_{i^*+1} is the smallest stable cluster;
the number of atoms condensed in the stable clusters

$$N_a = \sum_{i=i^*+1}^{\infty} i \cdot n_i \tag{6}$$

and the mean cluster size

$$\langle i \rangle = N_a / N_c \tag{7}$$

from which the mean cluster radius can easily be derived.

Numerical solution of eqs. (4) is in fact possible. The only data required for such calculations are the binding energies, the lattice parameters, substrate temperature, and impingement rate. Figure 9 shows the detailed results for the case of gold on a rock salt substrate at 573 °K and an impingement rate of 10^{13} $cm^{-2} s^{-1}$. The desorption energy ($E_{des} = 20$ kcal/mol) and the diffusion energy ($E_{diff} = 8.5$ kcal/mol) have been chosen for best agreement with a wide range of measurements. Under such conditions the growth process is governed by the equilibrium between impingement and desorption, which is indicated by a constant value of monomer concentration for a considerable time interval. The stationary value determined by impingement rate J_{imp} and desorption probability α_{des} is

$$n_{1(sat)} = J_{imp}/\alpha_{des} \tag{8}$$

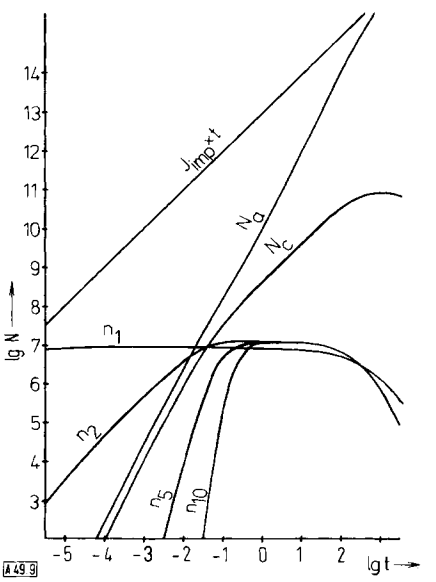


Fig. 9. Calculated dependence of some cluster concentrations n_i, the total number of stable clusters N_c, and the number of condensed atoms N_a on deposition time. Number of atoms presented to the substrate $J_{imp} \cdot t$ at deposition rate J_{imp} is also shown.

The induction period before the start of nucleation is 10^{-2} s and the nucleation ends by coalescence after 100 s; the maximum number $N_{c(sat)}$ of clusters is reached after 1000 s. The nucleation period is characterized by a linear increase in the number of clusters N_c. Another result that can be obtained from the theory concerns the size of the critical nucleus, *i.e.* of that cluster which is just more likely to grow than to decay under the conditions of the experiment. In this case the first stable cluster is a trimer. Each class of clusters has its own induction period; the rise of the cluster concentrations is steeper the larger the cluster. The number N_a of condensed

atoms increases with t^2 during the nucleation period, and then becomes linear. This is in general agreement with experiments on retarded condensation[17].

Unfortunately, the observation of the time dependence of film growth is limited to the final stages of the nucleation period (Fig. 8). This makes a direct comparison of experiments with the theoretical results (Fig. 9) difficult. However, the dependence of nucleation rate, saturation concentration, and mean radius at saturation upon temperature and impingement rate permits comparison of the properties of cluster growth with experiment over a wide range of conditions. Figure 10 shows the influence of the impingement rate on the above parameters. The plots of the nucleation rate $\dot{N}_c$ are almost linear over a wide range of impingement rates, and the slope is $2<\mathrm{d}(\ln N_c)/\mathrm{d}(\ln J_{imp})<2.5$. The size of the critical clusters is given alongside the curve plotted for 834 °K. The influence of the critical cluster size on $\dot{N}_c$ is much less pronounced than, *e.g.*, on nucleation of mist droplets because nucleation in film growth is determined by surface diffusion to a far greater extent than by the decay equilibrium. The dependence of the saturation concentration and the mean radius upon impingement rate is much weaker than that of the nucleation rate. Figure 11 shows the temperature dependence of film growth. At high temperatures the saturation concentrations of clusters decrease and the mean cluster size increases. This is of practical importance for the reduction of crystal defects in thin films. A comparison of experimental data obtained by *Robins et al.*[13] with theoretical results is shown in Figure 12. The dependences of nucleation rate and saturation concentration upon impingement rate (at 300 °C) and substrate temperature (at 10^{13} cm^{-2} s^{-1}) agree within the experimental scatter of data.

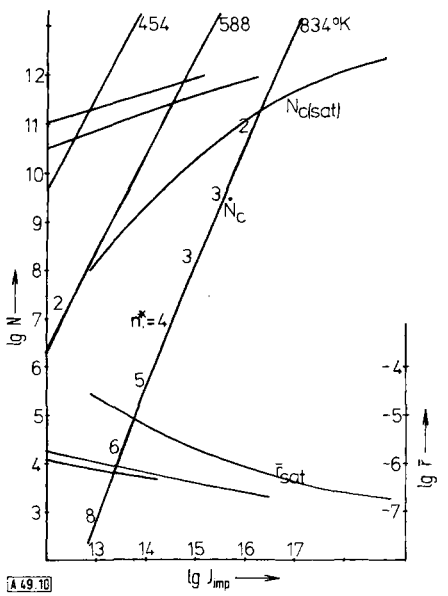


Fig. 10. Logarithmic dependence of characteristic film parameters on impingement rate J_{imp} for some temperatures. N_{cisat} is the saturation nucleus concentration, $\dot{N}_c$ the nucleation rate, $\bar{r}_{sat}$ the mean cluster radius at the time of saturation (in cm). n^* is the size of the critical nucleus at the points indicated.

This indicates that numerous growth experiments can be described by a kinetic theory. Extrapolations to experimentally unobservable regions therefore seem justified.

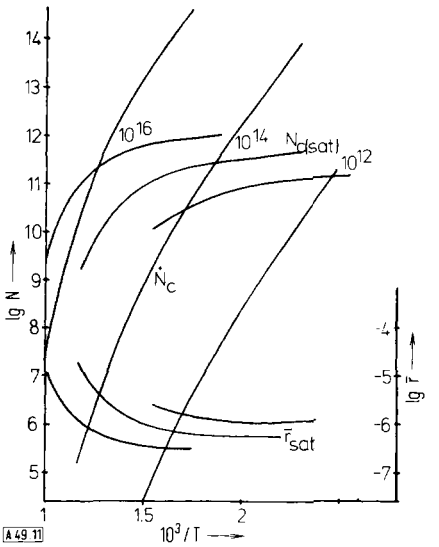


Fig. 11. Logarithmic dependence of characteristic film parameters on substrate temperature T for some impingement rates. Legend as in Fig. 10.

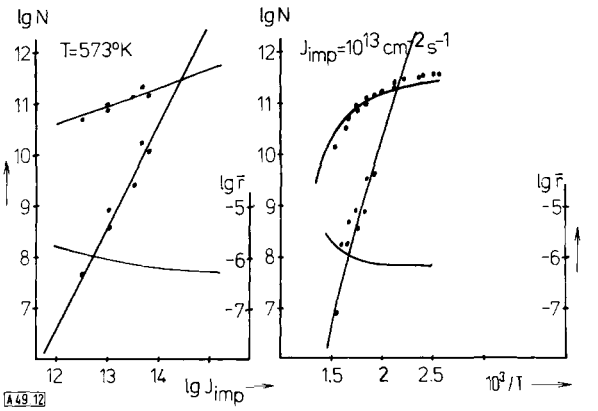


Fig. 12. Comparison between theoretical results for the growth of gold on a substrate with $E_{des}=20$ and $E_{diff}=8.5$ kcal/mol and experimental growth data for gold on rock salt (points from [13, 14]).

5. Low Temperature Condensation

Two examples of low temperature condensation will be presented: condensation of gold at 80 °K and an impingement rate of 10^{16} cm^{-2} s^{-1} on substrates characterized by (i) $E_{des}=5$ and $E_{diff}=2$ kcal/mol and (ii) $E_{des}=10$ and $E_{diff}=4$ kcal/mol. These substrate data might be representative for physical adsorption of a metal on a solid noble gas surface. Accurate experimental data are not yet available.

The low binding energy case is shown in Figure 13. The desorption equilibrium described by eq. (8) is not attained. Instead the monomer concentration is limited by twin formation before significant desorption can occur. The cluster concentrations and nucleus concentrations rise very steeply. No nucleation period, $N_c \sim t$, is observed. The growth under such conditions can be described by an induction period of 10^{-5} s, twin formation until 10^{-3} s, growth of the almost constant number of nuclei until 10^{-1} s, then coalescence. Diffusion is the governing feature of this mode of growth.

Both cases together are shown in Figure 14. In the high binding energy case diffusion of the monomers is largely restricted and film formation occurs directly by coalescence without involving clusters. The induction period is 10^{-2} s. This mode

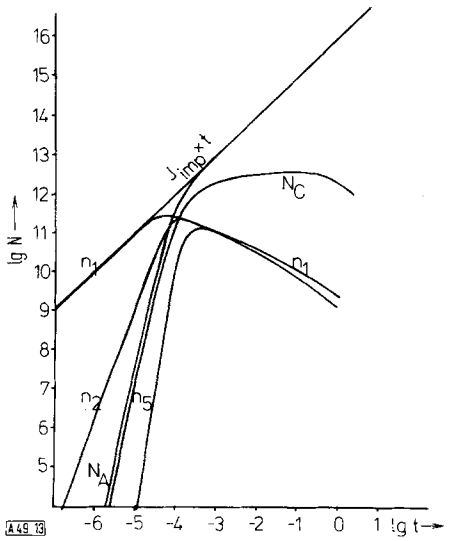


Fig. 13. Calculated dependence of cluster concentrations on deposition time. Legend as in Fig. 9. The calculations are for the case of weakly bound gold ($E_{des}=5$, $E_{diff}=2$ kcal/mol) on a substrate at 80°K.

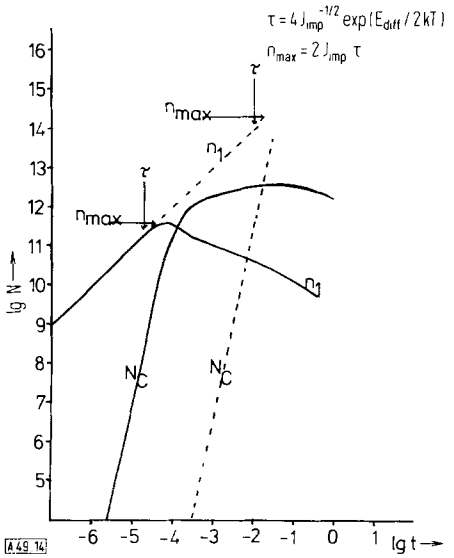


Fig. 14. Calculated dependence of cluster concentrations on deposition time for two different cases of binding. ——, binding as in Fig. 13; – – –, binding with $E_{des}=10$ and $E_{diff}=4$ kcal/mol. The induction time τ and the maximum monomer concentration as calculated from eqs. (9) and (11) are also indicated for the two cases.

of growth also gives two-dimensional layers, which are however strongly disordered compared to those described above.

The foregoing example of low temperature condensation may be of interest for chemical synthesis, especially in the case of reduced surface migration. Simple formulas permitting rapid assessment of growth can be derived from the general theory for the low temperature case, *i.e.* the case where twin formation dominates over desorption. Thus the induction time is

$$\tau = \sqrt{1/(8a\cdot s\cdot \nu_{diff})}\cdot J_{imp}^{-\frac{1}{2}}\cdot\exp(E_{diff}/2kT) \qquad (9)$$

The square root generally lies between 1 and 10 $cm^{-1}\,s^{1/2}$. The concentrations of monomers and twins at the end of the induction period are

$$n_1 = J_{imp}\cdot\tau = \sqrt{1/(8a\cdot s\cdot \nu_{diff})}\cdot J_{imp}^{\frac{1}{2}}\exp(E_{diff}/2kT) \qquad (10)$$
$$n_2 \approx 0.04\cdot J_{imp}\cdot\tau$$

The maximum concentration of monomers is attained at $t_{max}\approx 3\cdot\tau$, and its value is

$$n_{1max} \approx 2J_{imp}\cdot\tau \qquad (11)$$

At this time the numbers of twins and monomers are approximately equal. These formulas can be used as guidelines for the choice of rates, temperatures, and substrates for the attainment of a certain monomer concentration at a given time.

6. Final Remarks

A systematic experimental and theoretical investigation of cocondensation of metals and noble gases and organic materials at low temperatures is still unavailable. Extensions of theoretical considerations delineated above should, however, not be too difficult.

Meanwhile some conclusions can be derived from the simple one-component condensation theory. If the metal atoms react with the cocondensing atoms, a new substrate will be formed, generally with a new diffusion energy. Whatever this may be, a suitable surface temperature and rate of impingement can always adjust the induction time τ and the monomer concentration at this time to optimum values for a reaction with single metal atoms:

$$J_{imp} = n_1/\tau$$
$$T = (E_{diff}/k)/\ln(8a\,s\,\nu_{diff}\cdot n_1\cdot\tau) \qquad (12)$$

Whether reproducible reactions with dimers, trimers, or higher polymers can be achieved experimentally or whether the conditions for such reactions can be deduced theoretically must remain the object of future investigations.

List of symbols

Λ_0,	energy of sublimation
E_{des},	energy of desorption
E_{diff},	energy of diffusion
T,	substrate temperature
k,	Boltzmann constant
γ, J_{imp},	impingement rate
α_{des},	desorption probability
t,	time
B_i,	symbol for a cluster of i atoms
n_i,	concentration of clusters B_i
J_i,	growth probability of a cluster B_i
α_i,	decay probability of a cluster B_i
N_c,	total concentration of stable clusters
N_a,	number of condensed atoms
$\dot{N}_c$,	nucleation rate
i^*,	critical cluster size
$\langle i\rangle$,	mean cluster size
$N_{c(sat)}$,	saturation concentration of stable clusters
$\bar{r}$,	mean cluster radius
$\bar{r}_{sat}$,	mean cluster radius at saturation
$n_{1(stat)}$,	stationary monomer concentration at desorption equilibrium
$n_{1(max)}$,	maximum monomer concentration
τ,	induction time
a,	distance between adsorption sites
ν_{diff},	diffusion frequency
s,	cross-section for twin formation

Received: July 29, 1974 [A 49 IE]
German version: Angew. Chem. *87*, 233 (1975)

[1] *P. L. Timms*, Advan. Inorg. Chem. Radiochem. *14*, 121 (1972); J. Chem. Educ. *49*, 782 (1972); Angew. Chem. *87*, 295 (1975); Angew. Chem. internat. Edit. *14*, 273 (1975).

[2] *H. Mayer* in *H. G. Schneider* and *V. Ruth*: Advances in Epitaxy and Endotaxy. Deutscher Verlag für Grundstoffindustrie, Leipzig 1971, p. 63.

[3] *R. Niedermayer*, Krist. Tech. *5*, 2 (1970).
[4] Survey: *J. A. Venables* and *G. L. Price* in *J. W. Matthews:* Epitaxy. Academic Press, New York 1975 (in press), Chap. 4.
[5] *R. Niedermayer in H. G. Schneider* and *V. Ruth:* Advances in Epitaxy and Endotaxy. Deutscher Verlag für Grundstoffindustrie, Leipzig 1974, p. 21.
[6] *A. Mlynczak*, Dissertation, Universität Bochum 1974.
[7] *P. W. Steinhage*, Dissertation, Technische Universität Clausthal 1969.
[8] *H. Schmeisser* and *M. Harsdorff*, Z. Naturforsch. *25a*, 1896 (1970).
[9] *H. J. Stowell*, Thin Solid Films *21*, 91 (1974).
[10] *E. Bauer*, Z. Kristallogr. Kristallgeometrie Kristallphys. Kristallchem. *110*, 372, 395 (1958).
[11] *F. C. Frank* and *J. H. van der Merwe*, Proc. Roy. Soc. *A 198*, 205, 217 (1949).
[12] *R. Niedermayer*, Thin Solid Films *1*, 25 (1968).
[13] *V. N. E. Robinson* and *J. L. Robins*, Thin Solid Films *20*, 155 (1974); and literature quoted therein.
[14] *A. J. Donohoe* and *J. L. Robins*, J. Cryst. Growth *17*, 70 (1972).
[15] *V. Halpern*, J. Appl. Phys. *40*, 4627 (1969).
[16] *K. J. Routledge* and *H. J. Stowell*, Thin Solid Films *6*, 407 (1970).
[17] *A. Hölting*, Dissertation, Technische Universität Clausthal 1969.

Production and Condensation of Metal Vapors in Large Quantities[**]

By Walter Reichelt[*]

1. Introduction

Anybody working with evaporation or sputtering of metals under reduced pressure knows that chemical reactions can occur between the vaporized metals and organic components present in the residual gases. Such vapors arising from paraffin oils for instance may enter the working chamber if baffeling between diffusion pump and chamber is poor. The products can often be recognized by their smell.

Reactions of this kind have their uses, however, and when performed on a production scale they require efficient sources of metal vapors. Some aspects of these sources will be considered in the present report.

2. Binding Energy and Evaporation Rates

Many practical applications require a knowledge of the evaporation rate, a quantity deriving from the binding energy of the metal. Macroscopic material constants depending upon the binding energy include the melting point and the heat of evaporation. If we have reliable values of the heat of evaporation of a metal, then vapor pressures can be calculated for any desired temperature. The vapor pressure values yield evaporation rates *via* the expression due to *Hertz:*

$$G = \alpha \cdot p_s \sqrt{M/(2\pi RT)}$$

G: evaporation rate [g cm^{-2} s^{-1}]; p_s: saturation vapor pressure; α: Langmuir coefficient (approximately unity for most of the metals encountered in practice when evaporated from the melt)

Vapor pressure values reported in the literature sometimes show considerable variations. An estimation of the errors can draw upon the theory of metal binding energies. Table 1 lists the temperatures at which the vapor pressure of a number of metals warranting interest in this connection amounts to 1 torr; the melting points and heats of sublimation are given in Figures 1 and 2.

[*] Dr. W. Reichelt
W. C. Heraeus GmbH
645 Hanau, Postfach 169 (Germany)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

Table 1. Temperatures at which the metals listed have a vapor pressure of 1 torr.

Metal	T [°C] [1]	[2]	[3]
Ti	—	2180	2191
Cr	1578	1610	1695
Mo	3118	3300	3280
W	—	3980	3874
Fe	1798	1780	1790
Ni	2730	1800	1408
Co	—	1910	1471
Pt	2646	2600	2531

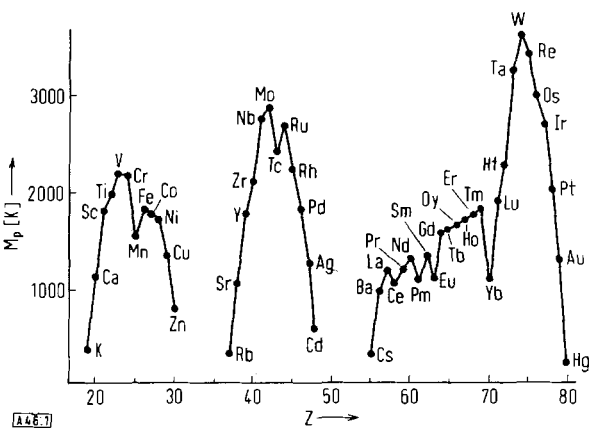


Fig. 1. Melting points m.p. *versus* atomic number Z.

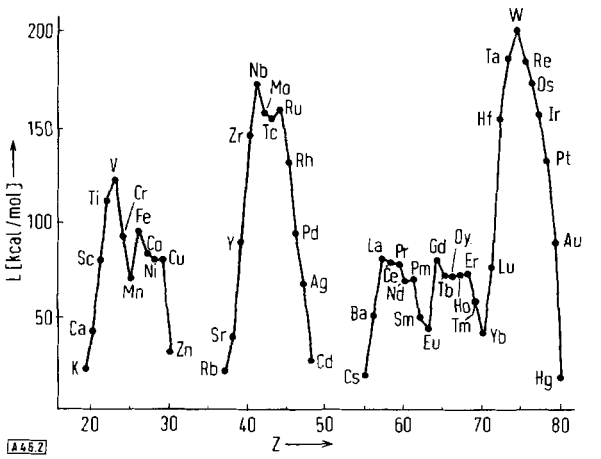


Fig. 2. Heats of sublimation *versus* atomic number Z.

3. Electron-Beam Evaporation

3.1. Crucible Material

The process that gives highest evaporation rates is electron-beam evaporation. Since evaporation is generally from the liquid phase the choice of crucible material is of great importance. Although a water-cooled copper crucible can be used in all cases, cooling must be extremely effective for some metals, *e.g.*, aluminum, in spite of the high thermal conductivity of copper; otherwise intermetallic compounds may be formed. Moreover, water-cooled copper crucibles lead to high energy losses because of the extremely high temperature gradient at the boundary between liquid metal and solid copper and the very low temperature gradient that can be maintained in solid copper. Experience shows that the heat loss is 10 to 30 times higher for a water-cooled copper crucible than for ceramic crucibles.

The ceramic crucible material has to be chosen so that the reaction between the molten metal and the oxide is limited to the surface. Considerable differences are observed in this respect. For example, molten aluminum reacts with quartz within the first few hours of operation to form a layer of solid compound several mm thick. This compound affords excellent protection against further attack.

Satisfactory solutions exist for the metals Cr, Nb, Mo, W, Fe, Co, Ni, Cu, Ag, Au, and the Pt metals. Some of the rare earth oxides are very resistant to molten metals. Molten oxides of mullite and sillimanite can also be used successfully.

3.2. Power Density of the Electron Beam

On use of an electron beam of high power density energy transfer can be restricted to a very small volume of the substance to be vaporized, thus resulting in higher efficiency. Too high a power intensity must be avoided, however, because it would cause spitting of molten metal particles owing to an excessive vapor pressure along the electron beam.

3.3. Energy Balance

Evaporation of 1 cm^3 of nickel in one second (8.9 g/s or 32 kg/h) requires 13.6 kcal/s or 57 kW of sublimation power. In practice the total power that has to be raised for evaporation of 32 kg of nickel per hour is approximately 164 kW and can be supplied for instance by four electron guns of 40 kW each. An approximate analysis of the total power consumption is given in Table 2. The efficiency is about 35%.

Table 2. Breakdown of power requirements for evaporation of nickel with an electron gun.

High tension rectifiers	9%
Electron guns (cathode heating, magnetic fields for beam deflection)	6%
Ionization and X-rays	4%
Thermal conduction through crucible (using a ceramic crucible)	18%
Thermal radiation from melt surface	10%
Electron backscattering	18%
Total power losses	65%
Evaporation	35%

Comparable results are obtained for metals having sublimation energies in the range 70 to 120 kcal/mol. (see Fig. 2; the heat of sublimation of nickel is 81 kcal/mol). With the refractory metals, *e.g.* W, Ta, Re, heat losses by conduction, radiation, and backscattering are higher. The dependence on angle of incidence, atomic number, primary energy, and the phase state has been investigated by *Sommerkamp*[4]. Figure 3 shows the power losses by electron backscattering as a function of atomic number. For the refractory metals Hf, Ta, W, Re the backscattered intensity is as high as 38%.

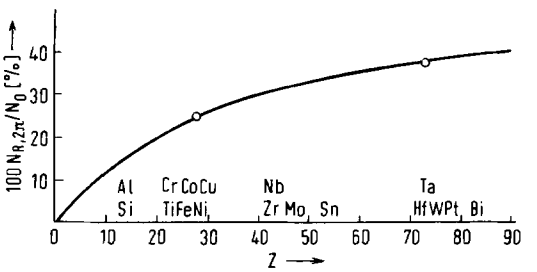


Fig. 3. Power loss by electron backscattering (power ratio $N_{R,2\pi}/N_0$) *versus* atomic number Z. $E_0 = 10$ keV, normal incidence of electron beam.

3.4. Interference

Parasitic electrons and X-rays produced by impact of the electrons on the metal in the crucible can lead to interference if the liberated metal atoms are to be reacted with various substrates.

Parasitic electrons can be eliminated by supplementary magnetic fields or by a negatively charged mesh of metal wire. The most effective method, however, is to chose the polarity such that the crucible is at a positive potential relative to the condensation surface.

X-rays can be largely avoided by reducing the accelerating voltage to a level below the threshold potential for the generation of characteristic X-rays. On reducing the voltage the current must be increased in order to maintain the power density of the electron beam. This can be accomplished by using a cathode of larger area.

3.5. Types of Electron Guns

A high power electron gun (Fig. 4) is generally equipped with an indirectly heated cathode of the block type and an auxiliary cathode of the spiral type.

The gun shown is designed for a power of 250 kW at an accelerating voltage of 22 kV; the maximum current is 11 A. The perveance, a quantity derived from the space charge law which characterizes the performance of a gun, is 3.4×10^{-6}. The beam generating space is evacuated by an auxiliary diffusion pump. Beam-forming is accomplished with two focusing coils; a third coil at the lower end of the gun serves for deflection of the beam.

Figure 5 shows a gun of more modest power (35—50 kW at 20 kV). A water-cooled crucible is connected directly to the gun.

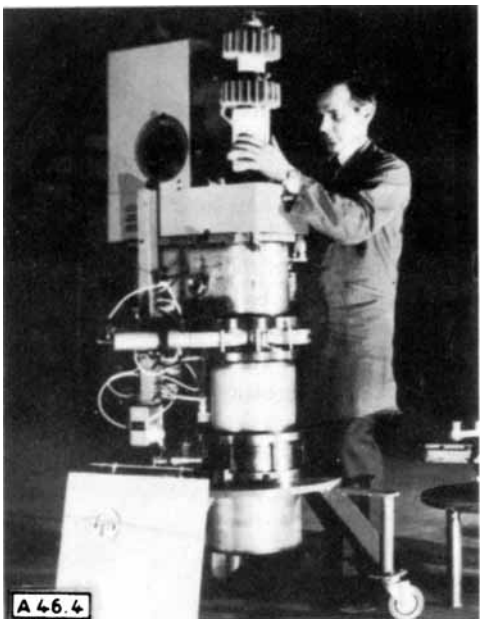


Fig. 4. High power electron gun (250 kW).

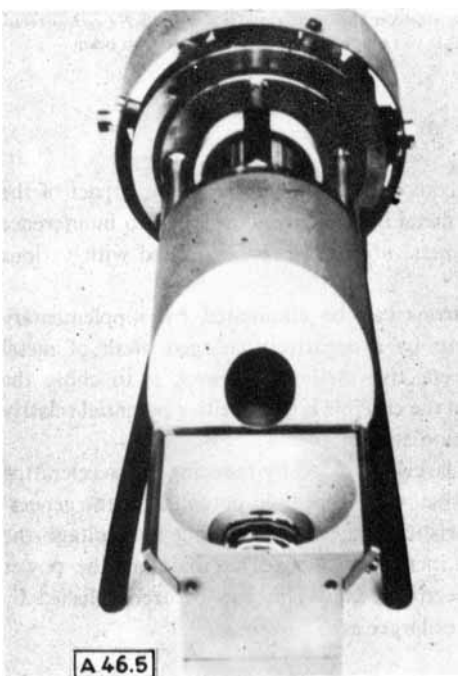


Fig. 5. 30 kW electron gun.

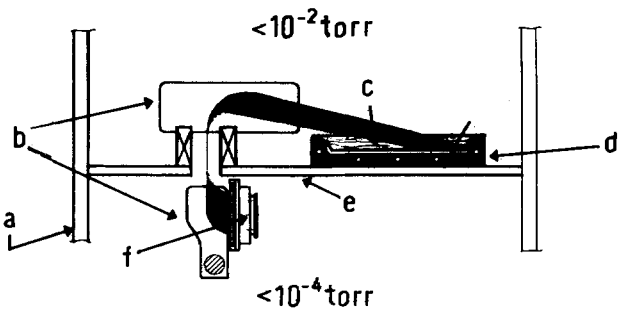


Fig. 6. Scheme of electron gun with linear cathode. a, vacuum tank walls; b, beam deflection system; c, molten material; d, water-cooled support; e, vacuum-tight barrier; f, electron gun.

In contrast to this circular gun concept there are modifications (Fig. 6) in which the cathode is a linear wire that can be of considerable length. The gun consists of a Wehnelt-type linear electrode and a parallel linear anode. In order to protect the cathode against ions and spitting particles the beam is deflected through 270°. With this concept, the beam generating space can also be kept under a higher vacuum than the crucible.

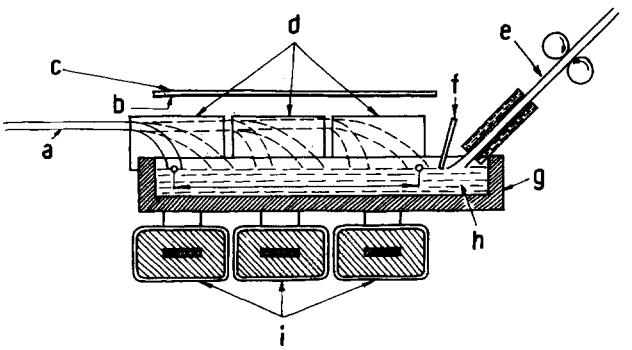


Fig. 7. Electron-beam evaporation unit with one electron gun. a, electron beam; b, deposited layer; c, steel strip; d, pole pieces of deflection magnets; e, feeding system for material; f, shielding; g, crucible; h, evaporation material; i, magnet coils (System: *M. v. Ardenne*).

The life-time for a cathode ranges between 50 and 200 h of operation, where the smaller value holds for spiral type cathodes and the larger one for block type cathodes.

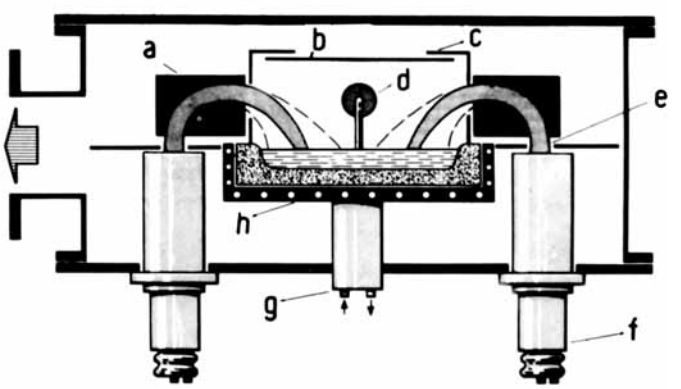


Fig. 8. Electron-beam evaporation unit with two electron guns. a, pole pieces of deflection system; b, steel strip; c, shielding; d, feeding system for material; e, electron beam; f, separately pumped Pierce gun; g, water-cooled crucible support; h, ceramic crucible.

The circular as well as the linear-beam guns are used in connection with either of the two following applications: In Figure 7 only one electron gun is present at the left; the beam is sequentially deflected down to the bath by operating the three magnet coils in turn. Material in solid form is fed on the right into the melt. Figure 8 shows an arrangement where the beams are laterally deflected by magnetic fields, but to a smaller extent. Fig. 9 depicts a 120 kW electron beam evaporation unit with four separately pumped guns; the wire feeding is carried out from an atmospheric environment.

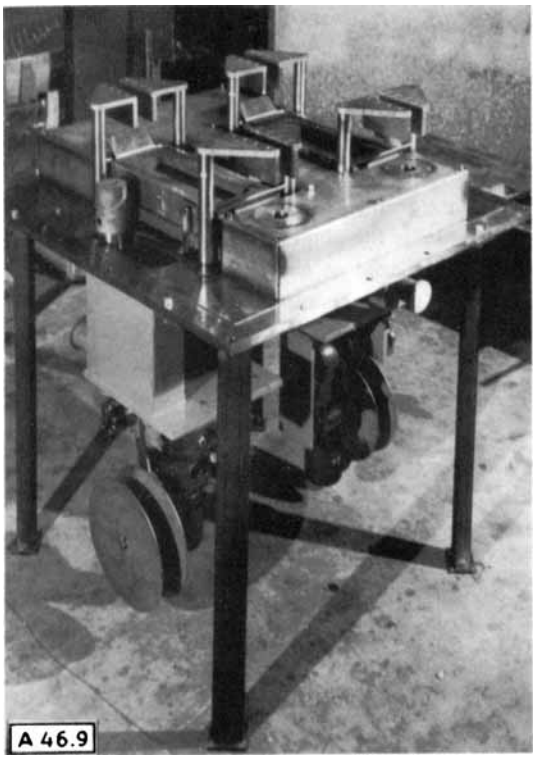


Fig. 9. Electron-beam evaporation unit with four electron guns.

4. Sputter Processes

Timms detailed paper[5] includes the remark that sputter processes have not yet been used in metal-atom syntheses.

For a long time the low sputtering rates precluded use of these processes, and significant advances have only recently been registered. A process that is well suited for sputtering of large quantities of metals (Ta, Mo, W, Re) is plasma sputtering at pressures from 10^{-2} to 10^{-4} torr. The plasma is generated by a high frequency (5 to 30 MHz) electromagnetic field.

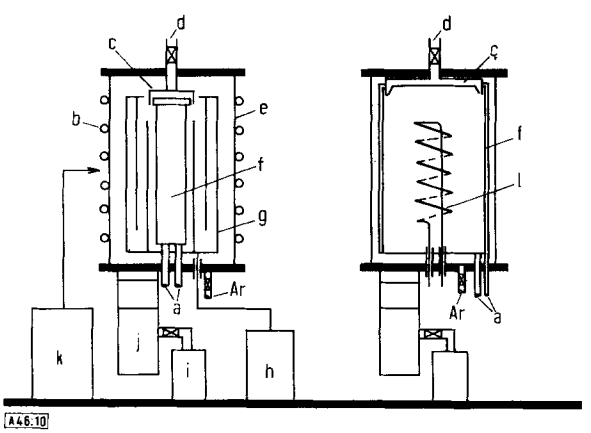


Fig. 10. Arrangement for RF frequency sputtering of metals. a, cooling circuit; b, high frequency coil; c, diffusor; d, reactive gas; e, glass vessel; f, condensed film; g, target of material to be sputtered; h, DC power supply; i, mechanical pump; j, diffusion pump; k, RF frequency generator; l, RF frequency coil made of metal to be sputtered.

There are two possible arrangements: Figure 10 (left) shows an apparatus in which the HF coil for electrodeless plasma generation is located on the outside of a glass cylinder, and a negatively charged target on the inside is bombarded by argon ions. The sputtered material is condensed on coaxially arranged substrates. Higher plasma densities are possible with the apparatus on the right of Fig. 10, where the HF coil is inside the working chamber and consists of the material to be sputtered. For low melting point metals the coil must be water-cooled. The coil need not be cylindrical, but may be composed of linear elements, so that almost all interesting metals, transition metals for instance, can be sputtered by this method.

The present state of the art permits sputtering rates of about 500 g/h with the equipment shown.

The main disadvantage of all sputtering processes is their low power efficiency of only 5—10%, compared with the 35% of electron-beam evaporation (see Section 3.3).

Another difficulty also has to be taken into account. If the metal atoms produced by sputtering are to be reacted with organic compounds then the equipment should be constructed so as to avoid their entering the central region of the plasma where they will easily be decomposed.

5. Condensation and Cooling

The evaporated metal atoms transport energy, *viz.* kinetic energy and heat of sublimation, which has to be removed from the condensation surface by a convenient cooling system. The contribution of the kinetic energy is usually less than 10%. At 2100 K, for instance, iron vapor has a kinetic energy of 6.7 kcal/mol and a heat of sublimation of 97 kcal/mol.

In order to estimate the condensation power we shall consider the example of chromium. For condensation of 1 kg of chromium per hour at 80 K it amounts to approximately 1700 kcal/h or 2 kW. Allowance must also be made for heat radiation from the walls. Since refrigerators employing liquid nitrogen have an efficiency of only about 20%, approximately 10 kW are necessary for removal of the heat liberated.

If the evaporated metals do not unite to form metal lattices on the condensation surface but undergo chemical reactions with various compounds then the cooling power will also change.

6. Evaporation Plants and Their Modification for Chemical Synthesis

Low temperature reactions of metal atoms with organic compounds can be carried out as batch or continuous pro-

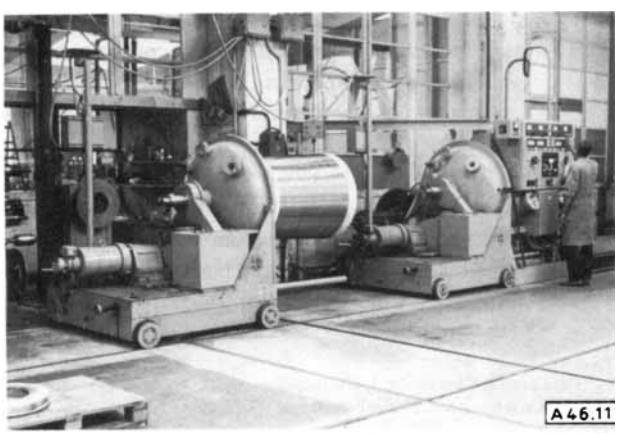


Fig. 11. Evaporation plant used in batchwise metal cladding.

cesses. At present no specially designed equipment for such reactions is commercially available.

Apparatus for a batch process will resemble that already used in metal cladding by evaporation.

Figure 11 shows a large rotating and refrigerated drum which can be introduced into an evacuated chamber. Vaporized compounds can be carefully distributed from above on the cooled surface and reacted with the metal vapor coming from sources located below the drum. The condensation surface may be as large as several square meters. In order to ensure uniform deposition several electron guns situated along a line parallel to the axis of the drum must be used.

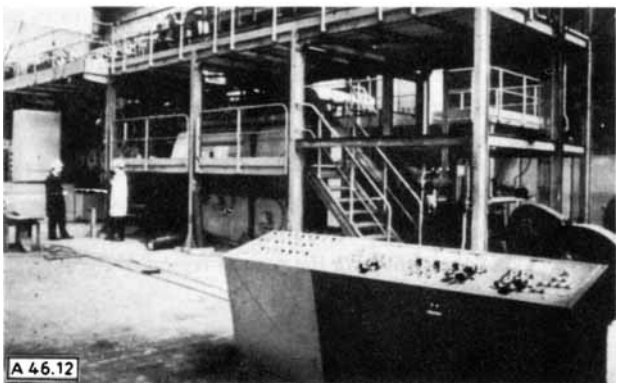


Fig. 12. Evaporation plant for continuous coating of steel strip.

Apparatus for the continuous process could be derived from the continuous band coaters used for coating steel strip with metals (Fig. 12). The strip would pass through a set of seals on entering and leaving the machine. When used for chemical synthesis the plant would have to be equipped with cooling rolls instead of heating rolls and with devices for distributing the gaseous compound over the moving strip. The reaction products could be scraped or brushed from the strip either inside the machine or outside in the atmosphere; the strip might also take the form of a closed loop.

Received: July 26, 1974 [A 46 IE]
German version: Angew. Chem. 87, 239(1975)

[1] *D'Ans-Lax:* Taschenbuch für Chemiker und Physiker. Springer, Berlin 1949, p. 864.
[2] Handbook of Chemistry and Physics. 41st Edit. The Chemical Rubber Co., Cleveland, Ohio 1959/60.
[3] *A. N. Nesmeyanov:* Vapor Pressure of the Chemical Elements. Elsevier, Amsterdam 1963.
[4] *P. Sommerkamp,* Z. Angew. Phys. *28,* 220 (1970).
[5] *P. L. Timms,* Advan. Inorg. Chem. Radiochem. *14,* 121 (1972).

New synthetic methods (9)

Chemistry of Phosphorylcarbenes[1][**]

By Manfred Regitz[*]

Phosphorylcarbenes, which have become known only recently during synthetic experiments in the field of phosphoryldiazoalkanes, have twofold preparative value. In the first place, they can be used to introduce phosphoryl groups into organic compounds, as in the phosphorylcyclopropanation of alkenes or arenes and in the phosphorylcyclopropenation of alkynes. Secondly, phosphorylcarbenes readily undergo rearrangements; hydride, alkyl, aryl, or acyl shifts lead to phosphorylated alkenes. The phosphorylcarbene/methylenephosphane oxide rearrangement provides access to the short-lived P analogs of the ketenes. Finally, the vinylcarbene/allene rearrangement was first discovered in this connection; it competes with ring closure to the cyclopropene.

1. Introduction

Progress in the synthesis of aliphatic diazo compounds leads almost of necessity to corresponding developments in carbene chemistry, since photochemical decomposition of diazoalkanes ensures universal access to carbenes. Thus, investigations into the synthesis of phosphoryldiazoalkanes, begun in our school several years ago, led us to study the reactivity of phosphorylcarbenes. The preparation of organophosphorus compounds by carbene reactions was of interest mainly from the point of view of whether, and in relevant cases to what extent, phosphorylcarbenes differ from their carbonyl analogs, which have been investigated very thoroughly.

2. Preparation of Phosphoryldiazoalkanes

The simplest of the compounds considered in this section, namely the α-diazophosphonate *(1)*, α-diazophosphane oxide *(2)*, and α-diazophosphinate *(3)*, are accessible by diazotization of amines[2] (method A); the only other application of this method was for preparation of the α-diazophosphane oxide *(4)* (Table 1).

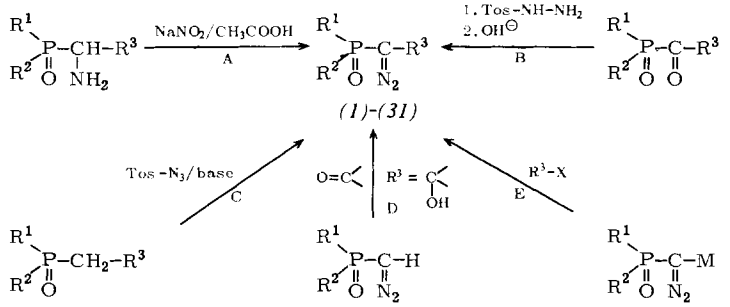
The Bamford-Stevens reaction[2] (method B) has a very wide scope, as shown by examples *(5)*—*(15)* (Table 1). The starting materials in this method are α-oxophosphoryl compounds, whose preparation involves the Michaelis-Arbusov reaction[3] between methoxyphosphanes and acyl chlorides

[*] Prof. Dr. M. Regitz
Fachbereich Chemie der Universität
675 Kaiserslautern, Pfaffenbergstrasse (Germany)

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

as an essential step; however, failure of the latter reaction has hitherto precluded synthesis of diazomethylphosphane oxides by method B. Only in the case of dimethyl cyclopropyldiazomethylphosphonate *(12)*, R^3 = cyclopropyl, was isolation of the diazo compound impossible for the compound decomposes spontaneously (see Section 4.1).

The phosphoryldiazoalkanes *(16)*—*(20)* containing a carbonyl group or a strongly proton-activating aryl group as a second substituent are obtained only by diazo group transfer[2, 4, 5] (method C) (Table 1). The active methylene compounds serving as starting materials can again be produced by the Michaelis-Arbusov reaction[3].

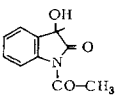
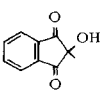
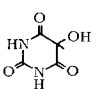


phenylphosphane oxide *(2)* by carbonyl compounds (Table 1). This aldol-like addition[2, 5] (method D) is generally straightforward when catalyzed by triethylamine [the addition of OH^- is necessary only for *(22)*] and is applicable to aldehydes, dicarbonyl, and tricarbonyl compounds. In the last of these cases the high carbonyl reactivity makes addition of base superfluous.

Reaction of metal derivatives of *(2)* with S_N1-active halides[2, 5] (method E) represents a further variant of the alkylation (Table 1). With benzyl iodide, *(2)*, M = Ag, affords the diazo compound *(30)*; compound *(31)* is obtained from *(2)*, M = Hg—CN_2—$PO(C_6H_5)_2$ and triphenylmethyl bromide. These two metal derivatives are readily accessible from *(2)* and the metal oxides in chloroform[7].

With few exceptions the phosphoryldiazoalkanes are unusually stable thermally, and in this respect they are far superior to the respective carbonyl analogs[19, 20]. If the temperature at which the decomposition constant k_1 amounts to 0.1 min^{-1} is chosen as a measure of comparison, this behavior can be pinpointed by the examples in Table 2. From these data consequences regarding the temperature and the duration of thermolysis can be drawn for thermal generation of phosphorylcarbenes from diazo compounds.

Table 1. Syntheses of the phosphoryldiazoalkanes *(1)*—*(31)*. Method A: Diazotization of amines, B: Bamford-Stevens reaction, C: Transfer of diazo groups, D: Aldol addition, E: Nucleophilic substitution.

	R^1	R^2	R^3	Method	Yield [%]	Ref.
(1)	OCH_3	OCH_3	H	A	46	[6]
(2)	C_6H_5	C_6H_5	H	A	45	[7]
(3)	C_6H_5	OCH_3	H	A	16	[8]
(4)	C_6H_5	C_6H_5	C_6H_5	A	29	[9]
(5)	OCH_3	OCH_3	C_6H_5	B	51	[10]
(6)	OCH_3	OCH_3	*p*-H_3CO—C_6H_4	B	97	[10]
(7)	OC_2H_5	OC_2H_5	C_6H_5	B	87	[11]
(8)	$OCH(CH_3)_2$	$OCH(CH_3)_2$	C_6H_5	B	54	[10]
(9)	OCH_3	OCH_3	CH_3	B	44	[12]
(10)	OCH_3	OCH_3	$(H_3C)_2CH$	B	72	[12]
(11)	OCH_3	OCH_3	$(H_3C)_3C$	B	64	[12]
(12)	OCH_3	OCH_3	cyclopropyl to cyclohexyl	B	80—82	[12]
(13)	C_6H_5	OCH_3	C_6H_5	B	66	[8]
(14)	OCH_3	OCH_3	$(H_3C)_2C{=}CH$	B	37	[12]
(15)	OCH_3	OCH_3	$H_3C(H_5C_6)C{=}CH$	B	83	[13]
(16)	OCH_3	OCH_3	$COOCH_3$	C	37	[14]
(17)	C_6H_5	C_6H_5	$CONH_2$	C	46	[15]
(18)	C_6H_5	C_6H_5	$COOC_2H_5$	C	57	[15]
(19)	C_6H_5	C_6H_5	COC_6H_5	C	100	[15]
(20)	OCH_3	OCH_3	*p*-O_2N—C_6H_4	C	35	[10]
(21)	C_6H_5	C_6H_5	$C_6H_5CH(OH)$	D	63	[16]
(22)	C_6H_5	C_6H_5	*p*-H_3C—C_6H_4—CH(OH)	D	48	[16]
(23)	C_6H_5	C_6H_5	*p*-NC—C_6H_4—CH(OH)	D	85	[16]
(24)	C_6H_5	C_6H_5	2-naphthyl-CH(OH)	D	68	[16]
(25)	C_6H_5	C_6H_5	2-thienyl-CH(OH)	D	68	[16]
(26)	C_6H_5	C_6H_5	$(H_5C_6{-}CO)_2COH$	D	83	[17]
(27)	C_6H_5	C_6H_5		D	93	[18]
(28)	C_6H_5	C_6H_5		D	70	[18]
(29)	C_6H_5	C_6H_5		D	78	[17]
(30)	C_6H_5	C_6H_5	$H_5C_6{-}CH_2$	E	54	[17]
(31)	C_6H_5	C_6H_5	$(H_5C_6)_3C$	E	66	[17]

The (α-diazo-β-hydroxyalkyl)diphenylphosphane oxides *(21)*—*(29)* are obtained on *C*-alkylation of (diazomethyl)di-

Normally therefore phosphoryldiazoalkanes are converted photolytically into phosphorylcarbenes, photolysis being car-

ried out under a Philips mercury high-pressure 125 W HPK lamp with a Duran 50 filter.

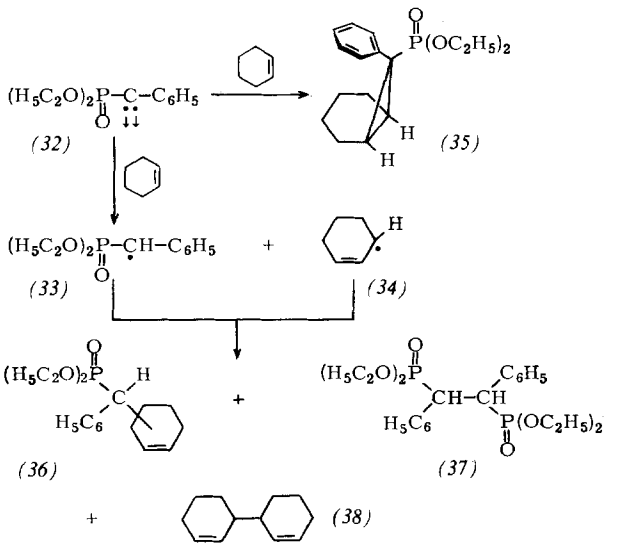
Table 2. Comparison of the thermal stability of phosphoryl- and carbonyldiazo compounds in mesitylene [19, 20]. $T_{0.1}$ is the temperature at which the decomposition constant $k_1 = 0.1\ min^{-1}$.

PO-Diazo cpd.	$T_{0.1}$ [°C]	CO-Diazo cpd.	$T_{0.1}$ [°C]
(4) $H_5C_6-\underset{\underset{N_2}{\|}}{\overset{\overset{O}{\|}}{C}}-P(C_6H_5)_2$	120	$H_5C_6-\underset{\underset{N_2}{\|}}{\overset{\overset{O}{\|}}{C}}-\overset{\overset{O}{\|}}{C}-C_6H_5$	75
(7) $H_5C_6-\underset{\underset{N_2}{\|}}{\overset{\overset{O}{\|}}{C}}-P(OC_2H_5)_2$	151	$H_5C_6-\underset{\underset{N_2}{\|}}{\overset{\overset{O}{\|}}{C}}-\overset{\overset{O}{\|}}{C}-OC_2H_5$	125
(19) $H_5C_6-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{C}}-\underset{\underset{N_2}{\|}}{\overset{\overset{O}{\|}}{C}}-P(C_6H_5)_2$	124	$H_5C_6-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{C}}-\underset{\underset{N_2}{\|}}{\overset{\overset{O}{\|}}{C}}-C_6H_5$	95

3. Intermolecular Reactions[21]

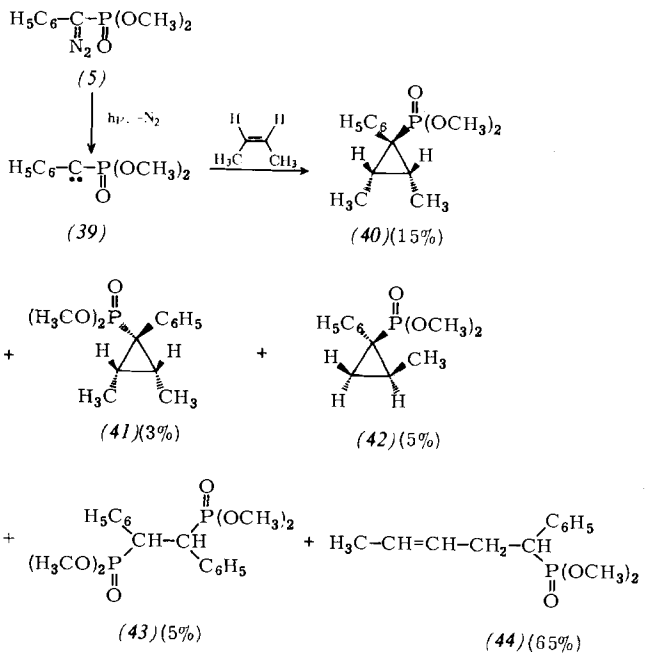
3.1. Phosphorylcyclopropanation of Alkenes

(Diethoxyphosphoryl)phenylcarbene *(32)* produced photolytically from *(7)* adds stereoselectively to cyclohexene, giving the norcarane derivative *(35)* with an *endo*-phenyl and an *exo*-phosphoryl group. The configuration at C-7 is the same as in 7-phenylnorcaradien-7-yl phosphonates *(51)*[10, 22]. At the same time, as an indication of its triplet character, *(32)* abstracts hydrogen from the cyclohexene with the formation of the two radicals *(33)* and *(34)*, the three possible products *(36)*—*(38)* of their combination also being isolated.



The fact that (dimethoxyphosphoryl)phenylcarbene *(39)* is also distinguished by triplet character follows from its reactions with *cis*- and *trans*-2-butene at −20 to −25 °C[23]. The *cis*-olefin undergoes stereospecific [2+1]-cycloaddition to give the diastereoisomers *(40)* and *(41)* alongside non-specific cycloaddition yielding *(42)*; the H-abstraction products *(43)* and *(44)* are also formed[24]. The last-mentioned compound could not be isolated but was determined quantitatively by NMR spectroscopy and coulometric titration with bromine. *trans*-2-Butene affords only two of the three possible cyclopropanes, namely *(40)* and *(42)*, the product picture being otherwise the same[23].

A decision whether the triplet behavior of *(32)* and *(39)* should be assigned specifically to the PO group will have to wait for conclusion of relevant experiments with (dialkoxyphosphoryl)carbenes.



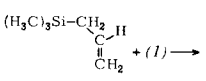
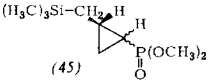
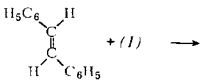
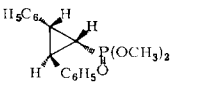
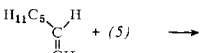
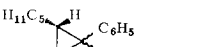
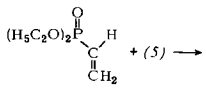
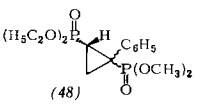
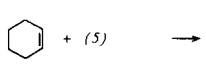
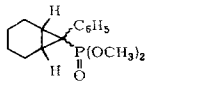
Cyclopropanations with phosphoryldiazoalkanes by the carbenoid route are more clear-cut and usually give a very high yield (Table 3); the H-abstraction that dominates on photochemical production of the carbenes is wholly suppressed. Usually the diazo compounds are decomposed on catalysis by copper [*(46)*—*(49)*]; it is surprising that cyclopropanation of 3-(trimethylsilyl)propene with *(1)*, to yield *(45)*, occurs already at 0—20 °C. The stereochemistry at the phosphoryl-carbon atom of the cyclopropanes is known only for *(46)*[10].

3.2. Phosphorylcyclopropanation of Arenes

Numerous examples are known of the preparation of 7-phosphorylnorcaradienes *(51)* by cyclopropanation of arenes with phosphorylcarbenes *(50)* (Table 4). In the case of the crystalline arenes (*p*-dichlorobenzene, naphthalene), the photolysis of the diazo compounds is carried out in the melt; their thermal stability guarantees photochemical generation of carbenes even under such conditions.

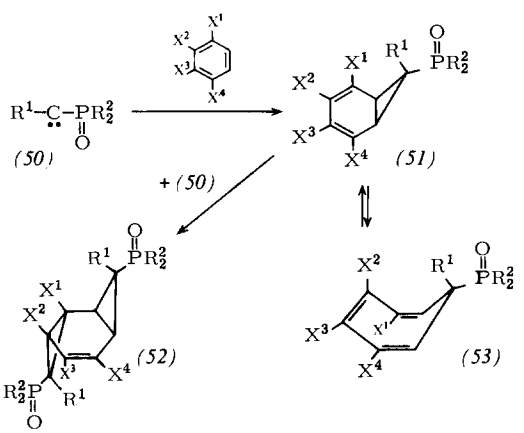
With *p*-xylene H-abstraction by *(50a)* completely swamps cyclopropanation, leading to the typical product picture of radical dimers[10]; in other cases further reaction of *(51)* is frequently observed, yielding tricyclo[5.1.0.0^{2,4}]oct-5-enes *(52)* (Table 4). Both reactions occur stereoselectively; the PO groups are always *exo*[10, 14]. This configuration follows from the *cis*-coupling of the phosphorus with β-cyclopropane protons (*ca.* 17 Hz), which differs distinctly from the corresponding *trans*-coupling (*ca.* 1—2 Hz)[10, 28]. The reference standard for this assignment is the cyclopropane derivative *(46)* (Table 3), for which the two possibilities have been verified. X-Ray structure analyses of *(51a)* and *(51f)* confirm the stereochemistry[29, 30].

Table 3. Phosphorylcyclopropanes *(45)*—*(49)* from olefins and the phosphoryldiazo compound *(1)* or *(5)* with copper catalysis.

Reactants	Cyclopropane	Yield [%]	Ref.
	 *(45)*	67 [a]	[6, 25]
	 *(46)*	8 [b]	[10]
	 *(47)*	73 [c]	[6]
	 *(48)*	90 [c]	[6]
	 *(49)*	96 [c]	[6, 26]

[a] Dichloromethane, 0—20 °C.
[b] Dichloromethane, reflux.
[c] Without solvent, reflux temperature of the olefin.

In some cases, *e.g. (51a)*, valence-tautomeric equilibria with 7-phosphorylcycloheptatrienes exist in solution[28, 31]. From temperature-dependent NMR spectra the equilibrium constants *(51)*⇌*(53)* in CS_2 are found to be 3.78 at −34 °C and 9.95 at −99 °C; at −116 °C the spectrum of the pure norcaradiene is observed[28].



Irradiation of *(1)* in *m*-bis(trifluoromethyl)benzene leads to two cyclopropanation products *(54)* and *(55)*, which in $CDCl_3$ occur in valence-tautomeric equilibrium with the cycloheptatrienes *(56)* and *(57)*, respectively, the trienes being dominant[14, 32]. On prolonged irradiation the *(54)*/*(56)* system is favored; it is possible that cycloelimination from *(55)* leads to (dimethoxyphosphoryl)carbene[33], which adds further to *m*-bis(trifluoromethyl)benzene. However, this is no longer a kinetically but now a thermodynamically controlled reaction.

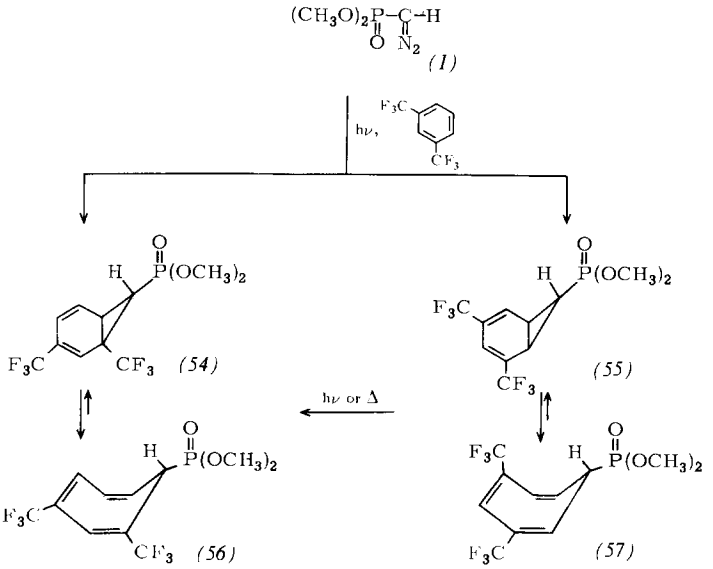
The same reaction can be brought about thermally; it can thus be regarded as a Berson-Wilcott rearrangement[34], *i.e.* as a sigmatropic [1,5]-carbon shift[35].

(Dimethoxyphosphoryl)(methoxycarbonyl)carbene *(58)* and benzene afford products that depend on the duration of the irradiation[14]. If the photolysis of *(16)* is interrupted before the reaction is complete, the norcaradiene *(59)* or the equilibrium system *(59)*⇌*(60)*, respectively, is produced (NMR spectroscopy in $CDCl_3$). More prolonged irradiation leads next to a not precisely determinable sequence of sigmatropic [1,5]- or [1,7]-shifts of ester groups or H atoms, producing the cycloheptatriene *(62)*. On still further irradiation

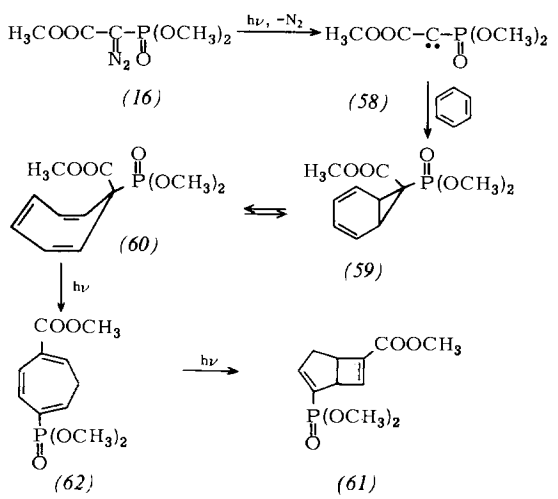
Table 4. Cyclopropanation of arenes by phosphorylcarbenes, yielding the valence tautomers *(51)*⇌*(53)* and the tricyclooctenes *(52)*.

	R^1	R^2	X^1	X^2	X^3	X^4	Yield [%] *(51)*⇌*(53)*	*(52)*	Ref.
a	C_6H_5	OCH_3	H	H	H	H	18	27	[10, 22]
b	C_6H_5	$OCH(CH_3)_2$	H	H	H	H	17	17	[10]
c	C_6H_4—OCH_3-(*p*)	OCH_3	H	H	H	H	15	11	[10]
d	C_6H_4—NO_2-(*p*)	OCH_3	H	H	H	H	12	24	[10]
e	C_6H_5	C_6H_5	H	H	H	H	40 [a]	—	[23, 27]
f	C_6H_5	OCH_3	Cl	H	H	Cl	35	—	[10]
g	$COOCH_3$	OCH_3	Cl	H	H	Cl	6	—	[14]
h	C_6H_5	OCH_3	H	H	Cl	Cl	15	10	[10]
i	H	OCH_3	H	H	—CH=CH—CH=CH—		53	—	[14]
j	C_6H_5	OCH_3	H	H	—CH=CH—CH=CH—		88	0.4	[10]

[a] On sensitization with cyclohexanone.

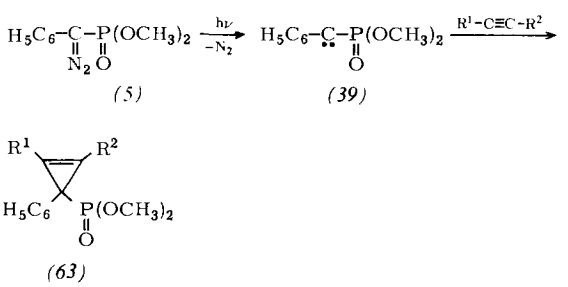


the photostable bicyclo[3.2.0]heptadiene *(61)* is formed from *(62)* by electrocyclic ring closure[36].



3.3. Phosphorylcyclopropenation of Alkynes

(Dimethoxyphosphoryl)phenylcarbene *(39)*, produced photolytically from *(5)*, reacts with alkynes to give satisfactory yields of dimethyl 1-phenyl-2-cyclopropenylphosphonates *(63)* (Table 5) if [3+2]-cycloaddition of *(5)* does not become operative[13].



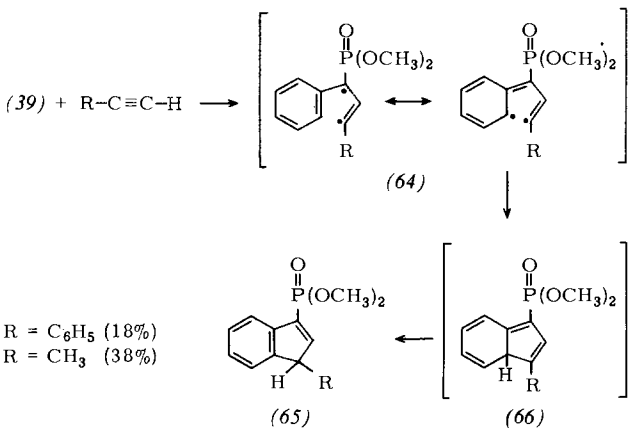
An interesting alternative is provided by monosubstituted alkynes, where ring closure to dimethyl 3-indenylphosphonates

Table 5. Dimethyl 1-phenyl-2-cyclopropenylphosphonates *(63)* from alkynes and (dimethoxyphosphoryl)phenylcarbenes *(39)* [13].

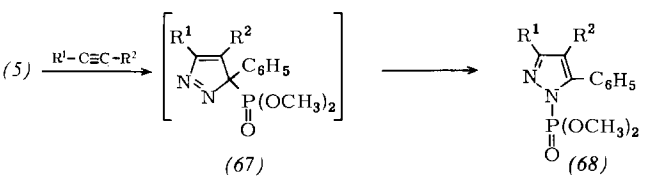
R^1	R^2	Yield [%]
C_6H_5	C_6H_5	61
CH_3	CH_3	55
C_6H_5	CH_3	41
C_6H_5	$COOCH_3$	39
C_6H_5	H	3
CH_3	H	59

(65) competes with the phosphorylcyclopropenation that yields *(63)*[13].

The carbene *(39)* apparently attacks the unsubstituted alkyne-carbon atom with formation of the diradical *(64)*, which cyclizes to *(66)*. Re-aromatization with a sigmatropic [1,5]-hydrogen shift leads to *(65)*[37].



Activated alkynes such as methyl propiolate, dimethyl acetylenedicarboxylate, acetylenedicarbonitrile, or hexafluoro-2-butyne do not undergo the carbene reaction at all, since photolytic carbene generation *(5)* → *(39)* occurs much more slowly than [3+2]-cycloaddition. The 3*H*-pyrazoles *(67)* that are undoubtedly formed initially cannot be isolated but are transformed, in a very rapid sigmatropic [1,5]-shift of the dimethoxyphosphoryl group, into the isomeric pyrazolides *(68)*[38].

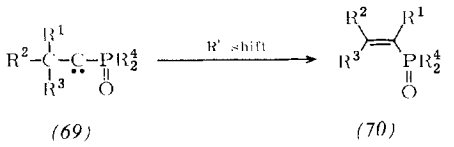


R^1 = $COOCH_3$, R^2 = H (100%) R^1 = R^2 = CN (63%)
R^1 = R^2 = $COOCH_3$ (100%) R^1 = R^2 = CF_3 (100%)

4. Intramolecular Reactions[21]

4.1. Hydride, Alkyl, Aryl, and Acyl Shifts

Phosphorylcarbenes with suitable substituents on the α-carbon, *e.g. (69)*, react extremely readily with migration of a substituent to the carbene center; phosphorylalkenes *(70)* are formed (Table 6).



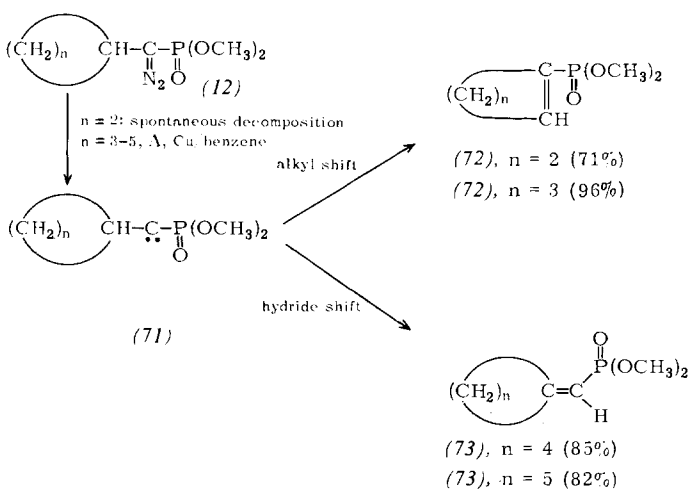
(69) (70)

Table 6. Phosphorylalkenes (70) prepared. Cu(acac)$_2$ = bis(2,4-pentanedionato)copper(II).

R^1	R^2	R^3	R^4	Reaction conditions	Yield [%]	Ref.
H	H	H	OCH_3	*hv*, benzene	22	[39]
H	CH_3	CH_3	OCH_3	Δ, Cu/benzene	87	[12]
				hv, benzene	55	[39]
CH_3	CH_3	CH_3	OCH_3	Δ, Cu/benzene	81	[12]
C_6H_5	H	H	C_6H_5	Δ, Cu(acac)$_2$/benzene	100	[17]
C_6H_5	C_6H_5	C_6H_5	C_6H_5	Δ, Cu(acac)$_2$/benzene	71	[17]

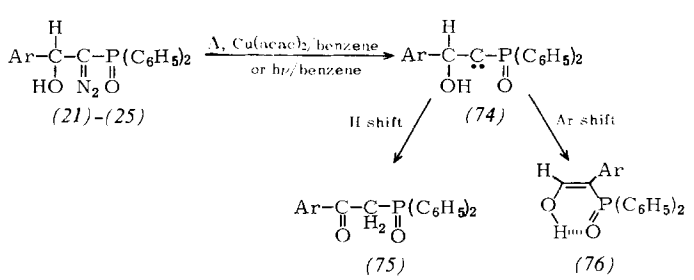
For these reactions the copper-catalyzed thermal decompositions of the diazo compounds corresponding to (69) always give higher yields of the olefin. If the carbenes are generated photolytically (Table 6), carbene dimerization and addition of carbene to solvent benzene also occur, though the latter is completely suppressed on copper catalysis[39].

The kind of substituent shift undergone by cycloalkyl(dimethoxyphosphoryl)carbenes (71) is controlled by the ring size. Cyclopropylcarbene (71), $n=2$, and cyclobutylcarbene (71), $n=3$, apparently prefer the alkyl shift to form cycloalkenes (72), because of ring strain, whereas cyclopentylcarbene (71), $n=4$, and cyclohexylcarbene (71), $n=5$, undergo a 5-hydride shift yielding the methylenecycloalkanes (73)[12].



(12) (71) (72), n = 2 (71%) (72), n = 3 (96%) (73), n = 4 (85%) (73), n = 5 (82%)

True competition between hydride and aryl shifts occurs with the [(arylhydroxymethyl)phosphoryl]carbenes (74) generated from (21)—(25). In the first case the enols that are undoubtedly formed initially are transformed into the ketones [(β-oxoethyl)phosphane oxides] (75), whereas in the second the (β-hydroxyvinyl)phosphane oxides (76) are isolated without any sign of ketone formation (Table 7)[16]. The hydride shift always predominates, irrespective of the mode of carbene generation (Table 7). Here too cyclopropanation of benzene is completely circumvented.

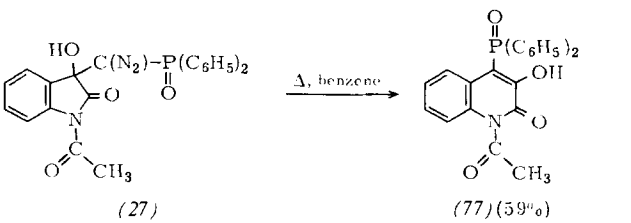


(21)–(25) (74) (75) (76)

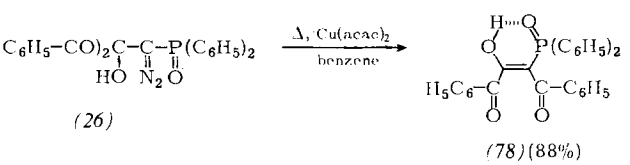
An aryl shift associated with ring expansion occurs in the reaction (27) → (77). Reactions of this type are mostly induced by acid catalysis (carbenium ion mechanism)[18]. The shift

Table 7. Competing H- and Ar shifts in (arylhydroxymethylphosphoryl)carbenes (74) [16].

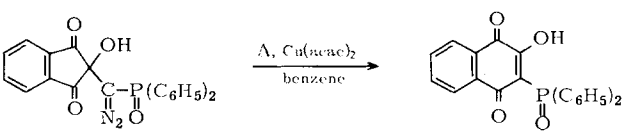
Ar	Thermolysis Yield [%] (75)	(76)	Photolysis Yield [%] (75)	(76)
C_6H_5	40	22	28	16
C_6H_4—CH_3-(*p*)	33	22	32	11
C_6H_4—CN-(*p*)	54	5	34	14
2-naphthyl	31	10	26	10
2-thienyl	43	33	27	16



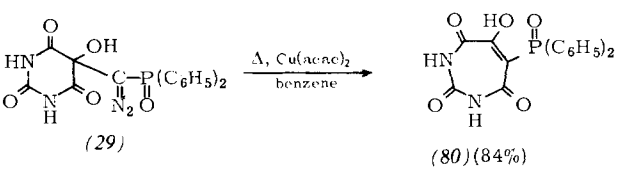
(27) (77) (59%)



(26) (78) (88%)



(28) (79) (80%)

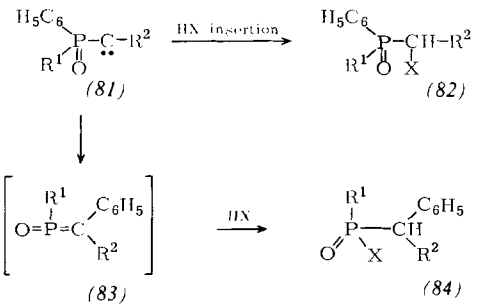


(29) (80) (84%)

of a benzoyl group to the carbene-carbon atom is responsible for the formation of (78) from (26)[17]. If this reaction is applied to cyclic systems, phosphorylated ring systems can be prepared in high yields, as is illustrated by the selected examples (28) → (79)[17] and (29) → (80)[17].

4.2. Phosphorylcarbene/Methylenephosphane Oxide Rearrangement

In a study of the reactivity of phosphorylcarbenes the question whether these compounds can afford the ketene analogs, methylenephosphane oxides such as *(83)*, in a reaction corresponding to the Wolff rearrangement is of particular interest. Methylenephosphane oxides are interesting in connection with the question whether compounds of pentavalent phosphorus with a coordination number of 3 can exist[40].



(81) *(82)* *(83)* *(84)*

When carbenes of type *(81)* are generated photolytically from diazo compounds in the presence of protic nucleophiles (water, methanol, aniline, or morpholine), they react in two ways: by one route the phosphane oxides *(82)* are formed with HX-insertion, by the other the phosphinic acid derivatives *(84)* are obtained, *i.e.* the carbenes *(81)* partly undergo P/C-phenyl shift to give the methylenephosphane oxides *(83)*[43] which add the nucleophile very rapidly, yielding *(84)* (Table 8).

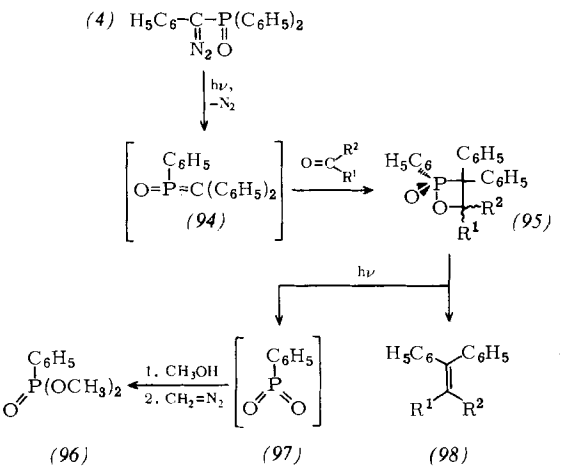
Irradiation of *(19)* in methanol leads to much more complicated reactions. Competition occurs between the phosphorylcarbene/methylenephosphane oxide rearrangement *(85)* → *(86)*[43] → *(90)* and the equally possible classical Wolff rearrangement *(85)* → *(89)* → *(93)*; the methyl esters *(90)* and *(93)* are formed in the ratio of approximately 4:1. It is possible, however, to reverse this ratio by introducing a *p*-dimethylamino group into the benzoyl group of *(19)* (phosphinic ester: carboxylic ester ≈ 1:2)[41].

Furthermore, *(85)* reacts with methanol by OH insertion, although the phosphane oxide *(87)* cannot be isolated; it undergoes intramolecular, photochemical reduction of the CO group to form the diradical *(91)*, which then cyclizes to the oxetane *(92)*[41]. Finally, reductive elimination of the diazonitrogen[44] also occurs, with formation of *(88)*[44].

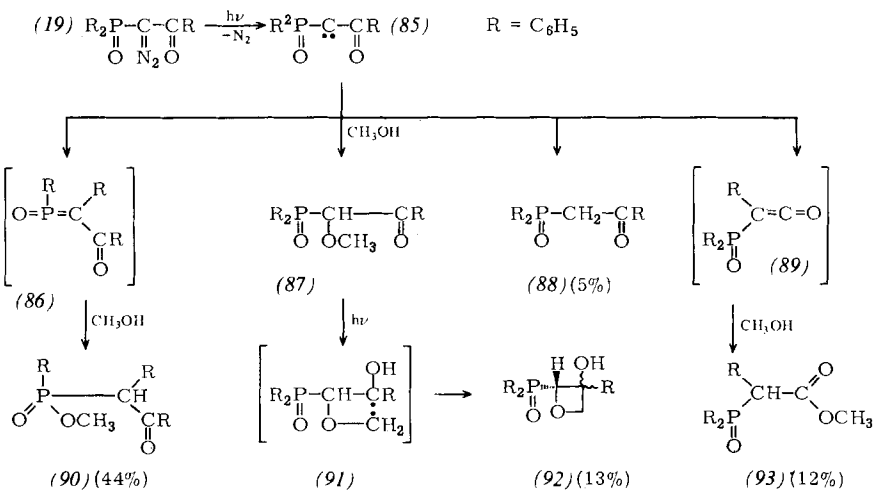
Table 8. Phosphane oxides *(82)* and/or phosphinic acid derivatives *(84)* from phosphorylcarbenes *(81)*.

R^1	R^2	X	Yield [%] *(82)*	Yield [%] *(84)*	Ref.
C_6H_5	H	OH	—	84	[41]
C_6H_5	H	OCH_3	—	61	[22, 41]
C_6H_5	H	$NH-C_6H_5$	—	55	[41]
C_6H_5	H	morpholino	—	54	[41]
H_3CO	H	OCH_3	30	26	[42]
C_6H_5	C_6H_5	OH	32	2	[19, 41]
C_6H_5	C_6H_5	OCH_3	100	—	[22, 41]
C_6H_5	C_6H_5	$NH-C_6H_5$	83	—	[41]
C_6H_5	$CONH_2$	OCH_3	81	—	[22, 41]
C_6H_5	$COOC_2H_5$	OCH_3	22	61	[22, 41]
H_3CO	C_6H_5	OCH_3	87	—	[42]

Yet another possibility of detecting the short-lived methylenephosphane oxide consists in trapping by carbonyl compounds. If *(4)* is irradiated in benzene in the presence of an aldehyde or a ketone, the latter undergoes orientation-specific [2+2]-cycloaddition to the methylenephosphane oxide, yielding the 1,2-oxaphosphetanes *(95)*. These products can be isolated if, like the adducts of aromatic aldehydes (Table 9), they are photostable (no absorption at $\lambda \geq 280$ nm). Photounstable 1,2-oxaphosphetanes fragment in whole or in part into butadienes or hexatrienes *(98)* (Table 9) and dioxophenylphosphorane *(97)*[45], which was detected in a model experiment.



(4) *(94)* *(95)* *(96)* *(97)* *(98)*



(19) *(85)* *(86)* *(87)* *(88)* (5%) *(89)* *(90)* (44%) *(91)* *(92)* (13%) *(93)* (12%)

Table 9. Reaction of (diphenylmethylene)phenylphosphane oxide *(94)* with carbonyl compounds, yielding 1,2-oxaphosphetanes *(95)* and/or alkenes *(98)*.

	R^1	R^2	Yield [%] *(95)*	Yield [%] *(98)*	Ref.
a	H	C_6H_5	17	—	[9, 27, 46]
b	H	C_6H_4—Cl-(*p*)	20	—	[9, 27]
c	H	1-naphthyl	18	—	[9, 27, 46]
d	H	CH=CH—C_6H_5	—	9	[9, 27]
e	H	CH=CH—C_6H_4—OCH_3-(*p*)	—	12	[9, 27]
f	CH_3	CH=CH—C_6H_5	—	10	[9, 27]
g	CH_3	CH=CH—C_6H_4—OCH_3-(*p*)	—	13	[9, 27]
h	C_6H_5	CH=CH—C_6H_5	11	8	[9, 27]
i	C_6H_5	CH=CH—C_6H_4—OCH_3-(*p*)	19	8	[9, 27]
j	C_6H_4—CH_3-(*p*)	CH=CH—CH=CH—C_6H_5	28	9	[9, 27]
k	CH=CH—C_6H_4—OCH_3-(*p*)	CH=CH—C_6H_4—OCH_3-(*p*)	—	10	[9, 27]
l	—CH_2—CH_2—	CH_2—CH=CH—	—	7	[9, 27]

Irradiation of *(95i)* (Table 9) in methanol afforded the butadiene *(98)* together with the methyl benzenephosphonate formed by addition of methanol to *(97)*; this was esterified to *(96)* by diazomethane and identified[9]. In all cases the rearrangement of *(4)* in benzene was accompanied by cyclopropanation of the benzene which yields the norcaradiene *(51e)* (Table 4). The reaction sequence *(94)* → *(95)* → *(97)* + *(98)* is reminiscent of Wittig carbonyl olefination.

Methylenephosphane oxide *(94)* produced thermally from *(4)* initially reacts with benzylideneacetophenone as in the photoreaction, *i.e.* by [2+2]-cycloaddition to give *(95h)* and partial fragmentation of the adduct to *(98h)*. Additionally, *(94)* and the α,β-unsaturated ketone undergo Diels-Alder reaction giving the 1,2-oxaphosphorin *(99)*. An analogous product picture has been found for diphenylketene and the same ketone[47]. It is not yet clear why the other carbonyl compounds (R^1R^2CO in Table 9) do not react thermally by [4+2]-cycloaddition.

(α-Benzoylbenzylidene)phenylphosphane oxide *(86)* can also be trapped by cycloaddition to carbonyl compounds if the diazo compound *(19)* is irradiated in a *p*-dichlorobenzene melt. If, as is permissible because of the different electronegativities of oxygen and phosphorus, one regards the heterocumulenes as 1,4-dipoles, it becomes understandable why *(86)* undergoes [4+2]-cycloaddition to aldehydes and ketones[48].

If the groups R^1 and R^2 are not identical, the 1,5,2-dioxaphosphorins are produced as diastereoisomers *(100)* and *(101)*, which can often be separated (Table 10).

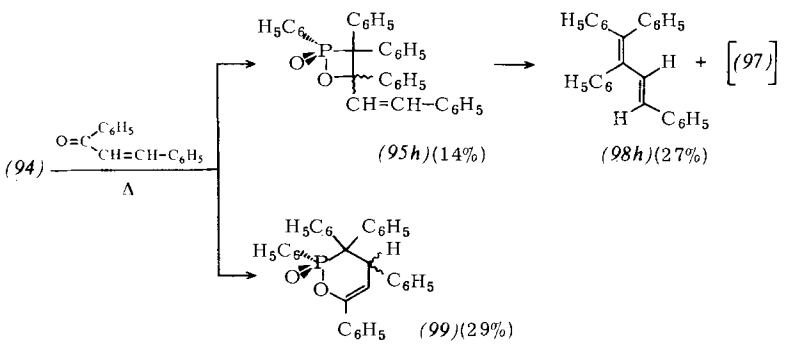
Table 10. 2*H*-1,5,2-Dioxaphosphorins *(100)* and *(101)* from (α-benzoylbenzylidene)phenylphosphane oxide *(86)* and carbonyl compounds [46, 48].

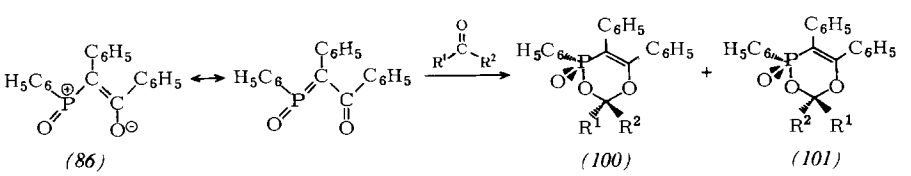
R^1	R^2	Yield [%] *(100)* + *(101)*
C_6H_5	H	28 [a]
C_6H_5	CH_3	22 [b]
C_6H_5	C_6H_5	14
CH_3	H	27 [c]
CH_3	CH_3	45
CH_3	$C(CH_3)_3$	26 [d]
—CH_2—	CH_2—CH_2—CH_2—CH_2—	32

[a] *(100)* and *(101)* can be separated.
[b] *(100)* and *(101)* cannot be separated; ratio ≈ 2:1 (NMR-spectroscopy).
[c] *(100)* and *(101)* can be separated; ratio ≈ 1:1.
[d] *(100)* and *(101)* can be separated; ratio ≈ 20:1.

Thermal fragmentation (215 °C, 5×10^{-3} torr) of *(100)*, $R^1 = R^2 = C_6H_5$, to diphenylacetylene, benzophenone, and the hypothetical *(97)* is in accord with the proposed structure, as is its alkaline hydrolysis to (α-benzoylbenzyl)phenylphosphinic acid and benzophenone[46].

Four dimers of *(86)* are obtained in all the trapping reactions. Their structures are currently being elucidated.

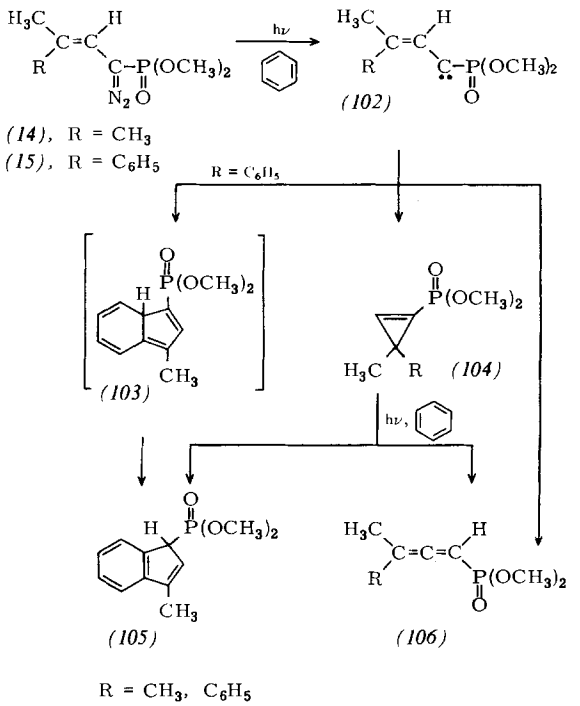




4.3. Vinylcarbene/Cyclopropene Ring Closure and Vinylcarbene/Allene Rearrangement

The carbenes *(102)* produced photolytically from the vinyl diazomethanephosphonates *(14)* and *(15)* in benzene initially avoid the possible formation of norcaradiene in favor of intramolecular reactions. The cyclopropene ring closure giving *(104)* (33 or 45 %, respectively) is preferred, but is accompanied to a minor extent by the hitherto unknown rearrangement to the propadienylphosphonates *(106)* (4 or 7%, respectively)[49].

The carbene *(105)*, R = C_6H_5, cyclizes to dimethyl 1-indenylphosphonate *(105)* (5%). *(103)* should be an intermediate along this route, arising by intramolecular insertion



of the carbene-carbon atom into the *ortho*-CH bond of the phenyl residue; the subsequent sigmatropic [1,5]-shift *(103)*→*(105)* is thermally allowed[49]. The cyclopropenylphosphonates *(104)* are also converted into *(105)* and *(106)* on irradiation[49], the most obvious explanation for this being ring opening of *(104)* to give *(102)*[50], followed by the reactions mentioned above.

A further route to phosphorylvinylcarbenes starts from phosphorylalkynes *(107)*. These alkynes add disubstituted diazoalkanes such as 2-diazopropane or diazodiphenylmethane with the usual orientation, giving 5-phosphoryl-3*H*-pyrazoles *(108)* of considerable stability.

On irradiation in benzene these pyrazoles isomerize with ring opening to yield the diazo compounds *(109)*[51], as can be readily observed by IR spectroscopy. Formation of the carbene *(112)* with loss of N_2 is followed by the reactions already discussed for *(102)*, giving the cyclopropenes *(110)* and the allenes *(111)* (Table 11)[52].

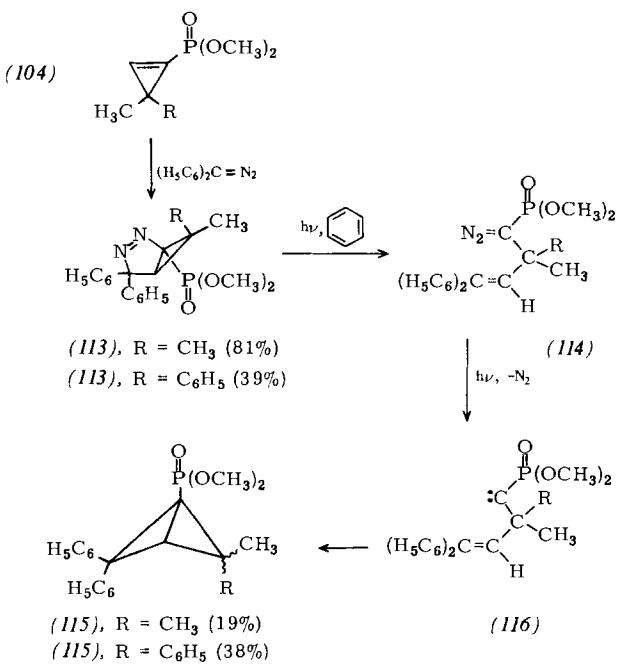
Table 11. 1-Cyclopropenylphosphane oxides *(110)* and propadienylphosphane oxides *(111)* from phosphorylvinylcarbenes *(112)* [52].

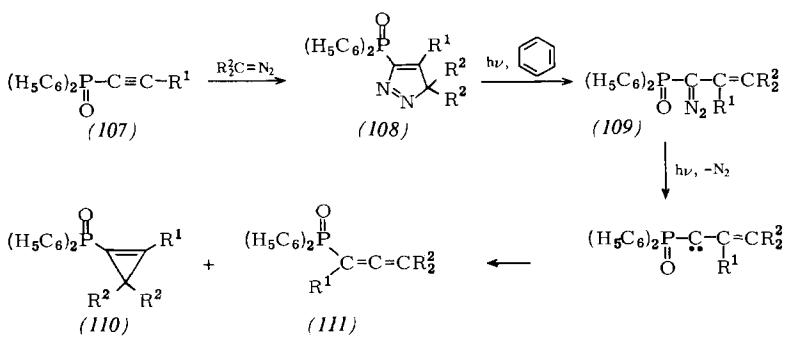
R^1	R^2	Yield [%] *(110)*	Yield [%] *(112)*
C_6H_5	CH_3	77	—
$(C_6H_5)_2P(O)$	CH_3	21	12
$(C_6H_5)_2P(O)$	C_6H_5	60	3

It should be noted that in these cases the shift of the diphenylphosphoryl group in *(112)* must precede allene formation and that the cyclopropene *(110)*, $R^1=(C_6H_5)_2PO$, $R^2=C_6H_5$, can be rearranged photochemically and quantitatively to the allene *(111)*, *(112)* again being a probable intermediate[52].

4.4. Vinylcarbene/Allylcarbene Homologation

This homologation is an extension of cyclization of phosphorylvinylcarbenes to phosphorylcyclopropenes, *e.g.*





(102) → *(104)*. From the latter, by cycloaddition of disubstituted diazoalkanes such as diazodiphenylmethane, one obtains the diazabicyclo[3.1.0]hexenes *(113)*, which on irradiation are converted into the allylcarbenes *(116)* in a photochemical two-step reaction[49].

Ring opening of *(113)* to *(114)* (detectable by IR spectroscopy)[53], which can be interpreted as a [3+2]-cycloreversion, is followed by loss of N_2 to give *(116)*. These carbenes *(116)* undergo intramolecular cyclopropanation to yield the 1-phosphorylbicyclo[1.1.0]butanes *(115)*[49].

Numerous co-workers participated in obtaining the results recorded from our own school. To them I offer my heartfelt thanks for the preparative opening up of phosphorylcarbene chemistry.

Received: August 30, 1974 [A 58 IE]
German version: Angew. Chem. *87*, 259 (1975)
Translated by Express Translation Service, London

[1] Carbenes, Part 8.—Part 7: ref. [49].
[2] Most recent review: *M. Regitz* in *F. Korte:* Methodicum Chimicum. Thieme, Stuttgart 1974. Vol. 6, p. 212.
[3] Review: *H. G. Henning* and *G. Hilgetag*, Z. Chem. *7*, 169 (1967).
[4] Review: *M. Regitz*, Angew. Chem. *79*, 786 (1967); Angew. Chem. internat. Edit. *6*, 733 (1967).
[5] Review: *M. Regitz*, Synthesis *1972*, 351.
[6] *D. Seyferth, R. S. Marmor*, and *P. Hilbert*, J. Org. Chem. *36*, 1379 (1971).
[7] *M. Regitz, A. Liedhegener, U. Eckstein, M. Martin*, and *W. Anschütz*, Liebigs Ann. Chem. *748*, 207 (1971).
[8] *U. Felcht* and *M. Regitz*, Chem. Ber. *108*, (1975), in press.
[9] *H. Eckes* and *M. Regitz*, Tetrahedron Lett. *1975*, 447.
[10] *H. Scherer, A. Hartmann, M. Regitz, B. D. Tunggal*, and *H. Günther*, Chem. Ber. *105*, 3357 (1972).
[11] *M. Regitz, W. Anschütz*, and *A. Liedhegener*, Chem. Ber. *101*, 3734 (1968).
[12] *R. S. Marmor* and *D. Seyferth*, J. Org. Chem. *36*, 128 (1971).
[13] *A. Hartmann*, Dissertation, Universität Saarbrücken 1974.
[14] *G. Maas*, Dissertation, Universität Saarbrücken 1974.
[15] *M. Regitz* and *W. Anschütz*, Chem. Ber. *102*, 2216 (1969).
[16] *W. Disteldorf*, Dissertation, Universität Saarbrücken 1974.
[17] *U. Eckstein*, Dissertation, Universität Saarbrücken 1973.
[18] *M. Regitz, W. Disteldorf, U. Eckstein*, and *B. Weber*, Tetrahedron Lett. *1972*, 3979.
[19] *M. Regitz, W. Anschütz, W. Bartz*, and *A. Liedhegener*, Tetrahedron Lett. *1968*, 3171.
[20] *M. Regitz* and *W. Bartz*, Chem. Ber. *103*, 1477 (1970).
[21] For general carbene reactivity see a) *W. Kirmse:* Carbene Chemistry. Academic Press, New York 1971, 2nd Edit.; b) *M. Jones* and *R. A. Moss:* Carbenes. Wiley, New York 1973.
[22] *M. Regitz, H. Scherer*, and *W. Anschütz*, Tetrahedron Lett. *1970*, 753.
[23] *H. Scherer*, Dissertation, Universität Saarbrücken 1971.
[24] *(44)* can be formed, at least partially, by direct insertion into a CH bond.
[25] *D. Seyferth* and *R. S. Marmor*, Tetrahedron Lett. *1970*, 2493.
[26] *D. Seyferth, P. Hilbert*, and *R. S. Marmor*, J. Amer. Chem. Soc. *89*, 4812 (1967).
[27] *H. Eckes*, Dissertation, Universität Saarbrücken 1974.
[28] *H. Günther, B. D. Tunggal, M. Regitz, H. Scherer*, and *T. Keller*, Angew. Chem. *83*, 585 (1971); Angew. Chem. internat. Edit. *10*, 563 (1971).
[29] *G. Maas, K. Fischer*, and *M. Regitz*, Acta Crystallogr. *30*, 1140 (1974).
[30] *G. Maas, K. Fischer*, and *M. Regitz*, Acta Crystallogr. *B30*, 2853 (1974).
[31] Review: *G. Maier:* Valenzisomerisierungen. Verlag Chemie, Weinheim 1972, pp. 105ff.
[32] The cyclopropanation product from benzene and (dimethoxyphosphoryl)carbene also exists at low temperatures in the cycloheptatriene form: *B. Weber*, Dissertation, Universität Saarbrücken, planned for 1975.
[33] Such a reaction is known for dimethyl 7-phenylnorcaradien-7-ylphosphonate; see [23].
[34] *J. A. Berson*, Accounts Chem. Res. *1*, 152 (1968).
[35] *N. Trong Anh:* Die Woodward-Hoffmann-Regeln und ihre Anwendung. Verlag Chemie, Weinheim 1972, p. 80.
[36] See [35], p. 46.
[37] Analogous reaction of diphenylcarbene: *J. Baron, M. E. Hendrick*, and *M. Jones*, J. Amer. Chem. Soc. *95*, 6286 (1973).
[38] *A. Hartmann* and *M. Regitz*, Phosphorus *5*, 21 (1974).
[39] *H. Heydt*, Diplomarbeit, Universität Saarbrücken 1972; over a wide temperature range the valence tautomer equilibrium is shifted wholly in favor of the cycloheptatriene form.
[40] *E. Niecke* and *W. Flick*, Angew. Chem. *86*, 128 (1974); Angew. Chem. internat. Edit. *13*, 134 (1974); *O. J. Scherer* and *N. Kuhn*, Chem. Ber. *107*, 2123 (1974); *J. Wiseman* and *F. H. Westheimer*, J. Amer. Chem. Soc. *96*, 4262 (1974).
[41] *M. Regitz, A. Liedhegener, W. Anschütz*, and *H. Eckes*, Chem. Ber. *104*, 2177 (1971).
[42] *U. Felcht*, Dissertation, Universität Kaiserslautern, planned for 1975.
[43] Attempted isolation or spectroscopic detection of the heterocumulene *(86)* has so far been unsuccessful.
[44] Mechanism and definition of term: *L. Horner* and *H. Schwarz*, Liebigs Ann. Chem. *747*, 1, 21 (1971).
[45] The same problems concerning valence and coordination number arise as with the methylenephosphane oxides.
[46] *M. Regitz, H. Scherer, W. Illger*, and *H. Eckes*, Angew. Chem. *85*, 1115 (1973); Angew. Chem. internat. Edit. *12*, 1010 (1973).
[47] *H. Staudinger* and *R. Endle*, Liebigs Ann. Chem. *401*, 263 (1913).
[48] *W. Illger*, Dissertation, Universität Saarbrücken 1974.
[49] *A. Hartmann, W. Welter*, and *M. Regitz*, Tetrahedron Lett. *1974*, 1825.
[50] See *L. Schrader* and *W. Hartmann*, Tetrahedron Lett. *1973*, 3995.
[51] See ref. [21b], p. 337.
[52] *H. Heydt*, Dissertation, Universität Kaiserslautern, planned for 1975.
[53] Comparable reactions of 2-diazopropane with carbonylcyclopropenes: *M. Franck-Neumann* and *C. Buchecker*, Tetrahedron Lett. *1969*, 2659.

New Element-Carbon (p-p)π Bonds

By Peter Jutzi[*]

Recent years have seen the preparation of π systems containing novel (p-p)π bonds between carbon and elements from the third, fourth, and fifth Main Groups of the Periodic Table; most of these compounds are predicted to be incapable of existence according to the classical concepts of the double bond. (p-p)π Bonds between carbon and phosphorus, arsenic, and antimony have been successfully stabilized in resonance-stabilized colored compounds of the cyanine and triphenylmethane type, and also in aromatic systems deriving from benzene, naphthalene, and anthracene. Bismuth-carbon and boron-carbon (p-p)π bonds have likewise been confirmed in aromatic systems. Silicon-carbon and germanium-carbon (p-p)π bonds have been detected in extremely reactive derivatives of silaethylene and germaethylene, respectively. The present report describes characteristic reactions of the new π systems. Their bonding follows from X-ray structure analysis, from photoelectron, UV, and NMR spectra, and from calculations. Criteria for the existence of π systems which are not allowed by the classical double bond rule are discussed; these criteria remain valid on generalization.

1. Introduction

Of the Main Group elements, boron, carbon, nitrogen, and oxygen occupy a special position, being able to form stable (p-p)π bonds. Such bonds are virtually unknown for all other elements with few exceptions. This becomes very clear on comparing element modifications (C-Si, N_2-P_4, O_2-S_8) and also on observation of the structures of comparable compounds (NO_3^--PO_3^-, CO_2-SiO_2, *etc.*).

Experimental failures in attempts to form such π bonds and theoretical work instigated by *Pitzer*[1] and *Mulliken*[2] led to formulation of the so-called "classical double bond rule" which states that elements having a principal quantum number greater than 2 should not be able to form (p-p)π bonds with themselves or with other elements. In strict accord with this rule, relevant compounds possessing El=El bonds were classed as "non-existent compounds".

The highly attractive task of disproving a theory by experiment has recently prompted a number of research groups to undertake renewed studies in this area. As a result, several exceptions to the classical double bond rule have become known.

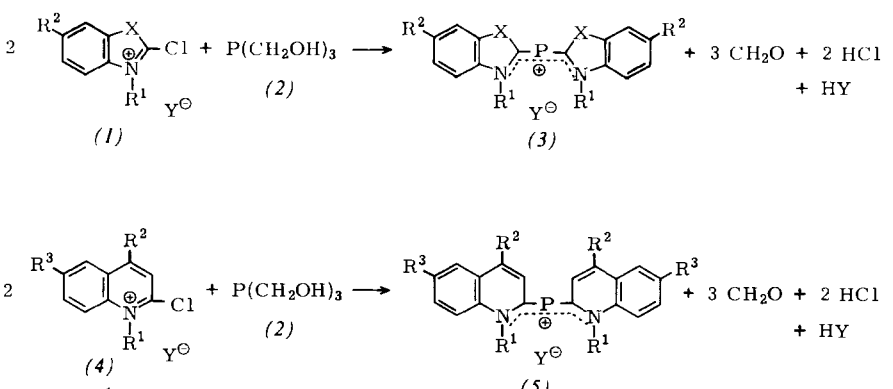
This progress report will present a series of compounds in which (p-p)π bonding has been accomplished for the first time between P, As, Sb, Bi, Si, or Ge on the one hand and carbon on the other. Moreover, bond systems having a B=C double bond will also be described. Although such bonds do not contravene the classical double bond rule, they were also unknown until very recently.

2. P=C, As=C, Sb=C, Bi=C Bonds

2.1. Dyes Having P=C, As=C, and Sb=C Bonds

2.1.1. Phospha- and Arsamethine Cyanines

After *Gier*[3] had demonstrated the existence of P≡C π bonds in 1961 by detection of HC≡P, a species which polymerizes at −130 °C, the first preparation of a stable compound containing a phosphorus-carbon (3p-2p)π bond was accomplished by *Dimroth*'s research school in 1964[4]. Reaction of 2-chlorobenzothiazolium and 2-chloroquinolinium salts [*(1)* and *(4)*, respectively] with tris(hydroxymethyl)phosphane yields resonance-stabilized phosphamethine cyanines *(3)* and *(5)* as stable, yellow to dark red crystalline compounds.



X = S, NR^1

Y = BF_4, ClO_4

R^1 = CH_3, C_2H_5; R^2 = H, Br, OCH_3, CH_3, C_2H_5, $CH(CH_3)_2$; R^3 = H, Br, OCH_3

This synthetic principle was later modified by *Märkl et al.*[5], who used tris(trimethylsilyl)phosphane in place of *(2)*.

[*] Doz. Dr. P. Jutzi
Institut für Anorganische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

The presence of divalent phosphorus having the coordination number 3 could be unequivocally demonstrated by studies on crystal structure[6, 7]. Thus "bis[*N*-ethyl-2-benzothiazole]-monophosphamethine cyanine perchlorate"[6] (Fig. 1) is in complete accord with the structure postulated by *Dimroth et al.* The two P—C bond lengths of 1.76 Å are significantly shorter than P—C single bonds [for comparison: $(CH_3)_3P$, 1.87 Å; $(C_6H_5)_3P$, 1.83 Å]. The CPC angle is 105° [$(CH_3)_3P$, 100°; $(C_6H_5)_3P$, 103°].

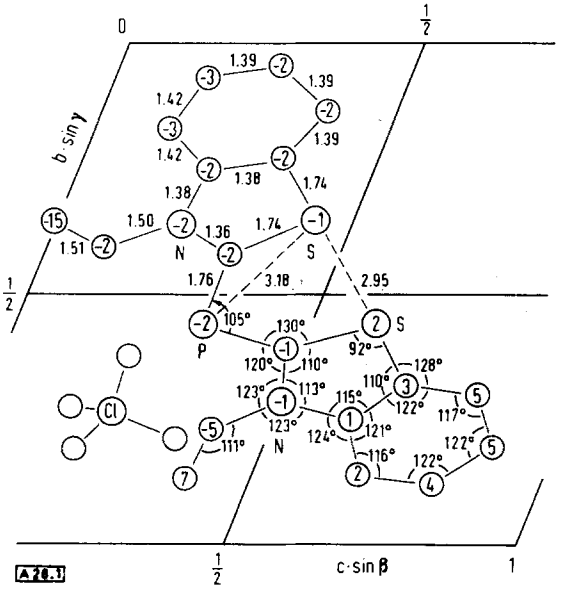
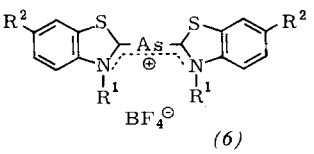


Fig. 1. *y,z* Projection of a perchlorate anion and a phosphacyanine cation with averaged bond lengths [Å] and angles. Deviations from the $2x+y+2z=2$ plane in 1/10 Å are given in the circles.

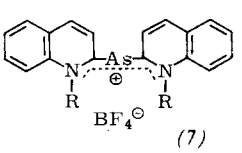
Spectroscopic and chemical investigations on phosphamethine cyanines have recently been reviewed by *Dimroth*[9].

The existence of stable arsenic-carbon (4p-2p)π bonds was first proved by *Märkl*[5] when he synthesized arsamethine cyanines. As in the above synthesis of phosphamethine cyanines, reaction with tris(trimethylsilyl)arsane affords dyes of type *(6)* and *(7)* which are stable in bulk but slowly decompose in solution.



(6)

$R^1 = CH_3, C_2H_5$; $R^2 = H, OCH_3$



(7)

$R = CH_3, C_2H_5$

The ultraviolet/visible spectra of phospha- and arsamethine cyanines closely resemble those of methine- and azamethine cyanines. In accord with the perturbation of the cyanine π-electron system discussed by *Kuhn*[8], decreasing electronegativity of the hetero atom is paralleled by a bathochromic shift of the long-wave absorption maxima (Fig. 2)[5, 9].

2.1.2. Resonance-Stabilized Triarylarsenic(v) and Triarylantimony(v) Cations

Pronounced delocalization extending over the central carbenium ion is assumed to occur in purely organic triphenylmethane dyes. The synthesis of analogous compounds having

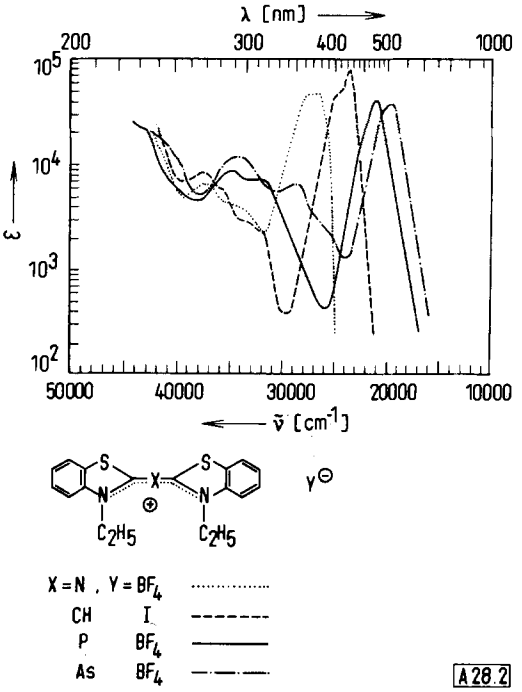
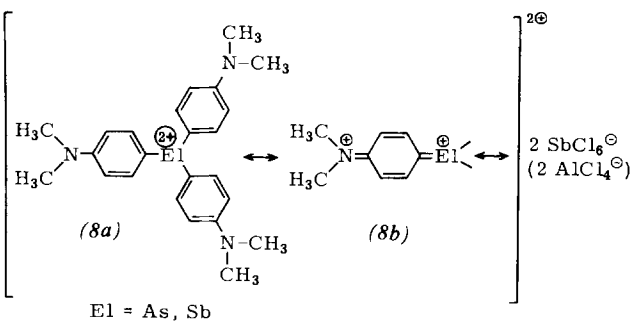


Fig. 2. Ultraviolet/visible spectra of comparable cyanine systems having N, C, P, or As as central atom.

a central arsenic or antimony atom was recently reported by *Klar et al.*[10]. Heating of tris(4-dimethylaminophenyl)arsenic dichloride or -antimony dichloride with antimony pentachloride or aluminum trichloride yields the air- and moisture-sensitive, highly insoluble salts of type *(8)* displaying an intense blue color.



(8a) *(8b)*

El = As, Sb

The UV and ^{1}H-NMR spectra suggest the possibility of resonance *(8a)*⇌*(8b)* and hence a certain degree of double bond character for the element-carbon bonds. (p-p)π Interaction is facilitated in these systems because the higher effective nuclear charge of the central atoms renders the pertinent p orbitals less diffuse and therefore better able to overlap with the C_{2p} π orbitals.

2.2. Phospha-, Arsa-, Stiba-, and Bismutaarenes

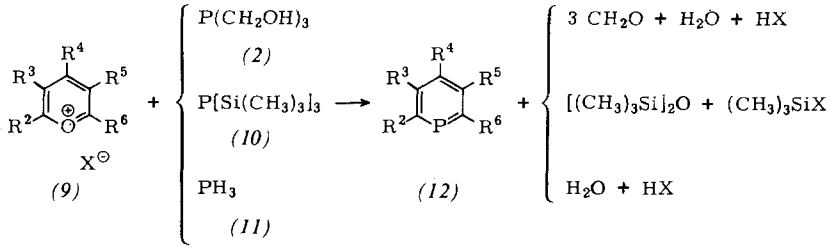
2.2.1. Preparation and Structure of Phosphaarenes

A phosphorus-carbon (3p-2p)π bond was first stabilized in a Hückel π system by *Märkl*[11] in 1966. Reaction of 2,4,6-triphenylpyranylium tetrafluoroborate *(9)* with tris(hydroxymethyl)phosphane *(2)* leads to the surprisingly stable yellow 2,4,6-triphenyl-1-phosphabenzene (2,4,6-triphenyl-λ^3-phosphorin) *(12)*, $R^{2,4,6} = C_6H_5$, $R^{3,5} = H$. Meanwhile more than

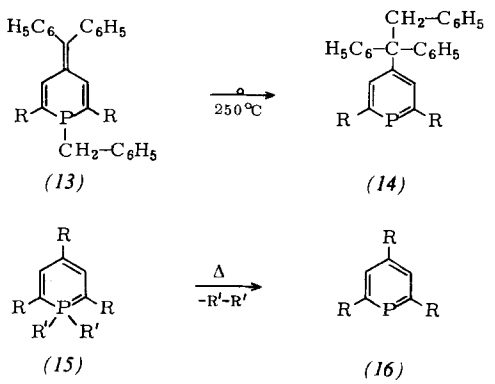
50 aryl-substituted phosphabenzenes have been prepared employing the same synthetic principle[9] under modified conditions. Thus *(9)* and tris(trimethylsilyl)phosphane *(10)* likewise afford compounds of type *(12)*[12], and acid-catalyzed reaction with unsubstituted phosphane itself *(11)* constituted the first preparation of mono-, di-, and trialkyl-substituted phosphabenzenes[13].

In analogous fashion, 4-substituted phosphabenzene derivatives are accessible from corresponding compounds of type *(17)*[19a, 30d].

Benzo-fused phosphabenzenes form much less readily than substituted phosphabenzenes. Thus although the pale-yellow, air-stable crystalline compound 2-phenyl-1-phosphanaphthalene *(21)*[19] is formed on thermolysis of 1-benzyl-2-phenyl-

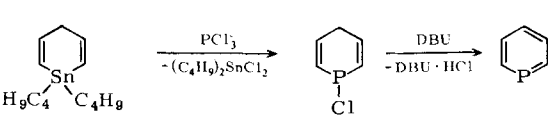


Further synthetic possibilities are provided by thermal rearrangement and elimination reactions. Intermolecular rearrangement of methylenephosphacyclohexadienes to phosphabenzenes *(13)*→*(14)*[14] and the transformation of "non-classical" phosphabenzene derivatives *(15)* into "classical" phosphabenzenes *(16)*[15] may be cited as examples. The reader is referred to the surveys by *Dimroth*[9] and *Märkl*[16] for a discussion of reaction mechanisms and for more detailed information.



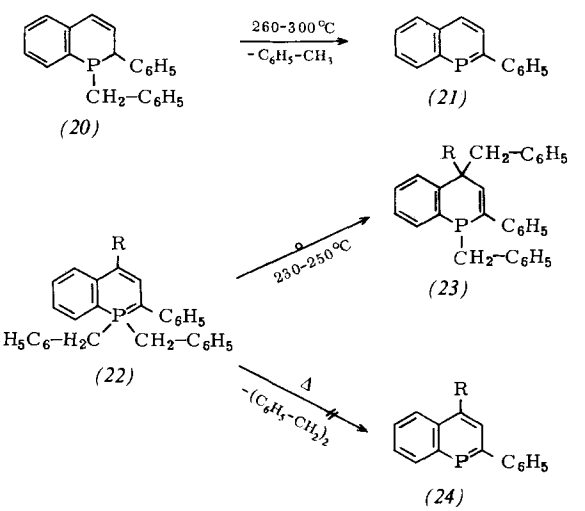
The unsubstituted parent compound of the phosphabenzene series was first prepared by *Ashe*[17] using a completely different approach. 1-Chloro-1-phospha-2,5-cyclohexadiene *(18)* (accessible from 1,1-dibutyl-1-stanna-2,5-cyclohexadiene *(17)* and PCl_3) readily eliminates hydrogen chloride on treatment with bases to give phosphabenzene *(19)* in good yield.

Phosphabenzene, a colorless volatile liquid, is highly reactive compared to its substituted derivatives. It proves to be extremely air- and moisture-sensitive and can only be stored for extended periods under an inert gas. Its structure has been confirmed by ^{1}H-NMR, ^{31}P-NMR, UV, IR, and mass spectra[17] and dipole moment determinations[18].

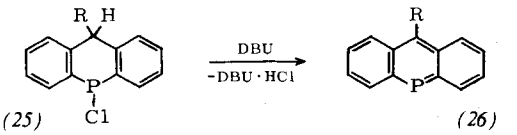


DBU = 1,5-Diazabicyclo[5.4.0]undec-5-ene

1,2-dihydro-1-phosphanaphthalene *(20)*, 1,1-dibenzyl-1-phosphanaphthalene *(22)* no longer reacts like *(15)* but rearranges instead with benzyl migration to form 1,4-dibenzyl-1,4-dihydro-1-phosphanaphthalenes *(23)*[20]. As tertiary phosphanes, these products are energetically favored over phosphanaphthalenes.

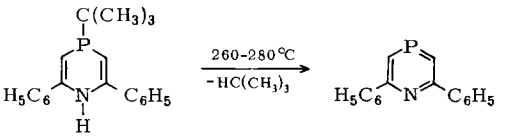


The dibenzo-fused derivative 9-phosphaanthracene (dibenzo[*b*,*e*]phosphorin) is already so unstable—corresponding to the reactivity of positions 9 and 10 of anthracene itself resulting from the π-electron density distribution—that it cannot be isolated. The 9-phosphaanthracene *(26a)* formed on reaction of 9-chloro-9,10-dihydro-9-phosphaanthracene *(25a)* with auxiliary bases can only be detected in solution by UV spectroscopy[21]. Only upon introduction of a phenyl group in position 10 is the reactivity reduced by steric shielding: 10-phenyl-9-phosphaanthracene *(26b)* is an isolable, crystalline, but extremely air-sensitive compound[22].



(a): R = H
(b): R = C_6H_5

The preparative route leading to phosphanaphthalene *(21)* also provides an entry to derivatives of 1-aza-4-phosphabenzene, a new type of aromatic compound with a P=C bond. Thus thermolysis of 2,6-diphenyl-4-*tert*-butyl-1,4-dihydro-1-aza-4-phosphabenzene *(27)* yields 2,6-diphenyl-1-aza-4-phosphabenzene *(28)* as a pale yellow viscous oil[23].



(27) *(28)*

Information concerning the aromatic character and the precise nature of the bonding in phosphabenzenes is provided by spectroscopic and crystal structure studies[24, 25]. The result of an X-ray structure analysis[24] of 2,6-dimethyl-4-phenyl-1-phosphabenzene is depicted in Figure 3. The particularly informative C—P—C distance of 1.74 Å is intermediate between the value for the P—C bond in triphenylphosphane (1.83 Å) and that for the P=C bond in triphenylmethylenephosphorane (1.65 Å). The larger angle in the heterocycle relative to benzene is due to the longer P—C bond. The phosphabenzene ring is almost planar.

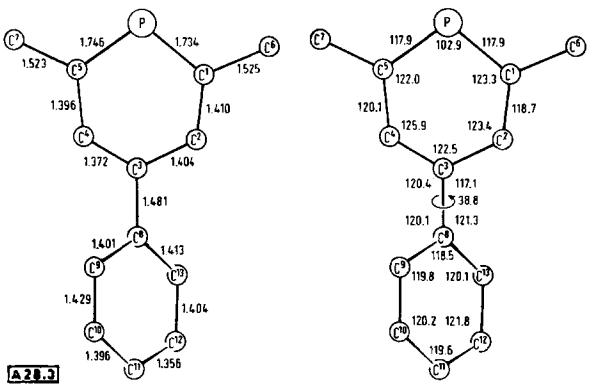


Fig. 3. Projection of a 2,6-dimethyl-4-phenyl-1-phosphabenzene molecule along *a*. Left-hand side: bond lengths [Å]; maximum standard deviation ±0.012 Å. Right-hand side: bond angles [°]; maximum standard deviation ±0.8°.

The ^{1}H-NMR spectra of all phosphabenzenes confirm their aromatic character. The π-electron delocalization follows from the ring current effect which causes the ring proton signals to appear at relatively low field strengths (cf. Section 2.2.4).

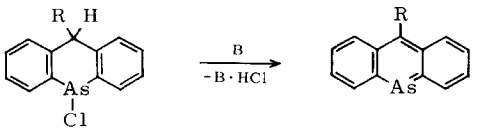
The unusual electronic situation at the phosphorus atom in compounds containing trivalent phosphorus of coordination number 2 is clearly seen in their ^{31}P-NMR spectra. In phosphabenzenes the phosphorus nucleus experiences only slight shielding; the ^{31}P resonance signals appear between $\delta = -170$ and -180 ppm [relative to 85% H_3PO_4, external standard], as against 0 to -60 ppm in normal tertiary phosphanes[9].

The UV spectra of phosphabenzene derivatives are very similar to those of corresponding pyridine and benzene derivatives (cf. Section 2.2.4).

2.2.2. Preparation of Arsa-, Stiba-, and Bismutaarenes

The first indication that it might be possible to stabilize an arsenic-carbon (4p-2p)π bond in a Hückel aromatic compound was obtained when we[26], and almost simultaneously *Bickelhaupt et al.*[27] too, examined the reaction of 9-chloro-9,10-dihydro-9-arsaanthracene *(29a)* with auxiliary bases such as DBU or triethylamine. The product is yellow 9-arsaanthracene *(30a)*, which is however only stable in solution and polymerizes on attempted isolation.

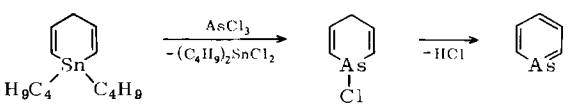
Meanwhile, 10-substituted 9-arsaanthracene derivatives *(30b)—(30e)* have also been prepared; the stability of these heteroarenes shows a significant increase on introduction of a phenyl group[28].



(29) *(30)*

	(a)	*(b)*	*(c)*	*(d)*	*(e)*
R	H	C_6H_5	Cl	Br	OCH_3

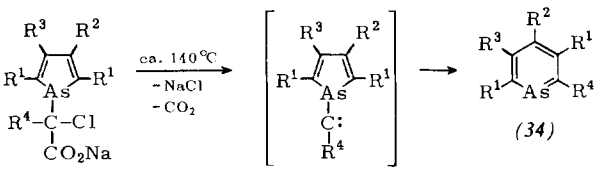
Synthesis of unsubstituted arsabenzene was accomplished by *Ashe* by the same method as was successfully employed for phosphabenzene[17]. Reaction of 1,1-dibutyl-1-stanna-2,5-cyclohexadiene *(17)* with arsenic trichloride to give *(31)* and subsequent elimination of HCl lead to arsabenzene *(32)* as a colorless, highly reactive compound.



(17) *(31)* *(32)*

The ^{1}H-NMR and UV spectra of *(32)* indicate aromatic character (cf. Section 2.2.4).

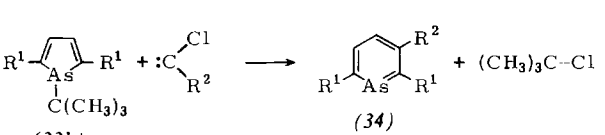
Aryl-substituted arsabenzenes *(34)*, obtained on thermolysis of arsoles *(33a)* by intramolecular carbene insertion[29, 30], are much more stable compounds.



(33a) *(34)*

R^1 = C_6H_5, Naphthyl, *p*-Tolyl
$R^{2,3}$ = C_6H_5, H
R^4 = C_6H_5, Cl, H

Substituted arsabenzenes *(34)* are also accessible by reaction of arsoles of type *(33b)* with phenylchlorocarbene or dichlorocarbene. This synthesis is analogous to the classical pyridine synthesis by ring expansion of pyrroles[30a, b].



(33b) *(34)*

R^1 = C_6H_5
R^2 = C_6H_5, Cl

Further arsabenzenes, some of which bear interesting functional substituents in position 4 ($R = C_6H_5$, *c*-C_6H_{11}, *tert*-C_4H_9, OCH_3, OC_2H_5, CHO, $COOC_2H_5$, $Si(CH_3)_3$, $Ge(CH_3)_3$) can be prepared starting from corresponding stannacyclohexadienes *(17)*[30c, d]. The formyl group in "arsabenzaldehyde", which smells strongly of benzaldehyde, displays a perfectly normal electrophilic reactivity (aldol reaction and aldol condensation with acetone)[30e].

An X-ray structure analysis[31] of 2,3,6-triphenyl-1-arsabenzene (Fig. 4) shows the heterocycle to be planar within the limits of experimental error (C_{2v} symmetry). The As—C bond length of 1.872 Å is shorter than a standard As—C σ bond (1.96 Å). Deviations from 120° in the ring are again a consequence of unequal As—C and C—C bond lengths.

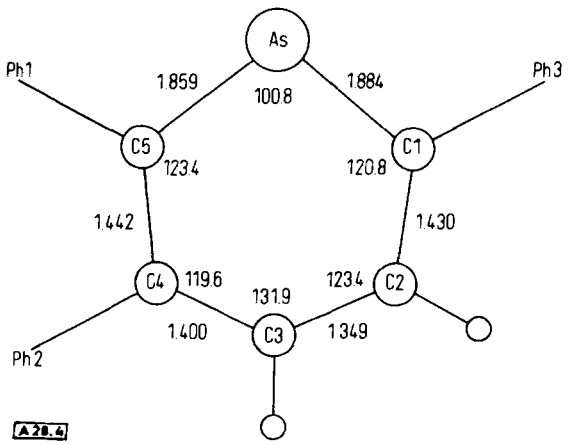
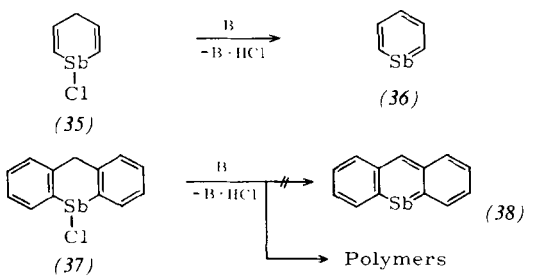


Fig. 4. Bond lengths [Å] and angles [°] in the C_5As ring of 2,3,6-triphenylarsenin. Standard deviations: As—C 0.014, C—C 0.02 Å; C—As—C 0.6, As—C—C 1.0, C—C—C 1.3°.

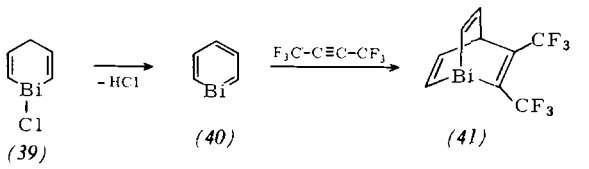
In the light of previous experience, it must be considered highly surprising that even compounds with (5p-2p)π orbital overlapping should be stable under certain conditions. Nevertheless, *Ashe*[32] succeeded in preparing stibabenzene *(36)* by elimination of HCl from 1-chloro-1-stiba-2,5-cyclohexadiene *(35)* and in its unequivocal characterization. The compound is stable only at low temperature ($\lesssim -80$ °C) in bulk and polymerizes on warming. It can, however, be conveniently handled in solution under an inert atmosphere.

Attempts to prepare 9-stibaanthracene *(38)* by the method employed in the synthesis of *(30)* were unsuccessful[33]. Although HCl can be eliminated quantitatively from 9-chloro-9,10-dihydro-9-stibaanthracene *(37)* with auxiliary bases, the reaction only yields polymeric products even at low temperature. The lower gain in resonance energy in the anthracene system no longer suffices to stabilize an Sb=C bond.

It is even possible to detect a (6p-2p)π bond by trapping reactions at low temperature. On elimination of HCl from 1-chloro-1-bismuta-2,5-cyclohexadiene *(39)* *Ashe*[34] obtained



bismutabenzene *(40)*, which is only stable in solution. The compound was characterized as the Diels-Alder adduct *(41)* formed on reaction with hexafluoro-2-butyne.

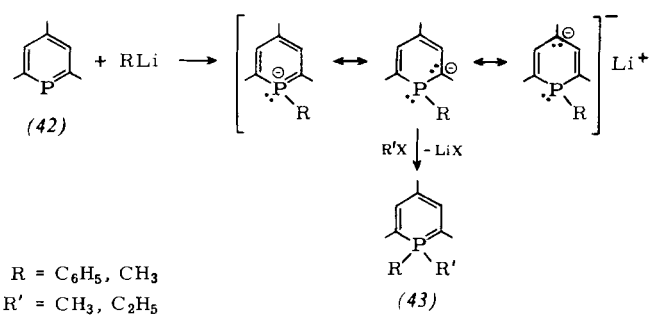


2.2.3 Reactions of Phospha-, Arsa-, Stiba-, and Bismutaarenes

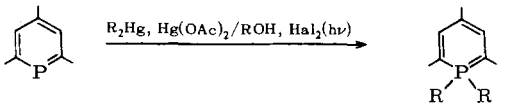
Among the new heteroaromatic compounds the chemistry of substituted phosphabenzenes has been investigated particularly thoroughly and already described in reviews by *Dimroth*[9] and *Märkl*[16]. The most interesting results will be summarized briefly and supplemented in this Section.

In comparison with pyridine, the very slight nucleophilic character of phosphabenzenes is rather striking. According to *Pearson*'s acid-base concept[35] they are classed as "soft" bases, and fail to react with "hard" acids. Attempted protonation, alkylation, and acylation gave negative results. The calculated pK_a value (≈ -10) of phosphabenzenium salts differs considerably from that of the pyridinium ion (≈ 5)[36]. In contrast, reactions with "soft" acids are feasible: 2,4,6-triphenyl-1-phosphabenzene *(12)* ($R^{2,4,6} = C_6H_5$) forms σ complexes with transition metals such as tantalum[37], chromium[38], molybdenum[38], tungsten[38], ruthenium[37], rhodium[37], palladium[37], copper[37], and gold[39]. Of these complexes, those containing Cr, Mo, W, and Au have been unequivocally confirmed by spectroscopic and structural studies. Thus the crystal structure of pentacarbonyl(2,4,6-triphenyl-1-phosphabenzene)chromium(0)[40] shows that all the bond lengths in the heteroaromatic ring of the σ complex correspond to those in the free ligand. The geometry of the complexed phosphabenzene is best described by assuming sp^2 hybridization of the phosphorus atom.

Substituted phosphabenzenes *(42)* display marked electrophilic behavior in numerous reactions. Thus they react with organolithium or organomagnesium compounds to give intensely colored anions which are attacked by electrophiles either at the P atom or at C-2 or C-4[41]; with S_N1-reactive alkyl halides the thermodynamically most stable products are 1,1-disubstituted "non-classical" phosphabenzenes *(43)*, deeply colored, generally strongly fluorescing compounds with phosphorus-carbon (d-p)π bonds.



Oxidation of "classical" to "non-classical" phosphabenzenes can also be achieved by radical reactions, as demonstrated by reactions with mercurials and with halogens[9].

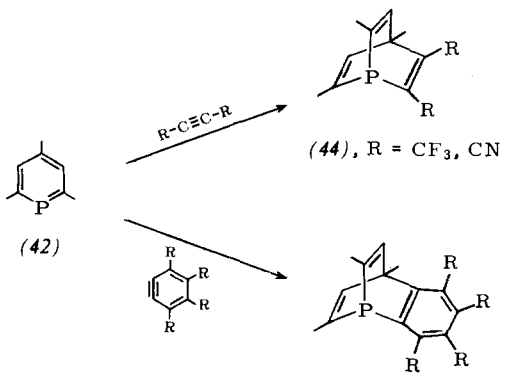


(42) (43)

R = CH_3, C_2H_5, C_6H_5, CH_3–C_6H_4, $CH_3OC_6H_4$, $(CH_3)_2N$–C_6H_4, C_6H_5–CH_2, 2,2'-Biphenyldiyl, OCH_3, OC_2H_5, Cl, Br

Oxidizing agents such as oxygen, halogen, nitric acid, or hydrogen peroxide lead to attack at various ring positions, depending upon how the reaction is conducted. The products are either 1,1-disubstituted λ^5-phosphabenzenes or phosphinic acid derivatives and other oxidation products formed by degradation of the 6π system[9].

The diene character of phosphabenzenes is only slight. As in the case of benzene, Diels-Alder $[\pi 4_s + \pi 2_s]$ cycloadditions occur only with highly reactive dienophiles such as hexafluoro-2-butyne, dicyanoacetylene, or arynes, to form compounds *(44)* and *(45)*, respectively[42–44].

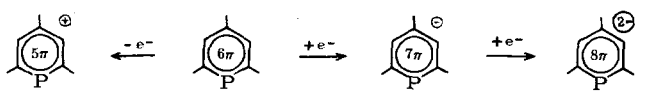


(42) (44), R = CF_3, CN

(45), R = H, Cl

Substituted phosphabenzenes react all the more readily the greater their "electron richness". Retro-Diels-Alder reactions are not observed.

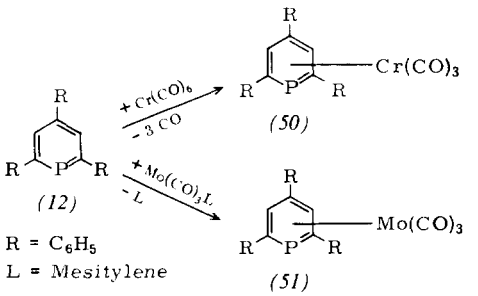
Electron transfer reactions in the π system of phosphabenzenes have led to interesting results. Thus substituted phosphabenzenes can be oxidized very easily to air-stable cation radicals *(46)* which are also highly stable in solution. ESR studies show that these radicals contain an intact phosphabenzene ring. The phosphabenzene anions *(47)* and *(48)* formed on electron addition are much less stable.



(46) (42) (47) (48)

ESR experiments and redox reactions evidence a stepwise reduction *via* the paramagnetic monoanion *(47)* to the diamagnetic dianion *(48)*[9]. Ready formation of anions *(47)* and *(48)* is in accord with the lower half-wave reduction potentials of phosphabenzenes relative to pyridine.

In their complexes with transition metals, phosphaarenes act not only as σ-bonded but also as π-bonded ligands. Thus reaction of 2,4,6-triphenyl-1-phosphabenzene *(12)* with $Cr(CO)_6$ in boiling dibutyl ether leads to tricarbonyl(2,4,6-triphenyl-η^6-1-phosphabenzene)chromium(0) *(50)*, and with tricarbonyl(mesitylene)molybdenum(0) at room temperature to the analogous molybdenum compound *(51)*[45].

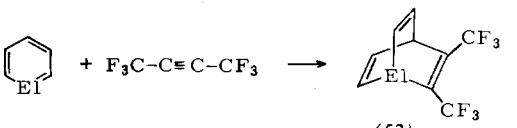


(12) (50) (51)

R = C_6H_5
L = Mesitylene

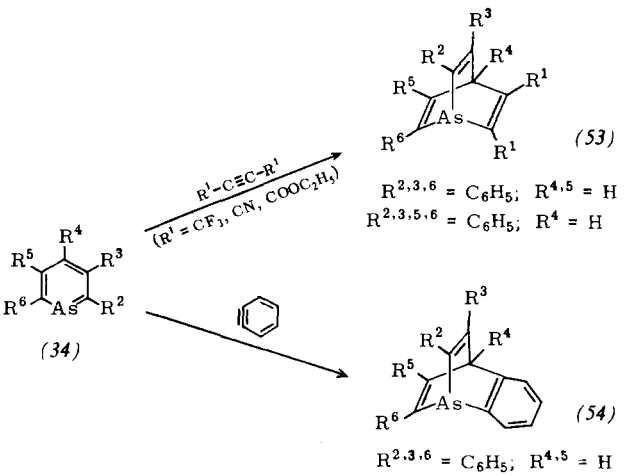
X-Ray structure analysis[46] of *(50)* confirms the presence of a true π-arene complex, the $Cr(CO)_3$ group being bound centrically to the phosphabenzene ring.

In contrast, little is known about the properties of arsa-, stiba-, and bismutaarenes. Only their Diels-Alder reactions have so far been described. For instance, arsabenzene, stibabenzene, and—as already mentioned—bismutabenzene afford corresponding cycloadducts *(52)* with hexafluoro-2-butyne[44].



El = As, Sb, Bi (52)

Unlike aryl-substituted phosphabenzenes, aryl-substituted arsabenzenes can also add to less reactive dienophiles to yield compounds of type *(53)*, and thus exhibit a more pronounced diene reactivity; cycloadditions with arynes lead to arsabarrelenes *(54)*[47].



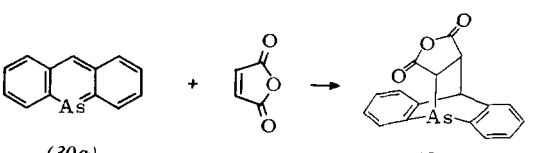
(34) (53)

$R^{2,3,6}$ = C_6H_5; $R^{4,5}$ = H
$R^{2,3,5,6}$ = C_6H_5; R^4 = H

(54)

$R^{2,3,6}$ = C_6H_5; $R^{4,5}$ = H

Expectedly, the anthracene system is also susceptible to Diels-Alder reactions with weak dienophiles under very mild conditions: *e.g.*, 9-arsaanthracene adds maleic anhydride to form *(55)*[26].



(30a) (55)

2.2.4. Photoelectron, UV, and ^{1}H-NMR Spectra

Photoelectron (PE) Spectra

The highest occupied molecular orbitals (HOMO) are of fundamental significance for the properties and reactivity of

a compound. Information about their assignment and energy is provided by PE spectra. Of the series of new heterocycles, photoelectron spectra have been published for phospha-, arsa-, and stibabenzene, for 2,4,6-tri-*tert*-butyl-1-phosphabenzene, 10-phenyl-9-phosphaanthracene, and 10-phenyl-9-arsaanthracene, and compared with previously recorded spectra of benzene and pyridine derivatives[48-50].

Table 1 lists the vertical ionization potentials of benzene, pyridine, and phospha-, arsa-, and stibabenzene. Assignment of the individual bands to π and n/σ ionization processes is based on both characteristic band shapes and on model calculations.

Table 1. Vertical ionization energies for benzene, pyridine, and phospha-, arsa-, and stibabenzene and their assignments.

PE Band		I_v [eV]		I_v [eV]		I_v [eV]		I_v [eV]		I_v [eV]
1	$a_1\ \sigma, n$	9.7	$b_1\ \pi$	9.2	$b_1\ \pi$	8.8	$b_1\ \pi$	8.3	$e_{1g}\ \pi$	9.24
2	$a_2\ \pi$	9.8	$a_2\ \pi$	9.8	$a_2\ \pi$	9.6	$a_2\ \pi$	9.4	$e_{2g}\ \pi$	11.24
3	$b_1\ \pi$	10.5	$a_1\ \sigma, n$	10.0	$a_1\ \sigma, n$	9.9	$a_1\ \sigma, n$	9.6	$a_{2u}\ \pi$	12.19
4	$b_2\ \sigma$	12.5	$b_2\ \sigma$	11.5	$b_2\ \sigma$	11.0	$b_2\ \sigma$	10.4		
5	$b_1\ \pi$	12.6	$b_1\ \pi$	12.1	$b_1\ \pi$	11.8	$b_1\ \pi$	11.7		

Decreasing electronegativity of the heteroatom is accompanied by a decrease in ionization energy. The sequence of MOs determined by *ab initio*[48] and CNDO/2[36] calculations is confirmed most convincingly by the PE data, especially by the sequence reversal of the two highest MOs first observed for these heteroaromatic compounds: while the $a_2(\pi)$ orbital [node at hetero atom] of pyridine is expectedly of higher energy than the $b_1(\pi)$ orbital [lobe at hetero atom], the situation is completely reversed in phospha-, arsa-, and stibabenzene, where the $b_1(\pi)$ orbital is always the HOMO. This reversal is understandable in view of the calculated electron density distribution[36,48]: the hetero atom nitrogen has an overall electron acceptor effect and stabilizes the $b_1(\pi)$ orbital; phosphorus, arsenic, and antimony have the opposite effect and thus stabilize the $a_2(\pi)$ orbital.

Unequivocal proof for this unusual sequence of the two highest occupied π-MOs is provided by comparison of the PE spectra of 9-phenylanthracene, 9-phenylacridine, 10-phenyl-9-phospha- and 10-phenyl-9-arsaanthracene[50] since, in contrast to the benzene system, the highest π-MO in anthracene is not degenerate.

The energies of the free electron pairs on the hetero atoms [$a_1\sigma$/n] are qualitatively of the same order owing to varying mixing of s and p atomic orbitals. Analogous effects are observed on comparison of NH_3 with PH_3, AsH_3, and SbH_3[51].

Estimates of the influence of hetero atom d orbitals on the bonding in the new aromatic compounds tend to vary: according to calculations by *Heilbronner et al.*[48] the effects of d orbitals can be neglected for all molecular orbitals, whereas *Schweig et al.*[36] consider the individual MOs to be stabilized to differing degrees by interaction with d orbitals.

Ultraviolet/visible Spectra

Comparison of the UV/vis spectra of analogous derivatives of benzene, pyridine, and phospha-, arsa-, and stibabenzene clearly reveals structural similarities in the band shapes and a systematic trend with regard to the longest wave absorption maxima. The influence of the hetero atom is manifested in a bathochromic shift of the π-π* transitions. A decreasing π-π* excitation energy runs parallel to the fall in electronegativity of the hetero atom and the likewise decreasing bond strength of corresponding El=C bonds.

Table 2. Longest-wave UV absorption of benzene, pyridine, and phospha-arsa-, and stibabenzene.

λ_{max} [Å]	256	250	246	268	312
	200	192	213	219	236
	180	175			

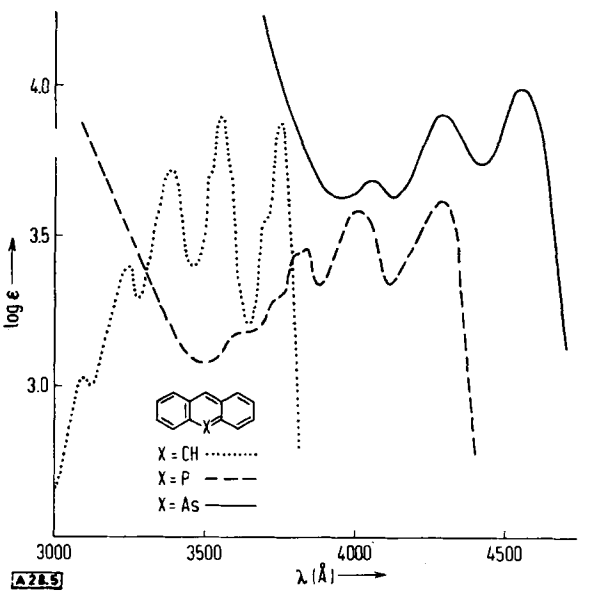


Fig. 5. UV spectra of anthracene (in cyclohexane), 9-phosphaanthracene (in toluene), and 9-arsaanthracene (in THF).

Table 2 shows a comparison of the longest wave absorptions of benzene, pyridine, and phospha-[17], arsa-[17], and stibabenzene[32] (the extinction values are not comparable owing to changes in selection rules). Figure 5 reproduces the long wave regions of the anthracene and phospha- and arsaanthracene spectra[26]; the almost superposable structure of the longest wave absorption bands of phospha- and arsaanthracene and their close similarity to the $1/L_A$ band of anthracene are striking.

^{1}H-NMR Spectra

According to their ^{1}H-NMR spectra, the new heterocycles are aromatic in so far as they display a pronounced ring current effect[9, 16, 17, 32]. The resonances of the ring protons lie at fairly low field. On comparison of the ^{1}H-NMR spectra of pyridine and phospha-, arsa-, and stibabenzene, the progres-

sive downfield shift for the CH protons α to the hetero atom is particularly striking (Table 3).

In molecules with strongly polar groups the electrical dipole moment may be expected to lead to a change in the charge density on certain protons. The dipole moment in pyridine causes deshielding of the α-protons. On going from pyridine to phospha-, arsa-, and stibabenzene this effect should be reduced and an upfield shift occurs in the α-proton signals.

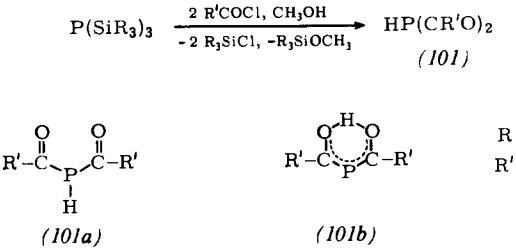


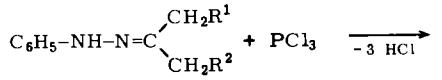
Table 3. Chemical shifts [ppm], coupling constants [Hz] in the ^{1}H-NMR spectra of pyridine [104] and phospha-, arsa-, and stibabenzene [105].

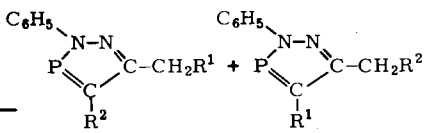
	$\delta_{2\text{-H}}$	$\delta_{3\text{-H}}$	$\delta_{4\text{-H}}$	J_{23}	J_{34}	J_{24}	J_{35}	J_{25}	J_{26}	J_{PCH}
	8.29	7.38	7.75	5.5	7.5	1.9	1.6	0.9	0.4	
	8.61	7.72	7.38	10.0	9.1	1.25	1.80	1.25	−1.90	38
	9.11	7.83	7.53	10.2	8.1	1.05	2.45	1.06	−1.3	
	10.94	8.24	7.78	9.0	11.5	1.0	1.0	4.0	−4.0	

The downfield shift actually observed is therefore attributed to the dominating influence of the magnetic anisotropy of the increasingly large hetero atom[32].

2.3. Other P=C Systems

As early as 1967, Russian authors described an astonishingly simple route to compounds having a phosphorus-carbon (3p-2p)π bond. Reaction of the phenylhydrazones of dimethyl, methyl ethyl, methyl propyl, and methyl butyl ketone with phosphorus trichloride affords isomeric mixtures of 1,2,3-diazaphospholes of type *(100)*[106].





	(a)	(b)	(c)	(d)
R^1	H	H	H	H
R^2	H	CH_3	C_2H_5	C_3H_7

(100)

The structures of these compounds have been confirmed by ^{1}H- and ^{31}P-NMR, IR, and UV spectra, as well as by electron diffraction experiments[107]. Comparison of the UV spectra of *(100)* with those of corresponding 1,2,3-triazoles reveals a slight bathochromic shift, such as is also observed on going from pyridines to phosphabenzenes. The P=C bond length of 1.75 Å also agrees with expectations.

A keto-enol tautomerism involving a P=C bond system has recently been reported for the first time[108]. Stepwise reaction of tris(trimethylsilyl)phosphane with pivaloyl chloride and methanol affords dipivaloylphosphane *(101)*, shown by spectroscopic findings to exist in the keto *(101a)* and in the enol form *(101b)*. Increasing solvent polarity favors the keto form.

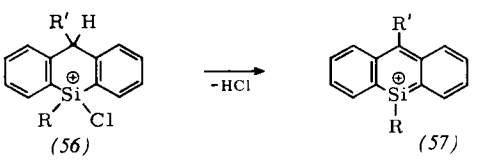
An X-ray structure analysis performed at −80 °C shows that *(101)* assumes the enol form in the solid state (*R* value, 7.4 %; P=C, 1.79 Å).

3. Si=C and Ge=C Bonds

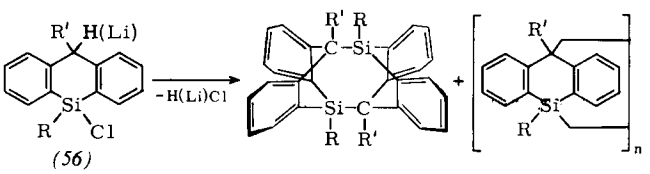
3.1. Experiments on Synthesis of Resonance-Stabilized π-Systems

The reactions described in Section 2 which lead to novel (p-p)π bonds between carbon and elements of the fifth Main Group have sometimes been applied to the formation of such bonds with elements of the fourth Main Group—so far without success.

Thus 9-R-10-R'-9-silaanthracenes cannot be obtained from 9-R-9-chloro-10-R'-9,10-dihydro-9-silaanthracenes *(56)* by elimination of HCl, or of LiCl after prior metalation. Although the desired silaarenes *(57)* appear at remarkable intensities in the mass spectrum[52, 53], the necessary elimination fails to occur in a chemical experiment and reaction proceeds *via* intermolecular substitution leading to dimeric or polymeric products[53–55].



(56) *(57)*



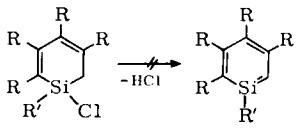
(56)

R = C_6H_5, $C_6H_2(CH_3)_3$, Cl, F, OC_2H_5, C_4H_9, CH_3

R' = $Si(CH_3)_3$, Cl, Br, $COOCH_3$

Analogous results are obtained with 9,10-dihydro-9-germaanthracene derivatives[54].

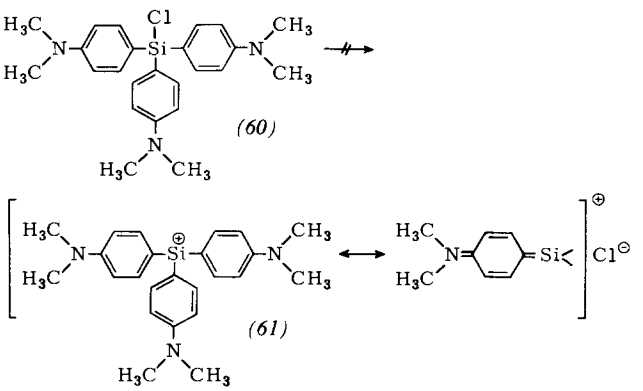
Even the greater gain in resonance energy in the benzene system compared with the anthracene system is not sufficient to stabilize a Si=C bond: although HCl can be eliminated quantitatively from 1-R'-1-chloro-1-sila-2,4-cyclohexadiene *(58)*, no silabenzene *(59)* can be detected, not even as intermediate[56–58].



(58) (59)

R = C_6H_5, H
R' = C_6H_5, CH_3

Attempts to synthesize dyes having a resonance-stabilized Si=C bond have also been described. Tris(4-dimethylaminophenyl)chlorosilane *(60)*, prepared by *Wannagat et al.*[59] in 1955, admittedly corresponds to a "silicocrystalviolet" in composition, but is not ionic in structure and therefore color-

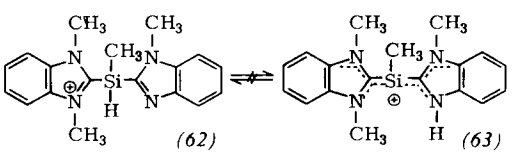


(60)

(61)

less. In this case (p→d)π interactions have such a pronounced stabilizing effect that ionization with resonance stabilization of cation *(61)* is energetically disfavored[59, 10].

Attempted preparations of silamethine cyanine dyes led as far as the successful synthesis of apparently suitable precursors of type *(62)*, but proton migration leading to a resonance stabilized Si=C bond as in *(63)* failed to occur. The proton attached to silicon is still bound as hydride in spite of electron withdrawal by the heterocycles[60].



(62) *(63)*

The first indication of a resonance-stabilized Ge=C bond was obtained by *Curtis*[103] on synthesis of 1-lithio-1,2,3,4,5-pentaphenyl-1-germacyclopentadiene. Investigations on the ionic character of this compound and on resonance stabilization in the anionic 6π system have yet to be performed.

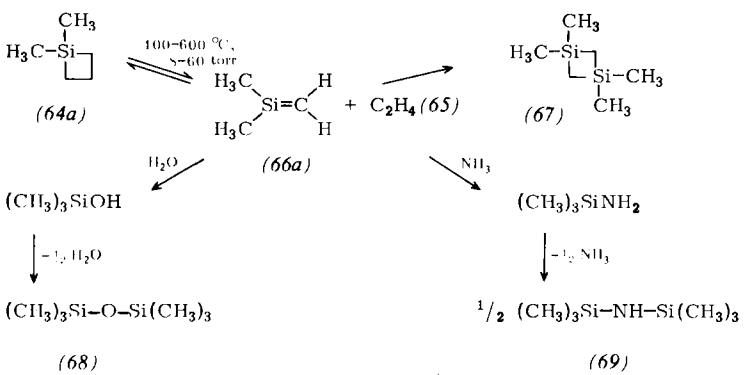
3.2. Silaalkenes and Germaalkenes

Alkene-analogous compounds containing Si=C or Ge=C bonds have frequently been postulated to explain reaction mechanisms[61], but definite proof of these short-lived species was obtained only recently from pyrolysis reactions and photochemical experiments.

3.2.1. Thermolysis Reactions

Studies performed by *Gusel'nikov et al.*[62-64] on 1,1-dimethyl-1-silacyclobutane *(64a)* showed the thermal behavior of this compound to differ in the liquid and gaseous states. Whereas *(64a)* decomposes at about 150°C under normal pressure to give polymeric products, in the gaseous phase it undergoes cleavage in clearly defined manner when heated above 400°C at pressures between 8 and 60 torr; the sole products are ethylene *(65)* and the highly reactive species 2-methyl-2-silapropene *(66a)*, which can only be kept for a short time. Compound *(66a)* dimerizes very rapidly to 1,1,3,3-tetramethyl-1,3-disilacyclobutane *(67)*, but can be trapped by water or ammonia to form hexamethyldisiloxane *(68)* or hexamethyldisilazane *(69)*, respectively.

Kinetic data[64] show the cleavage of *(64a)* to *(65)* and *(66a)*, like that of octafluorocyclobutane to tetrafluoroethylene[65], to be a reversible first order reaction with Arrhenius parameters resembling those for the thermal degradation of alkylcyclobutanes. A triplet ground state is ruled out for *(66a)*. The trapping reactions affording *(68)* and *(69)* are faster than the reverse reaction leading back to *(64a)* and dimerization to *(67)*.

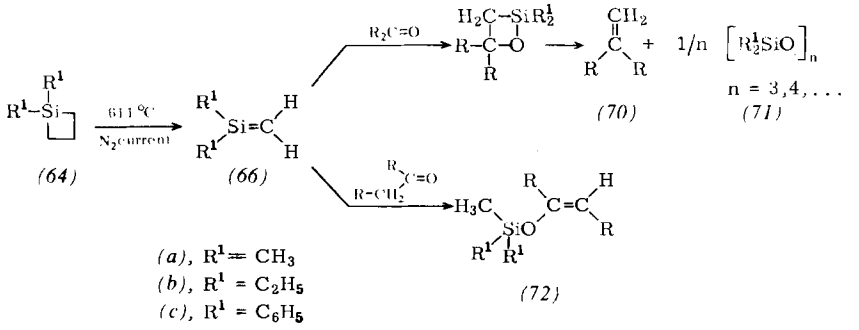


(64a) *(66a)* *(67)* *(68)* *(69)*

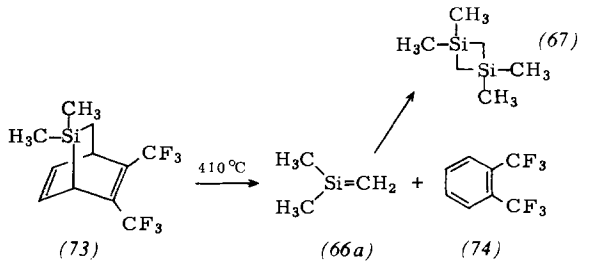
In similar manner, *Sommer et al.*[66a, b] prepared the silaalkenes *(66b)* and *(66c)*, and investigated their reactivity towards various trapping reagents. They undergo a kind of "Wittig reaction" with non-enolizable ketones to give olefins *(70)* and cyclic siloxanes *(71)*, while siloxyalkenes *(72)* are formed with enolizable ketones.

Trapping reactions with halosilanes provide arguments in favor of strongly polar Si=C double bonds[66c].

Another method of preparing silaalkenes has been developed by *Barton et al.*[67-69]. Thermal decomposition of 2,3-bis(trifluoromethyl)-7,7-dimethyl-7-silabicyclo[2.2.2]octa-2,5-diene *(73)* furnishes *o*-bis(trifluoromethyl)benzene *(74)* and 2-methyl-2-silapropene *(66a)*, which can be isolated in a matrix and characterized by its IR spectrum. The very intense band at 1407 cm^{-1} is assigned to the C=Si stretching vibration. This band disappears on heating, when *(66a)* dimerizes to disilacyclobutane *(67)*.

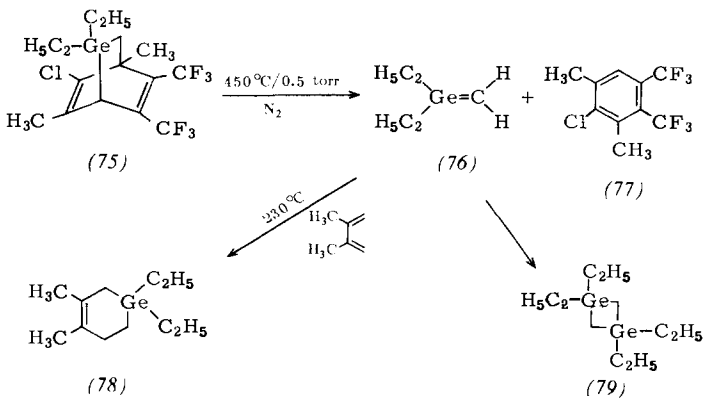


(a), $R^1 = CH_3$
(b), $R^1 = C_2H_5$
(c), $R^1 = C_6H_5$



Further evidence for the occurrence of short-lived silaalkenes was obtained from kinetic studies on the pyrolysis of tetramethylsilane[70]. The pyrolysis products of trimethylsilane can also be easily explained in terms of silaalkene intermediates[71, 72].

Analogous experiments were performed with the aim of forming germanium-carbon (4p-2p)π bonds. While pyrolysis reactions of germacyclobutane derivatives have not yet afforded unambiguous proof for the existence of a germaalkene[73], the decomposition products of 2,3-bis(trifluoromethyl-4,6-dimethyl-5-chloro-7,7-diethyl-7-germabicyclo[2.2.2]octa-2,5-diene *(75)* at 450°C/0.5 torr indicated formation of a short-lived 2-ethyl-2-germabutene *(76)*[74]. It can either be trapped with 2,3-dimethylbutadiene to give *(78)* or be detected as the dimerization product *(79)*.

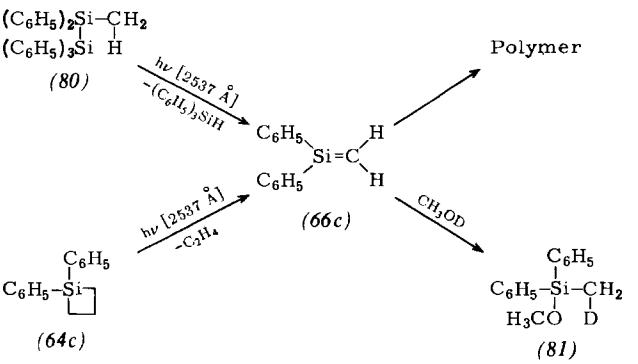


The above thermolytic studies show that sila- and germaalkenes can indeed exist in the gaseous phase at suitable dilutions but decompose very fast in the condensed state and in the usual solvents owing to their kinetic lability. Detection of these compounds by gas phase kinetic studies has been particularly successful.

3.2.2. Photochemical Reactions

Synthesis of extremely short-lived silaalkenes can be accomplished not only by thermal but also by photochemically induced homolysis. Thus irradiation ($\lambda = 2537$ nm) of pure 1,1-dimethyl-1-silacyclobutane *(64a)* at 28 and 77 K yields 2-methyl-2-silapropene *(66a)* which can be characterized by its uniform dimerization to 1,3-disilacyclobutane *(67)*. In cyclohexane solution the same reaction becomes very complicated and *(67)* is formed in only very small yield[67].

Nevertheless, *Sommer et al.* were also able to detect a transient silaalkene in photochemical reactions conducted in solution. Photolysis of both pentaphenylmethyldisilane *(80)*[75] and 1,1-diphenyl-1-silacyclobutane *(64c)*[76] yields 1,1-diphenyl-1-silaethylene *(66c)* which can be trapped as *(81)* with deuteriomethanol.



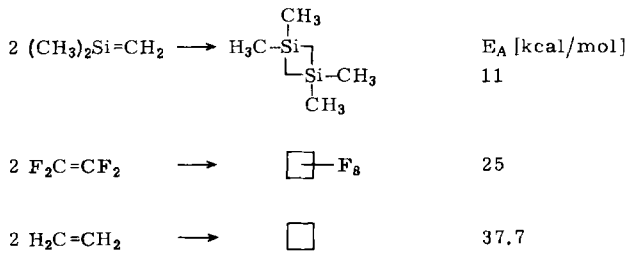
Although the dark reaction of *(64c)* with CH_3OD also entails ring cleavage it leads to different products. It is still unclear whether intermediates having paired electron spins or diradical species are formed in these photochemical experiments.

Intermediates having a Si=C bond have recently also been detected in photochemical and thermal isomerizations. Thus 1-sila-1,3,5-hexatrienes[109] appear transiently during photoisomerization of 1-sila-2,4-cyclohexadiene derivatives; thermally induced *cis-trans* isomerization of propenylallyldimethylsilane proceeds after the manner of a reversible Cope rearrangement *via* a 1,1,3-trimethyl-1-sila-1,5-hexadiene[110].

3.3. Bond Energies and Calculations of Molecules

The π-bond energy in silaalkenes has been crudely estimated from thermodynamic and kinetic data gained for the pyrolysis of 1,1-dimethyl-1-silacyclobutane and of trimethylsilane[77]. It lies between 29 and 45 kcal/mol for 2-methyl-2-silapropene and between 29 and 37 kcal/mol for 2-silapropene. The difference between the dissociation energies of the Si—C bonds in silicon carbide and tetramethylsilane gave a value of about 28 kcal/mol for the π-bond energy in silaethylene[78]. Hence a Si=C π bond is roughly half as strong as a C=C π bond.

EHMO and CNDO calculations[79] on the silaethylene bond system show that interaction between 2pπ(C) and 3pπ(Si) electrons is not particularly effective. This is due less to inadequate orbital overlapping than to the considerable energy difference between the participating C 2p and Si 3p orbitals, which is manifested in a very high polarity, especially in the readily polarizable π system: $H_2C{=}SiH_2 \leftrightarrow H_2\overset{\ominus}{C}{-}\overset{\oplus}{S}iH_2$. The dipole moment of 2.9 D obtained by CNDO calculations[79] for silaethylene is correspondingly high. Of course, the polarity of the C=Si bond facilitates cyclodimerization reactions, as is clearly seen from the low activation energies relative to C=C bond systems[64, 79].



Thus it becomes understandable that silaalkenes can only exist in the gas phase and at low pressures, and can most readily be detected under these conditions which are not nearly so conducive to dimerization as they are in the liquid phase. According to recent CNDO/2 calculations, however, suitable substitution should lead to Si=C bonds that are stable even under normal conditions[79].

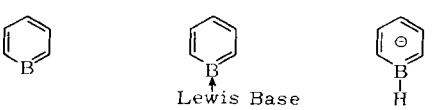
4. B=C Bonds

4.1. Preparation of Boraarenes

The pertinent literature contains several hints that the element boron is fundamentally capable of forming (p-p)π bonds[80]. Thus investigations in boron-nitrogen chemistry show that replacement of a C=C unit in benzene by the isoelectronic $\overset{\ominus}{B}{=}\overset{\oplus}{N}$ grouping leads to systems displaying aromatic properties. Stable bonds to the boron atom can also be deduced from overlap integrals[81, 82]. It is therefore astonishing that no aromatic compound having boron as sole hetero atom was known until very recently. In such compounds a (—CH=) unit in a Hückel π system is replaced by the isoelectronic $(-\overset{\ominus}{B}H{=})$ unit[83].

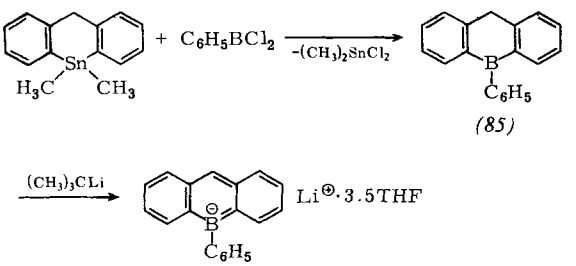
Even if it can exist at all, borabenzene will certainly be extremely unstable owing to its Lewis acidity and its inherent ring strain arising from the hybridization of the boron atom. However, it should be stabilized in compounds of type *(83)* by adduct formation with Lewis bases and attendant rehybridization to sp^2. Anions of type *(84)* isoelectronic with benzene are likewise conceivable.

During the past few years derivatives of *(83)* and *(84)* have been synthesized for the first time and studied with regard to their aromatic properties.

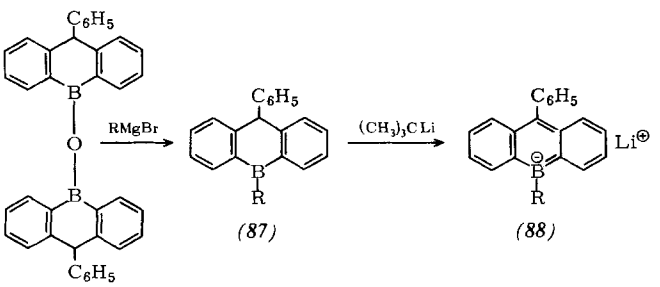


(82) *(83)* *(84)*

For example, metalation of 9-phenyl-9,10-dihydro-9-boraanthracene *(85)* in THF/pentane at −78 °C afforded the 9-phenyl-9-boraanthracene anion, which could be isolated as the solvent-separated ion pair *(86)*[84].



The same kind of reaction gives solvent-free 9-mesityl-10-phenyl-9-boraanthracene anion *(88)*[85] from 9-mesityl-10-phenyl-9,10-dihydro-9-boraanthracene *(87)*, and spectroscopic evidence has also been obtained for the 9-mesityl-9-boraanthracene anion[86].



R = Mesityl

The structure of the boraarene *(86)* is confirmed by its ^{1}H-NMR, ^{11}B-NMR, and UV spectra, and that of *(88)* by its UV spectrum and analytical and spectroscopic data of its deuterolysis product. Thus the proton resonance signals of *(86)* are compatible with a ring current and/or reduced negative charge on C^{10}; in the ^{11}B spectrum the π bond to boron and the consequently enhanced electron density on the boron atom shift the resonance signal upfield. The ultraviolet-visible spectra of *(86)* and *(88)* are especially characteristic of aromatic systems, and closely resemble those of 9-phospha- and 9-arsaanthracene [*(26a)* and *(30a)*] in structure. The longest wave absorption bands are almost identical, thus indicating comparable π-electron systems (Fig. 6).

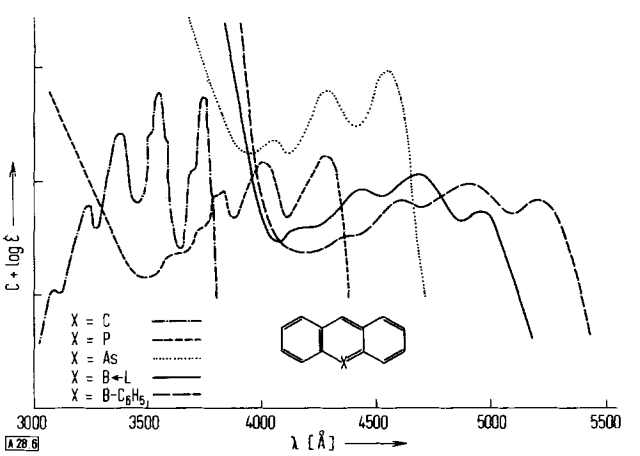
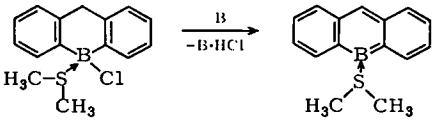


Fig. 6. Ultraviolet-visible spectra of anthracene, *(26a)*, *(30a)*, *(90)*, and *(86)*; measured in THF.

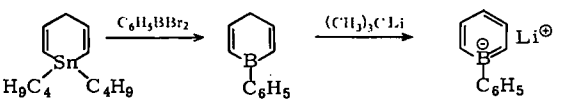
The bathochromic shift of the long-wave absorption maxima occurring on going from *(26a)* to *(30a)*, *(86)*, and *(88)* is attributable to the parallel drop in electronegativity of the hetero atoms in position 9 and the associated decrease in π-π^* excitation energy.

A donor-acceptor complex of type *(83)* has been detected by spectroscopy, but not yet isolated. For instance, reaction of the adduct *(89)* of 9-chloro-9,10-dihydro-9-boraanthracene and dimethylsulfane with auxiliary bases produces a low yield of the extremely unstable dimethylsulfane adduct of 9-boraanthracene *(90)*. Its ultraviolet-visible spectrum is expectedly almost identical with that of *(86)* (Fig. 6).



(89) *(90)*

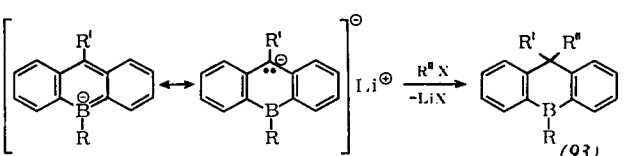
Ashe et al. have detected a non-fused derivative of the borabenzene anion *(84)* from NMR data[88]. 1-Phenyl-1-bora-2,5-cyclohexadiene *(91)* reacts with *tert*-butyllithium to form 1-phenyl-1-borabenzene anion *(92)*.



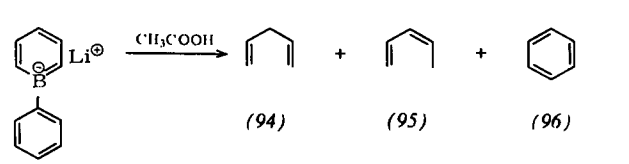
(17) *(91)* *(92)*

The resonance signals of *(92)* in the ^{1}H-NMR spectrum indicate a ring current and/or reduced negative charge on C^4, while a characteristic upfield shift is observed for *(92)* in the ^{11}B-NMR spectrum.

All boraarenes reported so far are extremely sensitive to atmospheric oxygen and moisture. The anionic aromatic compounds *(86)*, *(88)*, and *(92)* react as a resonance structure having a carbanionic center at C-10, C-2, or C-4 and a tervalent Lewis-acid boron atom: hence electrophilic and nucleophilic reactions are possible. Accordingly, reaction of *(86)* and *(88)* with electrophiles leads to 10-substituted 9,10-dihydro-9-boraanthracene *(93)* whereas reaction of *(92)* with an excess of glacial acetic acid involves degradation of the heterocyclic system; the pentadienes *(94)* and *(95)* and benzene *(96)* could all be detected.



(86), *(88)* *(93)*

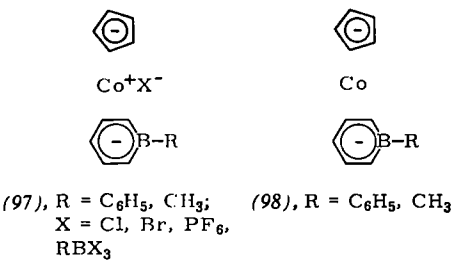


(92) *(94)* *(95)* *(96)*

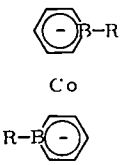
Only one case is known of a reaction retaining the aromatic system: *(92)* reacts with $FeCl_2$ to give the bis(borinato)iron complex[105].

4.2. π Complexes with Borabenzene Anions

Herberich et al. successfully stabilized derivatives of borabenzene anion by ring expansion reactions of complexed cyclopentadienyl anion. Reaction of bis(cyclopentadienyl)cobalt with boron halides is accompanied by complicated redox reactions; the diamagnetic salts of type *(97)* and paramagnetic neutral complexes *(98)* and *(99)* could be isolated as products[89-91].



(97), R = C_6H_5, CH_3; X = Cl, Br, PF_6, RBX_3 *(98)*, R = C_6H_5, CH_3



(99), R = C_6H_5, CH_3, Br, OH, OCH_3

The suspected bonding of the borabenzene anions (borinate ions) as η^6 ligands to the metal in *(97)*, *(98)*, and *(99)*, supported by ^{1}H- and ^{11}B-NMR data, has been confirmed by crystal structure studies on bis(1-methoxyborinato)cobalt *(99)* (R = OCH_3) and on bis(1-methylborinato)cobalt *(99)* (R = CH_3)[92].

These compounds possess a typical centrosymmetric sandwich structure with almost planar borinate ligands. The bonding closely resembles that in π-cyclopentadienyl- and π-benzene complexes. In both complexes, the B—C bond lengths are 1.52 Å and suggest a low double bond participation. The Co—B bonds are the longest metal-ring distances, leading to unsymmetrical bonding of the borinate ligands to the metal. Responsibility for this effect is attributed to the electron in excess of the noble gas configuration at the cobalt atom.

The ionization energies found for compounds of type *(98)* and *(99)* by mass spectrometry are remarkably low (6.5 to 7.1 eV)[91]. Comparison with the ionization energy of bis(cyclopentadienyl)cobalt (6.2 eV)[93] shows that the C_5H_5BR radical acts as a better electron acceptor in its bond to the metal than the C_5H_5 radical.

Borabenzene anions linked to cobalt by a π bond can be transferred to other transition metals[94, 95]. Thus reaction of *(99)* (R = C_6H_5) with $Mn_2(CO)_{10}$ yields 1-phenylborinato-tricarbonylmanganese, while *(99)* (R = C_6H_5, CH_3) and $Fe_2(CO)_9$ afford violet bis(borinato)tetracarbonyldiiron derivatives which can be thermolyzed to orange bis(borinato)iron complexes. These are the first diamagnetic neutral complexes to contain an η^6-borabenzene anion.

5. Conclusion

With the exception of B=C bonds, the novel element-carbon (p-p)π bonds should be incapable of existence according

to the classical double bond rule. This rule, which has been a topic of frequent discussion[96–99], is based in part on the fact that σ bonds between elements of the second long row are relatively long and the increasingly diffuse nature of p orbitals with increasing principal quantum number makes for poor overlap to form π bonds. This has received support from theoretical studies by *Pitzer*[1] and *Mulliken*[2].

However, these cannot be the sole criteria in the case of El=C (p-p)π bonds: π systems based on relatively long σ bonds and involving highly diffuse p orbitals (Table 4) certainly exist. Stable compounds containing S=C (3p-2p)π and Te=C (5p-2p)π bonds have long been known[96, 102], and compounds with Sb=C (5p-2p)π and even Bi=C (6p-2p)π bonds have been mentioned in this progress report.

Table 4. El—C σ bond lengths [Å] (cf. ref. [101]).

1.58	1.54	1.51	1.51
B—C	C—C	N—C	O—C
	1.94	1.87	1.81
	Si—C	P—C	S—C
	1.99	1.98	1.94
	Ge—C	As—C	Se—C
		2.18	2.14
		Sb—C	Te—C

Table 5. Electronegativities according to Pauling [101].

B	C	N	O
2.0	2.5	3.0	3.5
	Si	P	S
	1.8	2.1	2.5
	Ge	As	Se
	1.8	2.0	2.4
		Sb	Te
		1.9	2.1
		Bi	
		1.9	

The stability of these bonds might be explicable by participation of pd hybrids *(b)* as well as pure p orbitals *(a)* in π bonding between carbon and elements of the second long row and higher[79]. This would lead to significant improvement in overlap in spite of unfavorable bond lengths.

(a) *(b)*

Questions concerning the existence of El=C (p-p)π bonds must also take account of bond polarities which can be very great in some cases. They arise from electronegativity differences between the participating elements (Table 5) and lead to unequal electron distributions especially in the readily polarizable π system[79]. Thus varying contributions of the resonance hybrid *(B)* to the ground state of the π-bonded molecules must be expected, depending upon the element concerned.

(A) *(B)*

The elements sulfur, selenium, and carbon exhibit only slight electronegativity differences; corresponding El=C systems therefore exist predominantly as resonance structure *(A)* and some of them are remarkably stable[102]. The greatest electronegativity difference is found between carbon and the elements silicon and germanium; compounds with Si=C and Ge=C bonds contain a considerable proportion of the resonance hybrid *(B)* and therefore display a pronounced kinetic lability. The reactivity of these systems is presumably further affected by the d-orbital contraction resulting from the positive charge on the Si and Ge atom and the associated enhancement of electrophilic character[100]. Similar considerations also apply to B=C systems. Here the pronounced Lewis acid character of the boron atom precludes the formation of π bonds with sp hybridized boron and hence an unoccupied p orbital on the boron atom.

Experience gained so far with El=C bonds can also be applied to other π systems. New element-element (p-p)π bonds should then become available if it proves possible to prepare resonance-stabilized π-systems, to reduce the polarity in the π systems by appropriate substitution, and to avoid oligomerization reactions by steric effects.

I am indebted to J. Baumgärtner, H. Fetz, H. J. Hoffmann, and W. Sakriss for obtaining many of the above results. Thanks are also due to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

Received: December 20, 1973;
revised: February 21, 1975 [A 28 IE]
German version: Angew. Chem. *87*, 269 (1975)

[1] *K. S. Pitzer*, J. Amer. Chem. Soc. *70*, 2140 (1948).
[2] *R. S. Mulliken*, J. Amer. Chem. Soc. *72*, 4493 (1950); *77*, 884 (1955).
[3] *T. E. Gier*, J. Amer. Chem. Soc. *83*, 1769 (1961).
[4] *K. Dimroth* and *P. Hoffmann*, Angew. Chem. *76*, 433 (1964); Angew. Chem. internat. Edit. *3*, 384 (1964); Chem. Ber. *99*, 1325 (1966).
[5] *G. Märkl* and *F. Lieb*, Tetrahedron Lett. *1967*, 3489.
[6] *R. Allmann*, Angew. Chem. *77*, 134 (1965); Angew. Chem. internat. Edit. *4*, 150 (1965).
[7] *R. Allmann* and *I. Kawada*, Angew. Chem. *80*, 40 (1968); Angew. Chem. internat. Edit. *7*, 69 (1968).
[8] *H. Kuhn*, Helv. Chim. Acta *31*, 1441 (1948); *34*, 1308, 2371 (1951).
[9] *K. Dimroth*, Fortschr. Chem. Forsch. *38*.1 (1973).
[10] *J. M. Keck* and *G. Klar*, Z. Naturforsch. *27b*, 596 (1972).
[11] *G. Märkl*, Angew. Chem. *78*, 907 (1966); Angew. Chem. internat. Edit. *5*, 846 (1966).
[12] *G. Märkl*, *F. Lieb*, and *A. Merz*, Angew. Chem. *79*, 475 (1967); Angew. Chem. internat. Edit. *6*, 458 (1967).
[13] *G. Märkl*, *F. Lieb*, and *A. Merz*, Angew. Chem. *79*, 947 (1967); Angew. Chem. internat. Edit. *6*, 944 (1967).
[14] *G. Märkl* and *D. E. Fischer*, Tetrahedron Lett. *1972*, 4925.
[15] *G. Märkl* and *A. Merz*, Tetrahedron Lett. *1971*, 1215.
[16] *G. Märkl*, Lect. Heterocycl. *1*, 69 (1972).
[17] *A. J. Ashe III*, J. Amer. Chem. Soc. *93*, 3293 (1971).
[18] *R. L. Kuczkowski* and *A. J. Ashe III*, J. Mol. Spectrosc. *42*, 457 (1972).
[19] a) *G. Märkl* and *F. Kneidl*, Angew. Chem. *85*, 990 (1973); Angew. Chem. internat. Edit. *12*, 931 (1973); b) *G. Märkl* and *K. H. Heier*, *ibid. 84*, 1067 (1972); and *11*, 1017 (1972), resp.
[20] *G. Märkl* and *K. H. Heier*, Angew. Chem. *84*, 1066 (1972); Angew. Chem. internat. Edit. *11*, 1016 (1972).
[21] *P. deKoe* and *F. Bickelhaupt*, Angew. Chem. *79*, 533 (1967); Angew. Chem. internat. Edit. *6*, 567 (1967).
[22] *H. Vermeer* and *F. Bickelhaupt*, Angew. Chem. *80*, 912 (1968); Angew. Chem. internat. Edit. *7*, 889 (1968).
[23] *G. Märkl* and *D. Matthes*, Angew. Chem. *84*, 1069 (1972); Angew. Chem. internat. Edit. *10*, 1019 (1972).
[24] *J. C. J. Bart* and *J. J. Daly*, Angew. Chem. *80*, 843 (1968); Angew. Chem. internat. Edit. *7*, 811 (1968).
[25] *W. Fischer*, *E. Hellner*, *A. Chatzidakis*, and *K. Dimroth*, Tetrahedron Lett. *1968*, 6227.
[26] *P. Jutzi* and *K. Deuchert*, Angew. Chem. *81*, 1051 (1969); Angew. Chem. internat. Edit. *8*, 991 (1969).
[27] *H. Vermeer* and *F. Bickelhaupt*, Angew. Chem. *81*, 1052 (1969); Angew. Chem. internat. Edit. *8*, 992 (1969).

[28] a) *H. Vermeer* and *F. Bickelhaupt*, Tetrahedron Lett. *1970*, 3255; b) *R. J. M. Weustink*, *C. Jongsma*, and *F. Bickelhaupt*, *ibid. 1975*, 199.
[29] *G. Märkl*, *H. Hauptmann*, and *I. Advena*, Angew. Chem. *84*, 440 (1972); Angew. Chem. internat. Edit. *10*, 441 (1972).
[30] a) *I. Advena*, Dissertation, Universität Würzburg 1973; b) *G. Märkl*, *I. Advena*, and *H. Hauptmann*, Tetrahedron Lett. *1974*, 303; c) *G. Märkl* and *F. Kneidl*, Angew. Chem. *85*, 990 (1973); *86*, 745 (1974); Angew. Chem. internat. Edit. *12*, 931 (1973); *13*, 667 (1974); d) *P. Jutzi* and *J. Baumgärtner*, to be published; e) *G. Märkl* and *F. Kneidl*, Angew. Chem. *86*, 746 (1974); Angew. Chem. internat. Edit. *13*, 668 (1974).
[31] *F. Sang* and *J. J. Daly*, Angew. Chem. *84*, 679 (1972); Angew. Chem. internat. Edit. *10*, 630 (1972).
[32] *A. J. Ashe III*, J. Amer. Chem. Soc. *93*, 6690 (1971).
[33] *P. Jutzi*, unpublished.
[34] *A. J. Ashe III* and *M. D. Gordon*, J. Amer. Chem. Soc. *94*, 7596 (1972).
[35] *R. G. Pearson*, Surv. Progr. Chem. *5*, 1 (1969).
[36] *H. Oehling* and *A. Schweig*, Tetrahedron Lett. *1970*, 4941.
[37] *M. Fraser*, *D. G. Olah*, *A. N. Hughes*, and *B. C. Hui*, J. Heterocycl. Chem. *9*, 1457 (1972).
[38] *J. Deberitz* and *H. Nöth*, J. Organometal. Chem. *49*, 453 (1973).
[39] *K. C. Dash*, *J. Eberlein*, and *H. Schmidbaur*, Synth. Inorg. Metal. Org. Chem. *3*, 375 (1973).
[40] *H. Vahrenkamp* and *H. Nöth*, Chem. Ber. *106*, 2227 (1973).
[41] *G. Märkl*, *F. Lieb*, and *A. Merz*, Angew. Chem. *79*, 59 (1967); Angew. Chem. internat. Edit. *6*, 87 (1967).
[42] *G. Märkl* and *F. Lieb*, Angew. Chem. *80*, 702 (1968); Angew. Chem. internat. Edit. *7*, 733 (1968).
[43] *G. Märkl*, *F. Lieb*, and *C. Martin*, Tetrahedron Lett. *1971*, 1249.
[44] *A. J. Ashe III* and *M. D. Gordon*, J. Amer. Chem. Soc. *94*, 7596 (1972).
[45] *J. Deberitz* and *H. Nöth*, Chem. Ber. *103*, 2541 (1970); *106*, 2223 (1973).
[46] *H. Vahrenkamp* and *H. Nöth*, Chem. Ber. *105*, 1148 (1972).
[47] *G. Märkl*, *I. Advena*, and *H. Hauptmann*, Tetrahedron Lett. *1972*, 3961.
[48] *C. Batich*, *E. Heilbronner*, *V. Hornung*, *A. J. Ashe III*, *D. T. Clark*, *U. T. Cobley*, *D. Kilcast*, and *J. Scanlan*, J. Amer. Chem. Soc. *95*, 928 (1973).
[49] *H. Oehling*, *W. Schäfer*, and *A. Schweig*, Angew. Chem. *83*, 723 (1971); Angew. Chem. internat. Edit. *10*, 656 (1971).
[50] *W. Schäfer*, *A. Schweig*, *F. Bickelhaupt*, and *H. Vermeer*, Angew. Chem. *84*, 993 (1972); Angew. Chem. internat. Edit. *11*, 924 (1972).
[51] *A. W. Potts* and *W. Price*, Proc. Roy. Soc. London *A326*, 181 (1972).
[52] *P. Jutzi*, J. Organometal. Chem. *16*, P71 (1969).
[53] *G. L. van Mourik* and *F. Bickelhaupt*, Rec. Trav. Chim. Pays-Bas *88*, 868 (1969).
[54] *P. Jutzi*, Chem. Ber. *104*, 1455 (1971).
[55] *P. Jutzi* and *H. Fetz*, Chem. Ber. *106*, 3445 (1973).
[56] *V. Hagen* and *H. Rühlmann*, Z. Chem. *9*, 350 (1970).
[57] *P. Jutzi*, Habilitationsschrift, Universität Würzburg 1971.
[58] *P. Jutzi* and *J. Baumgärtner*, unpublished.
[59] *U. Wannagat* and *F. Brandmeier*, Z. Anorg. Allg. Chem. *280*, 223 (1955).
[60] *P. Jutzi* and *W. Sakriss*, Chem. Ber. *106*, 2815 (1973).
[61] *C. J. Attridge*, Organometal. Chem. Rev. *A5*, 323 (1970); *O. M. Nefedov* and *M. N. Manakov*, Angew. Chem. *78*, 1039 (1966); Angew. Chem. internat. Edit. *5*, 1021 (1966); *A. W. P. Jarvie* and *R. J. Rowley*, J. Organometal. Chem. *36*, C7 (1972); *M. Kumada*, *K. Tamao*, *M. Ishikava*, and *M. Matsumo*, Chem. Commun. *1968*, 614.
[62] *L. E. Gusel'nikov* and *M. C. Flowers*, Chem. Commun. *1967*, 64.
[63] *L. E. Gusel'nikov* and *M. C. Flowers*, Chem. Commun. *1967*, 864.
[64] *L. E. Gusel'nikov* and *M. C. Flowers*, J. Chem. Soc. *B1968*, 419.
[65] *J. N. Butler*, J. Amer. Chem. Soc. *84*, 1393 (1962).
[66] a) *D. N. Roark* and *L. H. Sommer*, J. C. S. Chem. Comm. *1973*, 167; b) *C. M. Golino*, *R. D. Bush*, *D. N. Roark*, and *L. H. Sommer*, J. Organometal. Chem. *66*, 29 (1974); c) *R. D. Bush*, *C. M. Golino*, and *L. H. Sommer*, J. Amer. Chem. Soc. *96*, 7105 (1974).
[67] *T. J. Barton* and *E. Kline*, J. Organometal. Chem. *42*, C21 (1972).
[68] *T. J. Barton* and *C. L. McIntosh*, J. C. S. Chem. Comm. *1972*, 861.
[69] *T. J. Barton* and *C. L. McIntosh*, J. C. S. Chem. Comm. *1972*, 861.
[70] *R. P. Clifford*, *B. G. Gowenlok*, *C. A. F. Johnson*, and *J. Stevenson*, J. Organometal. Chem. *34*, 53 (1972).
[71] *J. M. T. Davidson* and *C. A. Lambert*, J. Chem. Soc. *D1969*, 1276.
[72] *J. M. T. Davidson* and *C. A. Lambert*, J. Chem. Soc. *A1971*, 882.
[73] *N. S. Nametkin*, Dokl. Akad. Nauk SSSR *194*, 1096 (1970).
[74] *T. J. Barton*, *E. A. Kline*, and *P. M. Garvey*, J. Amer. Chem. Soc. *95*, 3078 (1973).
[75] *P. Boudjouk*, *J. R. Roberts*, *C. M. Golino*, and *L. H. Sommer*, J. Amer. Chem. Soc. *94*, 7926 (1972).
[76] *P. Boudjouk* and *L. H. Sommer*, J. C. S. Chem. Comm. *1973*, 54.
[77] *R. Walsh*, J. Organometal. Chem. *38*, 245 (1972).
[78] *R. A. Jackson*, Chem. Soc. Spec. Publ. No. *24*, 299 (1970).
[79] *M. D. Curtis*, J. Organometal. Chem. *60*, 63 (1973); 3rd Int. Organosilicon Symp., Madison, Wisconsin, 1972.
[80] *E. L. Muetterties:* The Chemistry of Boron and its Compounds. Wiley, New York 1967, pp. 482—495.
[81] *R. S. Mulliken*, Chem. Rev. *41*, 207 (1947).
[82] *D. A. Brown* and *C. G. McCormack*, J. Chem. Soc. *1964*, 5385.
[83] Comparisons between the π system in 9-borafluorene [83a], which is stabilized *via* the p_z orbital on the boron atom, and borepin [83b, c]: a) *R. Köster* and *G. Benedikt*, Angew. Chem. *75*, 419 (1963); Angew. Chem. internat. Edit. *2*, 323 (1963); b) *A. J. Leusink*, *W. Drenth*, *J. G. Noltes*, and *G. J. M. van der Kerk*, Tetrahedron Lett. *1967*, 1263; c) *E. E. van Tamelen*, *G. Brieger*, and *H. G. Untsch*, *ibid. 1960*, 14.
[84] *P. Jutzi*, Angew. Chem. *84*, 28 (1972); Angew. Chem. internat. Edit. *11*, 53 (1972).
[85] *R. van Veen* and *F. Bickelhaupt*, J. Organometal. Chem. *43*, 241 (1972).
[86] a) *R. van Veen* and *F. Bickelhaupt*, J. Organometal. Chem. *30*, C51 (1971); b) J. Organometal. Chem. *77*, 153 (1974).
[87] *P. Jutzi*, Int. Symp. Chem. Nonbenzenoid Aromatic Compounds, Sendai (Japan) 1970; Abstr. p. 147.
[88] *A. J. Ashe III* and *P. Shu*, J. Amer. Chem. Soc. *93*, 1804 (1971).
[89] *G. E. Herberich*, *G. Greiss*, and *H. F. Heil*, Angew. Chem. *82*, 838 (1970); Angew. Chem. internat. Edit. *9*, 805 (1970).
[90] *G. E. Herberich*, *G. Greiss*, *H. F. Heil*, and *J. Müller*, Chem. Commun. *1971*, 132.
[91] *G. E. Herberich* and *G. Greiss*, Chem. Ber. *105*, 3413 (1972).
[92] *G. Huttner*, *B. Krieg*, and *W. Gartzke*, Chem. Ber. *105*, 3424 (1972).
[93] *J. Müller* and *L. D'or*, J. Organometal. Chem. *10*, 313 (1967).
[94] *G. E. Herberich*, Chimia *26*, 475 (1972).
[95] a) *G. E. Herberich* and *H. J. Becker*, Angew. Chem. *85*, 817 (1973); Angew. Chem. internat. Edit. *12*, 764 (1973); b) *G. E. Herberich*, *H. J. Becker*, and *G. Greiss*, Chem. Ber. *107*, 3780 (1974); c) *G. Huttner* and *W. Gartzke*, Chem. Ber. *107*, 3786 (1974).
[96] *W. E. Dasent:* Non-existent Compounds. Dekker, New York 1965, Chap. 4.
[97] *B. J. Aylett*, Advan. Inorg. Chem. Radiochem. *11*, 249 (1968).
[98] *J. E. Huheey:* Inorganic Chemistry. Harper-Row, New York 1972, p. 617.
[99] *L. D. Pettit*, Quart. Rev. Chem. Soc. *25*, 1 (1971).
[100] *J. R. Beattie* and *T. Gilson*, Nature *193*, 1041 (1962).
[101] *L. Pauling:* Die Natur der chemischen Bindung. Verlag Chemie, Weinheim 1968.
[102] Comprehensive Inorganic Chemistry, Vol. 2. Pergamon-Press, London 1973, pp. 795, 935.
[103] *M. D. Curtis*, J. Amer. Chem. Soc. *91*, 6011 (1969).
[104] *W. G. Schneider*, *H. J. Bernstein*, and *J. A. Pople*, Can. J. Chem. *35*, 1487 (1957).
[105] *A. J. Ashe III*, personal communication.
[106] *N. P. Ignatova*, *N. N. Mel'nikov*, and *N. J. Shvetsov-Shilovskii*, Geterotsikl. Soedin. *4*, 753 (1967).
[107] *A. F. Vasilev*, *L. V. Vilkov*, *N. P. Ignatova*, *N. N. Mel'nikov*, *V. V. Negrebetskii*, *N. J. Shvetsov-Shilovskii*, and *L. S. Khaikin*, Dokl. Akad. Nauk SSSR *183*, 95 (1968).
[108] *G. Becker* and *H. P. Beck*, 2nd Symp. Inorg. Phosphorus Comp., Prague 1974, Abstr. p. 112.
[109] *Y. Nakadarira*, *S. Kanouchi*, and *H. Sakurai*, J. Amer. Chem. Soc. *96*, 5621 (1974).
[110] *I. Slutsky* and *H. Kwart*, J. Org. Chem. *38*, 3658 (1973).

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

Dialkylstannanediyls (Dialkylstannylenes)

By *Ulrich Schröer* and *Wilhelm P. Neumann*[*]

The tin analogs of the carbenes, the stannanediyls (stannylenes) R_2Sn, have long been sought after—ever since the beginning of organotin chemistry. We first came across this problem during our investigations on poly- and cyclostannanes when we observed that the growing poly-tin chain is always lengthened by only one chain link at a time[1], and that the substituted distannanes *(1)* readily undergo decomposition[2]. We have now found, for example, that tetrabutyl-1,2-dichlorostannane *(1a)* disproportionates quantitatively into Bu_2SnCl_2 and a (inhomogeneous) red Bu_2Sn polymer on heating in a sealed glass tube at 120—130 °C for 7 hours.

$$n\ XR_2Sn\text{–}SnR_2X \xrightarrow{\Delta} n\ R_2SnX_2 + (R_2Sn)_n$$

(1a), R = n-C_4H_9, X = Cl
(1b), R = n-C_4H_9, X = H

The assumption that the stannanediyl Bu_2Sn is present as intermediate during this heating—either in the free state or in a transition state complex[3]—finds support in the fact that addition of methyl iodide leads to almost quantitative trapping with insertion into the C—I bond.

$$(1a) \xrightarrow[-\,Bu_2SnCl_2]{\Delta} Bu_2Sn \xrightarrow{MeI} Bu_2Sn\begin{matrix}Me\\ \diagup\\ \diagdown\\ I\end{matrix}$$

A following reaction involving decomposition of initially formed polystannanes can be ruled out—as control experiments have shown[4]: $Bu_2Sn(Cl)Me$ and $Bu_2Sn(Cl)I$ are absent.

Radical chain reactions can also be ruled out, since trapping agents such as hydroquinone remain ineffective. Furthermore, the reaction proceeds no more rapidly than the spontaneous decomposition of *(1a)*. This is accelerated by UV light (high pressure mercury vapor lamp), and is then rapid even at room temperature.

The yield of insertion product (thermal reaction) with alkyl iodides R'I decreases in the series R' = CH_3 (85%), C_2H_5 (70%), n-C_3H_7 (50%), n-C_4H_9 (40%), n-C_5H_{11} (30%); once again, polystannane is formed at the same time. The decrease in yield along this series is doubtless due to the decreasing concentration of c_{C-I} and can also be achieved by dilution with an inert solvent. From this, and the independence of the rate of disproportionation on the presence of a trapping agent, we conclude the intermediary occurrence of free, short-lived dibutylstannanediyl.

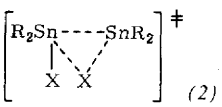
Alkyl iodides afford higher yields of insertion products than bromides, which, under the same conditions afford higher yields than the chlorides (for R' = n-C_3H_7: 50, 30, 20%). In the case of iodides the yields decrease in the series *n*-butyl > *iso*-butyl > *sec*-butyl (40, 35, 25%). Both the ease of bond cleavage and concentration of trapping reagent as well as steric effects thus influence capture of the short-lived stannanediyl.

Other alkyl halides, as well as Sn—Sn groups, are also suitable as R_2Sn trapping reagents (molar ratio 6:1, 120 to 130 °C):

$$\left.\begin{matrix}C_6H_5\text{–}CH_2Cl\\ H_2C{=}C{=}CHI\\ HC{\equiv}C\text{–}CH_2I\\ HC{\equiv}C\text{–}CH_2Br\\ H_2C{=}CH\text{–}CH_2Br\\ Me_3Sn\text{–}SnMe_3\end{matrix}\right\} + (1a) \xrightarrow[-\,Bu_2SnCl_2]{\Delta} \left\{\begin{matrix}C_6H_5\text{–}CH_2\text{–}Sn(Cl)Bu_2 & (15\%)\\ H_2C{=}C{=}CH\text{–}Sn(I)Bu_2 & (25\%)\\ H_2C{=}C{=}CH\text{–}Sn(Br)Bu_2 & (20\%)\\ H_2C{=}CH\text{–}CH_2\text{–}Sn(Br)Bu_2 & (15\%)\\ Me_3Sn\text{–}Bu_2Sn\text{–}SnMe_3\,[5] & (20\%)\end{matrix}\right.$$

Tolan, 1,4-diphenyl-, 2,3-dimethyl- and 1,2,3,4-tetraphenylbutadiene, however, do not react with the stannanediyl; only polystannane is formed. On using organotin hydrides as trapping reagents we obtained complex mixtures, as can be expected as a result of H—X exchange[2].

Other substituents X in *(1)*, as well as Cl and H, have proved useful as leaving groups. Thus, the thermal reaction with CH_3I is complete after 7—8 h at 120—130 °C for X = Cl, at 90—100 °C for X = Br, at 75—85 °C for X = I[6], and at 80—90 °C for X = $OCOCH_3$. For commencement of reaction (at *ca.* 60 °C) a loosening of X is essential; the simplest transition state would be *(2)*.



(2)

This reaction is probably more complicated, since *(1a)* is present as dimer even at 0.05—0.1 M in benzene (vapor pressure-osmometric measurements) bridged *via* Cl atoms (splitting of the Sn—Cl Raman lines at 250 cm^{-1}). A loosening of X in *(1a)*, even at room temperature, has been achieved with the aid of butyllithium; R_3SnX, LiX and the expected secondary products of R_2Sn, with distannane as trapping reagent, *e. g.* the corresponding tristannane[5, 7] are formed.

Received: September 4, 1974 [Z 139 IE]
German version: Angew. Chem. 87, 247 (1975)

[*] Prof. Dr. W. P. Neumann and Dipl.-Chem. U. Schröer
Lehrstuhl für Organische Chemie der Universität
46 Dortmund-Eichlinghofen, August-Schmidt-Strasse 6 (Germany)

CAS Registry numbers:
C_6H_5—CH_2Cl, 100-44-7; H_2C=C=CHI, 2936-44-9;
HC≡C—CH_2I, 659-86-9; HC≡C—CH_2Br, 106-96-7;

H_2C=CH—CH_2Br, 106-95-6; Me_3Sn—$SnMe_3$, 661-69-8; C_6H_5—CH_2—Sn(Cl)Bu_2, 54460-66-1; H_2C=C=CH—Sn(I)Bu_2, 54460-67-2; H_2C=C=CH—Sn(Br)Bu_2, 54460-68-3; H_2C=CH—CH_2—Sn(Br)Bu_2, 1802-97-7; Me_3Sn—Bu_2Sn—$SnMe_3$, 54460-69-4; Bu_2Sn, 1191-48-6; CH_3I, 74-88-4; C_2H_5I, 75-03-6; n-C_3H_7I, 107-08-4; n-C_4H_9I, 542-69-8; n-$C_5H_{11}I$, 628-17-1; n-C_3H_7Cl, 540-54-5; n-C_3H_7Br, 106-94-5; i-C_4H_9I, 513-38-2; s-C_4H_9I, 513-48-4; Br(n-$C_4H_9)_2$Sn—Sn(n-$C_4H_9)_2$Br, 54460-71-8; I(n-$C_4H_9)_2$Sn—Sn(n-$C_4H_9)_2$I, 54460-72-9; (CH_3CO_2)(n-$C_4H_9)_2$Sn—Sn(n-$C_4H_9)_2$($OCOCH_3$), 54460-73-0; (n-$C_4H_9)_2SnCl_2$, 683-18-1; (n-$C_4H_9)_2SnH_2$, 1002-53-5; (n-$C_4H_9)_2SnBr_2$, 996-08-7; (n-$C_4H_9)_2SnI_2$, 2865-19-2; (n-$C_4H_9)_2$Sn($OCOCH_3)_2$, 1067-33-0; *(1a)*, 54460-70-7; *(1b)*, 3849-97-6

[1] *W. P. Neumann, J. Pedain,* and *R. Sommer,* Liebigs Ann. Chem. *694,* 9 (1966). Cyclopentadienylstannylenes have recently been reported by: *H.-J. Albert* and *U. Schröer,* J. Organometal. Chem. *60,* C6 (1973); *K. D. Bos, E. J. Bulten,* and *J. G. Noltes, ibid. 67,* C13 (1974).

[2] *R. Sommer, B. Schneider,* and *W. P. Neumann,* Liebigs Ann. Chem. *692,* 12 (1966); *J. Pedain,* Dissertation, Universität Giessen 1965.

[3] Cf. the discussion concerning the corresponding carbenes; *W. Kirmse:* Carbene Chemistry. Academic Press, New York 1971; *G. Köbrich,* Angew. Chem. *79,* 15 (1967); Angew. Chem. internat. Edit. *6,* 41 (1967).

[4] The ready decomposition of polystannanes into stannylenes postulated by *M. O. Nefedov* and *M. N. Manakov* [Angew. Chem. *78,* 1039 (1966); Angew. Chem. internat. Edit. *5,* 1021 (1966)] does not occur, at least under the reaction conditions chosen by us.

[5] B.p. 122—123 °C/2 × 10^{-5} torr.

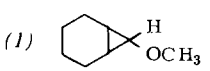
[6] *(1)*, X = Br, I, was prepared by an analogous method [2].

[7] This route is not recommended for reactions with alkyl halides as trapping reagents because of side reactions.

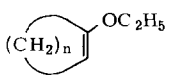
Anodic Oxidation of Cyclopropane Derivatives[1] [**]

By *Meinolf Klehr* and *Hans J. Schäfer*[*]

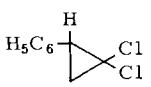
The reactivity of the three-membered ring towards electrophiles, radicals, and oxidizing agents resembles that of the double bond[2]. It appeared preparatively advantageous and



(1)

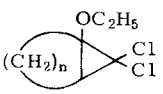


(6), n = 4
(7), n = 5
(8), n = 6



(2)

H_5C_6—CH=CH_2 *(9)*



(3), n = 4
(4), n = 5
(5), n = 6

Table 1. Voltammetric peak potentials of the cyclopropane derivatives *(1)*–*(5)* and the comparable olefins *(6)*–*(9)*.

Cyclopropane	E_p [V] [a]	Olefin	E_p [V] [a]
7-Methoxynorcarane *(1)*	+1.64	*(6)*	+1.28 [b]
1-Phenyl-2,2-dichlorocyclopropane *(2)*	+1.83	*(9)*	+1.70 [c]
1-Ethoxy-7,7-dichloronorcarane *(3)*	+1.65	*(6)*	+1.28 [b]
1-Ethoxy-8,8-dichlorobicyclo[5.1.0]octane *(4)*	+1.65	*(7)*	+1.28
1-Ethoxy-9,9-dichlorobicyclo[6.1.0]nonane *(5)*	+1.65	*(8)*	+1.30 [c]

[a] 10^{-3} mol/l in 0.5 M methanolic sodium perchlorate solution (anodic limit: +1.9 V referred to Ag/AgCl) at glassy carbon against Ag/AgCl, sweep rate: 20 mV/s.

[b] *D. Koch, H. Schäfer,* and *E. Steckhan,* Chem. Ber. *107,* 3640 (1974), see Table 1 therein.

[c] *E. Steckhan,* Dissertation, Universität Göttingen 1971.

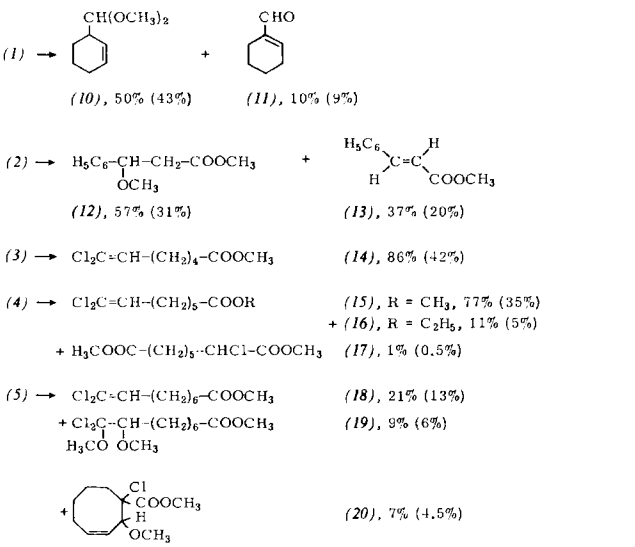
[*] Dipl.-Chem. M. Klehr and Prof. Dr. H. J. Schäfer
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)

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

mechanistically instructive to check how far the findings of anodic oxidation of olefins[3] apply in the case of cyclopropane derivatives. According to *Shono*[4] 1,3-addition of nucleophiles with ring-opening is to be expected. The cyclopropane derivatives *(1)*–*(5)* are only slightly more anodically oxidized than comparably substituted olefins (Table 1).

Anodic oxidation of *(1)*–*(5)* affords the products listed in Table 2.

Table 2. Oxidation products of the cyclopropane derivatives *(1)*–*(5)*. Yields referred to amount of reacted starting compound are given alongside or under the products; those in brackets are referred to current consumption.



(1) → *(10)*, 50% (43%) + *(11)*, 10% (9%)

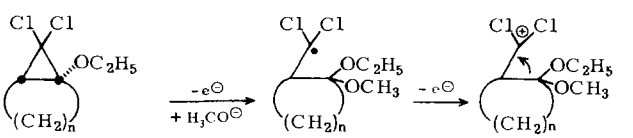
(2) → H_5C_6—CH(OCH$_3$)—CH_2—$COOCH_3$ *(12)*, 57% (31%) + H_5C_6(H)C=C(H)$COOCH_3$ *(13)*, 37% (20%)

(3) → Cl_2C=CH—$(CH_2)_4$—$COOCH_3$ *(14)*, 86% (42%)

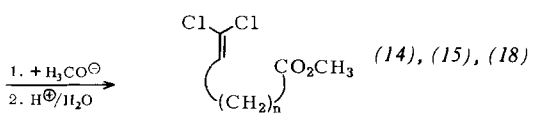
(4) → Cl_2C=CH—$(CH_2)_5$—COOR *(15)*, R = CH_3, 77% (35%) + *(16)*, R = C_2H_5, 11% (5%)
+ H_3COOC—$(CH_2)_5$—CHCl—$COOCH_3$ *(17)*, 1% (0.5%)

(5) → Cl_2C=CH—$(CH_2)_6$—$COOCH_3$ *(18)*, 21% (13%)
+ Cl_2C(OCH$_3$)—CH(OCH$_3$)—$(CH_2)_6$—$COOCH_3$ *(19)*, 9% (6%)
+ Cl, COOCH$_3$, H, OCH$_3$ *(20)*, 7% (4.5%)

The reaction probably proceeds *via* the radical cations of *(1)*–*(5)*, since controlled potential electrolysis was performed at the oxidation potential of the cyclopropanes. Unsaturated acetals or esters can be formed from the radical cations by C—C cleavage with ring opening and subsequent solvolysis, deprotonation, and oxidation. Remarkable is the transformation of the bicyclic compounds *(3)*, *(4)* and *(5)* into the acyclic unsaturated esters *(14)*, *(15)* and *(18)*, respectively, that could take place *via* a fragmentation.



(3)-*(5)*, n = 4-6



(14), *(15)*, *(18)*

Methyl 7,7-dichloro-6-heptenoate (14)

Compound *(3)* [19.8 g (*ca.* 0.1 mol)] was electrolyzed in a partitioned cell (diaphragm: ion-exchange membrane Amfion C-100) at +1.6 V (against Ag/AgCl) and a current density of 25 mA/cm^2 at a glassy carbon anode in methanol/lutidine (10:1) with 0.5 N $NaClO_4$ as supporting electrolyte until consumption of 0.1 F. Distillation of the crude product at 55—56.5 °C/0.05 torr gave 2 g of *(14)* (n_D^{20} = 1.4711) (gas chromatographic: 86% yield based on reacted *(3)*, SE 30 column: 120—180 °C, standard: n-$C_{13}H_{28}$).

Received: November 15, 1974 [Z 141 IE]
German version: Angew. Chem. *87,* 173 (1975)

[1] Anodic Oxidation of Organic Compounds, Part 14.—Part 13: *D. Koch, H. Schäfer,* and *E. Steckhan,* Chem. Ber. *107,* 3640 (1974).

[2] *D. Wendisch* in Houben-Weyl-Müller: Methoden der organischen Chemie. Thieme, Stuttgart 1971, Vol. 4/3, p. 575ff.; *M. Charton* in *J. Zabicky*: The Chemistry of Alkenes. Interscience, New York 1970, Vol. 2, p. 512; *R. J. Oullette* in *W. S. Trahanosky*: Oxidation in Organic Chemistry. Academic Press, New York 1973, Part B, p. 158.

[3] *H. Schäfer* and *E. Steckhan*, Angew. Chem. *81*, 532 (1969); Angew. Chem. internat. Edit. *8*, 518 (1969); *H. Schäfer*, Chem.-Ing.-Tech. *42*, 164 (1970); *B. Belleau* and *Y. K. Au-Young*, Can J. Chem. *47*, 2117 (1969); *T. Shono* and *A. Ikeda*, J. Amer. Chem. Soc. *94*, 7892 (1972); *T. Shono*, *Y. Matsumura*, and *Y. Nakagawa*, J. Org. Chem. *96*, 3532 (1974); *L. Eberson* and *H. Schäfer*, Fortschr. Chem. Forsch. *21*, 1 (1971) especially pp. 85, 108; *N. L. Weinberg* and *H. R. Weinberg*, Chem. Rev. *68*, 449 (1968), especially p. 469; *D. Koch*, *H. Schäfer*, and *E. Steckhan*, Chem. Ber. *107*, 3640 (1974); *J. M. Fritsch*, *H. Weingarten*, and *J. D. Wilson*, J. Amer. Chem. Soc. *92*, 4038 (1970); *E. Steckhan* and *H. Schäfer*, Angew. Chem. *86*, 480 (1974); Angew. Chem. internat. Edit. *13*, 472 (1974).

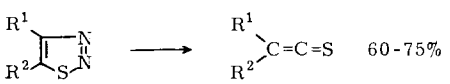
[4] *T. Shono*, *Y. Matsumura*, and *Y. Nakagawa*, J. Org. Chem. *36*, 1771 (1971).

Flash Thermolysis of 1,2,3-Thiadiazoles: A Simple Route to Thioketenes[**]

By *Günther Seybold* and *Christian Heibl*[*]

Thioketenes *(2)* were until now either difficultly accessible or only detectable indirectly as intermediates[2]. It is not surprising therefore that this class of compounds has been little studied and their synthetic potential rarely utilized.

We have now found that the flash thermolysis of 1,2,3-thiadiazoles *(1)* at 580 °C/10^{-4} torr constitutes a simple, convenient, and generally applicable method for the synthesis of thioketenes in good yields—simple, not least because the starting compounds are readily accessible from aldehydes and ketones[3].



(1a)-(1f) *(2a)-(2f)* 60-75%

(a), $R^1 = R^2 = p$-Cl-C_6H_4; *(b)*, $R^1 = R^2 = C_6H_5$;
(c), $R^1 = C_6H_5$, $R^2 = H$; *(d)*, $R^1 = C(CH_3)_3$, $R^2 = H$;
(e), $R^1 = CH_3$, $R^2 = C_6H_5$; *(f)*, $R^1 + R^2 =$

The idea to prepare thioketenes from thiadiazoles is not new. As long ago as 1916 *Staudinger* made attempts to obtain diphenylthioketenes by thermolysis of *(1)* in boiling naphthalene[4]. However, he was able to isolate only tetraphenylthiophene and a compound which was later identified as a 1,3-dithiol derivative[5].

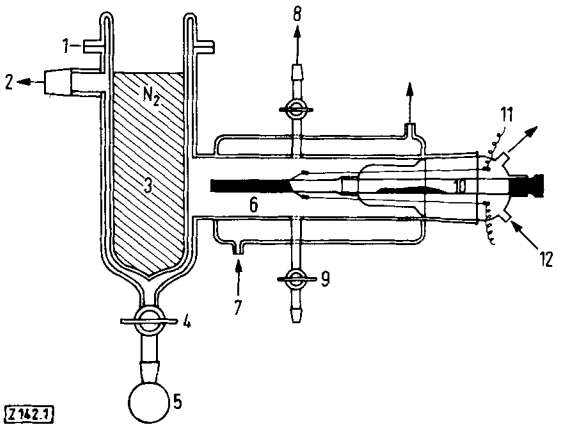


Fig. 1. Apparatus for flash thermolysis. 1: ground joint; 2: to pump; 3: cold finger; 4: coolable tap; 5: receiver; 6: heated quartz tube; 7: cooling water; 8: to manometer; 9: tap; 10: reservoir; 11: current supply; 12: thermostat.

The flash thermolysis was carried out with the apparatus illustrated in Fig. 1[6]. The thiadiazole *(1)* to be pyrolyzed is placed in the reservoir 10 whose temperature is regulated by a thermostat such that a slow but constant stream of substance into the electrically heated quartz tube 6 takes place. Immediately after leaving the hot zone—the residence time is of the order of 10^{-3} s—the pyrolyzate is chilled to −196 °C on the cold finger 3. During the pyrolysis a low-boiling solvent (*e.g.* CH_2Cl_2 or $CFCl_3$) is distilled into the vessel *via* tap 9. In this way dimerizations and oligomerizations are largely avoided when the cold finger is thawed off and dilute thioketene solutions are formed which drip through the coolable tap 4 into the receiver 5. The thioketene solutions obtained in this way are 0.1—0.4 molar and do not contain any by-products; they can be used directly for further reactions or spectroscopic investigations.

The yield of thioketene reached its maximum between 500 and 580 °C (temperature of the quartz tube 6). Above 600 °C decomposition into nitrogen, sulfur, and acetylene derivatives occurred as side reaction. The products found by *Staudinger* could not be detected. This is understandable since the flash thermolysis was carried out at 10^{-4} torr, so subsequent second order reactions of the particles initially formed can be ruled out.

As a rule, we worked at the gram level; however, if the cold finger is made rotatable by means of a ground joint

Table 1. Yields and physical properties of some thioketenes *(2)*.

Cpd.	Yield [%] [a]	IR [cm^{-1}] [b]	^{1}H-NMR δ	λ_{max} [nm] lg ε	Halflife [c]
(2a)	70	1725	—	627 2.31 in CH_2Cl_2	in CH_2Cl_2 at 40 °C: 6.10 h
(2b)	73	1725	—	624 2.51 in CH_2Cl_2	in CH_2Cl_2 at 30 °C: 6.13 h; 40 °C: 3.80 h
(2d)	65—75	1758	1.17 (s, 9H) 4.35 (s, 1H) in $CFCl_3$	575 1.00 in $CFCl_3$	in $CFCl_3$ at 22 °C: 0.98h

[a] Determined by trapping with dimethylamine. The structures of the thioamides were confirmed by elemental analysis, ^{1}H-NMR and IR spectra, and by comparison with authentic samples.
[b] Recorded at −50 °C in a low-temperature cuvette in CH_2Cl_2.
[c] Calculated for 0.01 M solutions [9].

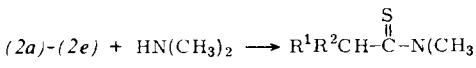
[*] Dr. G. Seybold and Dipl.-Chem. Ch. Heibl
Institut für Organische Chemie der Universität
8 München 2, Karlstrasse 23 (Germany)

[**] Flash Thermolysis of Organic Compounds, Part 3.—Part 2: [1].

1, amounts of up to 10 g can be reacted because of the increased cooling surface.

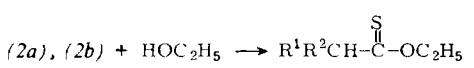
The yields and physical properties of a few thioketenes *(2)* which we have prepared by this method are listed in Table 1.

The structure of the reaction products *(1)* follows unequivocally from the IR bands between 1700 and 1800 cm^{-1} [1, 2, 7, 8] which are characteristic for thioketenes, from NMR, UV and mass spectra, and from chemical behavior. Reaction of *(2a)* to *(2e)* with dimethylamine at −80 °C leads to immediate and quantitative formation of the thioamide *(3)*. Since neither starting compounds nor secondary products of thioketenes react with dimethylamine in this way, this reaction is suitable for the quantitative determination of thioketene in solution. Thioketenes *(2a)* and *(2b)* react with alcohols at room temperature to give the *O*-alkylthiocarboxylic esters *(4)*.



(2a)-(2e) + $HN(CH_3)_2$ → $R^1R^2CH-\overset{S}{\overset{\|}{C}}-N(CH_3)_2$

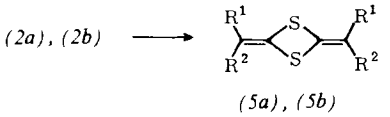
(3a)-(3e)



(2a), (2b) + HOC_2H_5 → $R^1R^2CH-\overset{S}{\overset{\|}{C}}-OC_2H_5$

(4a), (4b)

On warming (30 °C), the diarylthioketenes *(2a)* and *(2b)* dimerize to bismethylenedithietanes *(5)*, which have already been described by *Schönberg*[10].



(2a), (2b) → *(5a), (5b)*

In contrast, the thioketenes *(2c)*—*(2e)* oligomerize at room temperature to complex mixtures. *(2f)* already begins to polymerize at −120 °C and could therefore only be detected indirectly.

The dimerization or oligomerization of the thioketenes *(2a)*, *(2b)* and *(2d)* proceeds strictly according to a second order rate law. The halflives (Table 1) and ^{13}C-NMR spectra[11] of the thioketenes show that both electronic as well as steric effects are responsible for their different kinetic stabilities.

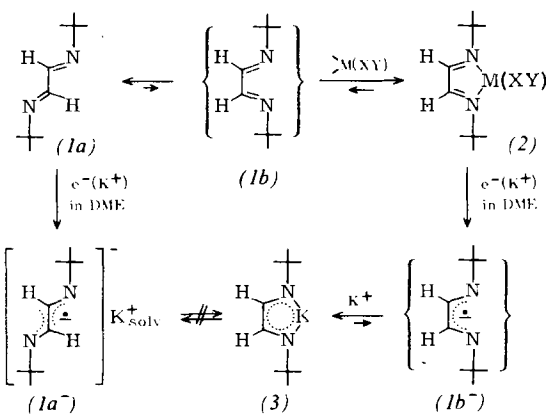
Received: November 26, 1974 [Z 142 IE]
German version: Angew. Chem. 87, 171 (1975)

[1] *G. Seybold*, Tetrahedron Lett. *1974*, 555.
[2] For literature survey see: *M. S. Raasch*, J. Org. Chem. *35*, 3470 (1970); *37*, 1347 (1972).
[3] *C. D. Hurd* and *R. I. Mori*, J. Amer. Chem. Soc. *77*, 5359 (1955); *L. Wolff*, Liebigs Ann. Chem. *333*, 1 (1904).
[4] *H. Staudinger* and *J. Siegwart*, Ber. Deut. Chem. Ges. *49*, 1918 (1916).
[5] *K. P. Zeller*, *H. Meier*, and *E. Müller*, Liebigs Ann. Chem. *766*, 32 (1972).
[6] *G. Seybold* and *U. Jersak*, unpublished.
[7] *A. Krantz* and *J. Laureni*, J. Amer. Chem. Soc. *96*, 6768 (1974).
[8] *E. Schaumann* and *W. Walter*, Chem. Ber. *107*, 3562 (1974).
[9] We thank Dr. *H. U. Wagner* for the spectroscopic investigations.
[10] *S. Schönberg*, *W. Knöfel*, *E. Frese*, and *K. Praefcke*, Chem. Ber. *103*, 1705 (1969).
[11] *J. Firl*, *Ch. Heibl*, and *G. Seybold*, unpublished.

Reductive Fixation of *cis*- and *trans*-1,4-Diazabutadienes[1]

By *Heindirk tom Dieck* and *Klaus-Dieter Franz*[*]

Like butadiene itself in the free state, simple 1,4-dialkyl-1,4-diazabutadienes such as *(1)* exist in the *(E)* conformation *(1a)*. No interaction between lone pairs (as expected for *(1b)*) is observed in the photoelectron spectra, and the IR and Raman spectra indicate the presence of a center of inversion[2]. *(1a)* is readily reduced to the paramagnetic anion *($1a^-$)* by potassium in dimethoxyethane (DME)[3]. The anion *($1a^-$)* displays a highly resolved ESR spectrum in which, at line widths below 0.1 G, not only the splitting by the two H and N atoms of the glyoxal bis(diimine) system (15 lines) but also the hyperfine structure of the 18 equivalent *tert*-butyl protons is visible (a_N 5.62, a_H 4.37, a_H (tBu) 0.15 G)[4, 5].

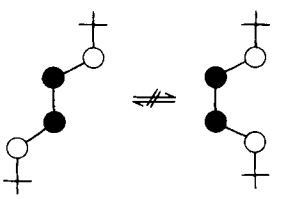


(1a) *(1b)* *(2)* *($1a^-$)* *(3)* *($1b^-$)*

The neutral (*Z*) conformer *(1b)* is not present in measurable concentration in solution; however, the conformational transition *(1a)*⇌*(1b)* occurs readily, as can be demonstrated by rapid formation of numerous chelate complexes *(2)*[6].

Some of the complexes *(2)* are sensitive to reduction (*e.g.* M(XY) = copper(I) halide[7] or π-allylbromodicarbonylmolybdenum[8]). In the course of cleavage by potassium or solvated electrons in DME the (*Z*) conformer of the ligand is reduced; the *cis* anion radical *($1b^-$)* corresponding to *($1a^-$)*, which is probably formed initially, rapidly complexes potassium ions to form the conformationally stable neutral potassium complex *(3)*.

With the reduced compounds of type *(1)* the (*Z*) or the (*E*) conformation can thus be fixed at will. No transition *($1a^-$)*⇌*(3)* is observed in the ESR spectrum at temperatures up to +30 °C; this is reasonable since reduction involves occupation of a molecular orbital with bonding interactions between the centers 2 and 3.



The potassium complex *(3)* displays an ESR spectrum which can be "built up" by superposition of four spectra of the

[*] Prof. Dr. H. tom Dieck and Dipl.-Chem. K.-D. Franz
Institut für Anorganische Chemie der Universität
6 Frankfurt am Main 70, Theodor-Stern-Kai 7 (Germany)

radical *(1a⁻)*. The number four arises from the nuclear spin of the commonest potassium isotope ^{39}K (*ca.* 93%, $I=3/2$).

The large K coupling constant (a_K 1.5 G) and the high resolution prove the conformational rigidity and also the presence of this unusual type of complex[9]. In general, potassium has a preference for a regular coordination sphere of oxygen ligands; in the present case, however, the ligand which is bonded only *via* nitrogen is not replaced by the chelating ether dimethoxyethane present in large excess. Hence specific potassium complexing agents are also conceivable with N ligands.

Received: April 10, 1974;
revised: September 5, 1974 [Z 144a IE]
German version: Angew. Chem. *87*, 244 (1975)

CAS Registry numbers:
(1), 28227-42-1

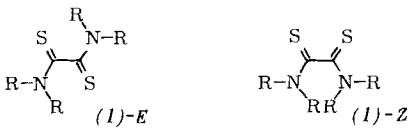
[1] Coordination and Conformation, Part 1. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.
[2] *K.-D. Franz* and *H. tom Dieck*, unpublished.
[3] *H. tom Dieck*, Habilitationsschrift, Universität Frankfurt 1971; *H. tom Dieck* and *I. W. Renk*, Chem. Ber. *104*, 110 (1971).
[4] *P. Clopath* and *A. v. Zelewsky*, Helv. Chim. Acta *55*, 52 (1972).
[5] *K. D. Franz, H. tom Dieck, U. Krynitz*, and *I. W. Renk*, J. Organometal. Chem. *64*, 361 (1974).
[6] *H. Bock* and *H. tom Dieck*, Angew. Chem. *78*, 549 (1966); Angew. Chem. internat. Edit. *5*, 520 (1966).
[7] *H. tom Dieck* and *I. W. Renk*, Chem. Ber. *104*, 92 (1971).
[8] *H. tom Dieck* and *H. Friedel*, J. Organometal. Chem. *14*, 375 (1968).
[9] The spectrum of *(3)* has actually already been recorded, without having been recognized as that of the potassium complex [4].

C—N Twisted Ethanedithioamides in Electron-Rich Complexes[1]

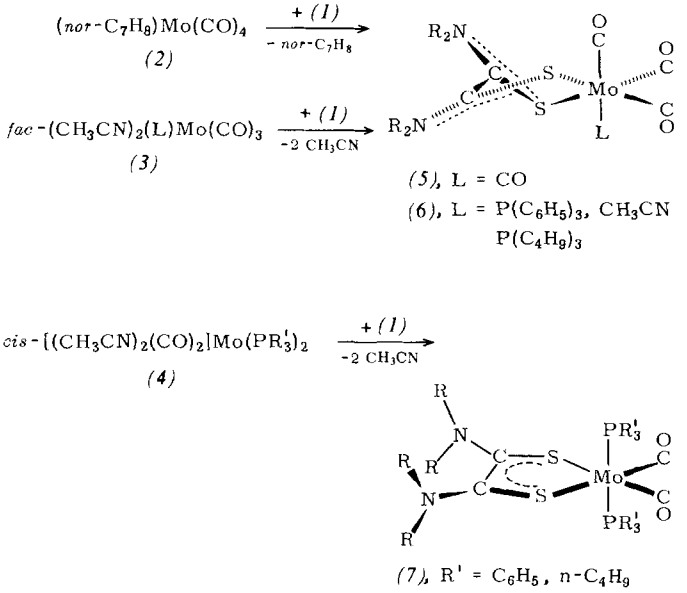
By *Heindirk tom Dieck* and *Michael Form*[*]

We have studied the reactions of carbonylmolybdenum complexes with ethanedithioamides ("dithiooxamides"), the only compounds possessing a S=C—C=S structure to be stable in the free state. Our choice fell upon the *N,N'*-tetraalkyl derivatives *(1)* in order to avoid side reactions (with R=H involving proton loss to give rubeanates).

Compounds *(1)* are not directly comparable with α-dithiones, the extremely readily reducible ligand systems in the so-called dithiolene complexes[2], since they are not planar in the (*E*) conformation but, according to UV[3] and NMR data[4], are twisted about the central C—C bond. A planar (*Z*) conformer of *(1)* is inconceivable owing to steric interactions; *(1)* should therefore be a poor *S,S*-chelating ligand.

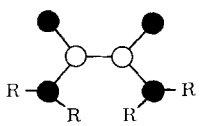


Reaction of *(1)* with the tetracarbonyl- *(2)* or the tricarbonylmolybdenum complexes *(3)* in ether affords moderately stable red ethanedithioamide complexes *(5)* and *(6)*; reaction with the dicarbonylmolybdenum derivatives *(4)* yields the fairly oxidation-resistant violet complexes *(7)*. (All reactions performed at 10—25 °C with the amides *(1)*, R=CH_3, C_2H_5; R_2=$-(CH_2)_4-$, $-(CH_2)_5-$.)



The CO stretching frequencies of *(5)* are low (R=CH_3: 2015, 1906, 1880, 1830 cm^{-1}) and fall even further in the case of *(6)* (R=CH_3, L=CH_3CN: 1910, 1780 cm^{-1}) as is generally observed on replacement of CO by stronger donors. On going to *(7)*, however, the CO frequencies increase markedly in spite of the replacement of CO by, *e.g.*, tributylphosphane (R=CH_3: 1930, 1850 cm^{-1}). This can only be explained by a significant change in the donor-acceptor properties of the *S,S*-coordinated ligands in the transition from *(5)* to *(7)*.

MO calculations show that twisting of *(1)* about C—C with retention of two planar thioamide systems is definitely favored over twisting about N—C, in accord with experiment[3, 4]. Formal reduction leads, however, to occupation of a molecular orbital that has bonding character between C—C and antibonding properties between N—C. Thus the dithiocarbonyl system with twisted R_2N groups becomes energetically more favorable.



The better a metal group is able to release electrons, the more the tetraalkylthioamide will prefer a planar S···C···C···S skeleton and form a "dithiolene" type complex with formally oxidized metal[5].

The NMR non-equivalence[6] of the R groups in *(1)*, well established for the carboxamides, has actually disappeared in the complexes *(7)* and a sharp signal is observed for the tetramethyl compound (R=CH_3: *(1)*, δ=3.25, 3.46 ppm in $CDCl_3$; *(7)*, δ=2.90 ppm in C_6D_6). All the experimental findings can therefore be explained by a conformational change in the ligand that is caused by electronic factors[7]. Complexes of divalent transition metals with *(1)* have been described previously[8, 9]. The preparation under highly acidic conditions described by *Peyronal et al.* presumably also involves a weakening of the thioamide interaction by protonation of the amide nitrogen.

[*] Prof. Dr. H. tom Dieck and Dipl.-Chem. M. Form
Institut für Anorganische Chemie der Universität
6 Frankfurt am Main 70, Theodor-Stern-Kai 7 (Germany)

Received: April 10, 1974;
revised: September 5, 1974 [Z 144b IE]
German version: Angew. Chem. *87*, 245 (1975)

CAS Registry numbers:
$(CH_3)_2NC(S)C(S)N(CH_3)_2$, 35846-78-9; $(C_2H_5)_2NC(S)C(S)N(C_2H_5)_2$, 13749-59-2; $(CH_2)_4NC(S)C(S)N(CH_2)_4$, 54460-65-0; $(CH_2)_5NC(S)C(S)N(CH_2)_5$, 24528-76-5; *fac*-$(CH_3CN)_2Mo(CO)_4$, 17594-19-3; *fac*-$(CH_3CN)_2(P(C_6H_5)_3)Mo(CO)_3$, 54460-81-0; *fac*-$(CH_3CN)_3Mo(CO)_3$, 17731-95-2; *fac*-$(CH_3CN)_2(P(C_4H_9)_3)Mo(CO)_3$, 54460-82-1; *cis*-$[(CH_3CN)_2(CO)_2]Mo(P(C_6H_5)_3)_2$, 23526-71-8; *cis* $[(CH_3CN)_2(CO)_2]Mo(P(n\text{-}C_4H_9)_3)_2$, 31264-80-9; *(2)*, 12146-37-1; *(5)*; R = CH_3, L = CO, 54460-83-2; *(6)*; R = CH_3, L = CH_3CN, 54460-84-3; *(7)*; R = CH_3, R' = *n*—C_4H_9, 54517-21-4

[1] Coordination and Conformation, Part 2. This work was supported by gifts of chemicals from BASF AG and Farbwerke Hoechst AG, and by the Fonds der Chemischen Industrie.—Part 1: *H. tom Dieck* and *K.-D. Franz*, Angew. Chem. *87*, 244 (1975); Angew. Chem. internat. Edit. *14*, 249 (1975).

[2] *J. A. McCleverty*, Progr. Inorg. Chem. *10*, 49 (1968).

[3] *B. Persson* and *J. Sandström*, Acta Chem. Scand. *18*, 1059 (1964).

[4] *H. tom Dieck* and *M. Form*, unpublished.

[5] *G. N. Schrauzer*, Accounts Chem. Res. *2*, 72 (1969).

[6] *J. W. Emsley*, *J. Feeney*, and *L. H. Sutcliffe*: High Resolution NMR Spectroscopy. Pergamon Press, Oxford 1965.

[7] The cyclic non-twistable dithioamide 1,4-dimethylpiperazine-2,3-dithione gives a "normal" complex *(7)* having CO frequencies at 1800 and 1730 cm^{-1} [4].

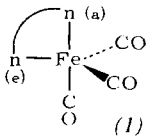
[8] *G. Peyronel*, *G. C. Pellacani*, *A. Pignedoli*, and *G. Benetti*, Inorg. Chim. Acta *5*, 263 (1971).

[9] *D. M. Hart*, *P. S. Rolfs*, and *I. M. Kessinger*, J. Inorg. Nucl. Chem. *32*, 469 (1970).

Unsymmetrical Coordination of a Symmetrical 1,4-Diazabutadiene to Iron(0)[1]

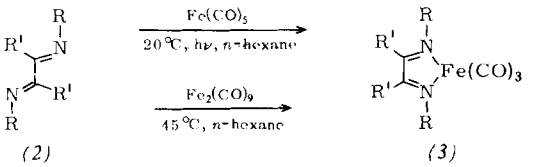
By *Heindirk tom Dieck* and *Alexander Orlopp*[*]

Pentacarbonyliron possesses a trigonal-bipyramidal structure and thus has two fundamentally distinguishable ligand sites. Olefins are known from experience to prefer the equatorial position (e), and n-donors the axial position (a) on substitution[2]. Bidentate n-donors should therefore form an a⌒e chelate *(1)*; however, coordinational asymmetry has never yet been detected with *a priori* symmetrical chelate ligands. Moreover, numerous trigonal-bipyramidal Fe^0 compounds display fluxional behavior[3].



(1)

We have studied the reaction of carbonyliron complexes with 1,4-diazabutadienes *(2a)–(2i)*. The air-sensitive violet [*(3a)*, *(3b)*] or red [*(3c)–(3i)*] tricarbonyl complexes are easily obtained photolytically from $Fe(CO)_5$ or thermally from $Fe_2(CO)_9$.



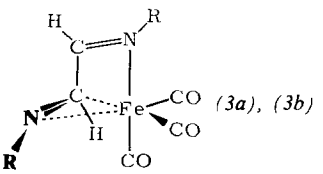
(2) *(3)*

The readily soluble complexes *(3c)–(3i)* closely resemble one another, and do not show any coordinational differences in the two half-ligands R—N=C(R') in their NMR spectra, in spite of the potentially different coordination sites (a,e). In contrast, the complexes *(3a)* and *(3b)*, having tertiary *N*-substituents, which were studied in detail because of their deviating solvatochromism, display some remarkable features. Both are monomeric compounds that can be sublimed or distilled in high vacuum. Apart from the usual CO frequencies, their IR spectra contain an intense band in the double bond region (1680—1690 cm^{-1}); the other complexes *(3)* exhibit no bands down to 1500 cm^{-1} or only those that are typical of aromatic compounds, like the molybdenum(0) complexes of these ligands[4]. In the ^{1}H-NMR spectrum of *(3a)* and *(3b)* all signal groups of the free ligands are doubled, thus indicating that the two halves must have become different as a result of coordination. In particular, the marked upfield shift of one of the two glyoxalic protons is reminiscent of the shift shown by olefinic protons on π-complex formation [*(2a)* in C_6H_6: δ = 1.2 and 7.9 ppm (9:1); *(3a)* in C_6D_6: δ = 1.44, 1.65, 6.35, and 8.01 ppm (9:9:1:1)].

The extreme difference between the glyoxalic C atoms in the ^{13}C-NMR spectrum of *(3a)* (Δδ = 36.4 ppm) also demonstrates the coordination induced non-equivalence of the two molecular halves originally identical in the free ligands[5].

The spectroscopic data suggest a structure with a C—C twisted ligand in *(3a)* and *(3b)*.

An axial n_N bond and an equatorial $\pi_{C=N}$ donor bond are in accord with the occurrence of an isolated C=N double bond (IR) and the olefin complex-type shielding of a proton (NMR).



(3a), *(3b)*

Table 1. IR and electronic spectral data of complexes *(3)*.

	R	R	ν_{CO} [a]			ν_{CN} [a]	ν_{max} [c]
			[cm^{-1}]				
(3a)	H	*t*-C_4H_9	2016	1938		1689	18400
(3b)	H	$C(CH_3)_2CH_2C(CH_3)_3$	2013	1935		1683	18020
(3c)	H	$CH(CH_3)_2$	2025	1950		[b]	20000
(3d)	H	C_6H_{11}	2020	1950		[b]	19800
(3e)	H	C_6H_4—OCH_3-(*p*)	2036	1971	1961	[b]	19570
(3f)	H	C_6H_3—$(CH_3)_2$-(2,6)	2041	1973	1965	[b]	20260
(3g)	H	C_6H_4—$N(CH_3)_2$-(*p*)	2035	1970	1960	[b]	19160
(3h)	CH_3	C_6H_5	2032	1964	1954	[b]	19880
(3i)	CH_3	C_6H_4—CH_3-(*o*)	2032	1967	1958		19920

[a] IR in *n*-hexane; [b] ν_{CN} below 1500 cm^{-1} or under the aromatic bands; [c] VIS/UV in *n*-hexane.

A clue as to the steric origin of this anomaly can be seen in the similar behavior of biacetylbis(imines) bearing secondary *N*-substituents[6]. A butadiene-type tetrahapto arrangement

[*] Prof. Dr. H. tom Dieck and Dipl.-Chem. A. Orlopp
Institut für Anorganische Chemie der Universität
6 Frankfurt am Main 70, Theodor-Stern-Kai 7 (Germany)

has been found in all the complexes of monoheterodienes whose structures have so far been established[7].

Received: April 10, 1974;
revised: September 5, 1974 [Z 144c IE]
German version: Angew. Chem. 87, 246 (1975)

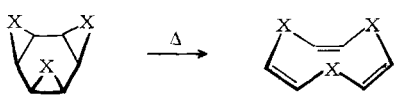
CAS Registry numbers:
(3a), 54446-66-5; (3b), 54446-61-6; (3c), 54446-62-7; (3d), 54446-63-8; (3e), 54446-64-9; (3f), 54446-65-0; (3g), 54446-66-1; (3h), 54515-24-1; (3i), 54446-67-2; (2a), 30834-74-3; $Fe(CO)_5$, 13463-40-6; $Fe_2(CO)_9$, 15321-51-4

[1] Coordination and Conformation, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 2: *H. tom Dieck* and *M. Form*, Angew. Chem. *87*, 245 (1975); Angew. Chem. internat. Edit. *14*, 250 (1975).
[2] *H. Haas* and *R. K. Sheline*, J. Chem. Phys. *47*, 2996 (1967).
[3] *E. L. Muetterties*, MTP Int. Rev. Sci., Inorg. Chem. Ser. 1, 9, 37 (1972); *B. E. Mann*, Advan. Organometal. Chem. *12*, 135 (1974).
[4] *I. W. Renk*, Dissertation, Universität Frankfurt 1970.
[5] *D. Leibfritz* and *H. tom Dieck*, unpublished.
[6] Biacetylbis(*sec*-alkylimines) are approximately as bulky as glyoxalbis(*tert*-alkylimines) in complexes: *H. tom Dieck* and *I. W. Renk*, Chem. Ber. *105*, 1403 (1972).
[7] *E. Koerner von Gustorf, F. W. Grevels, C. Krüger, G. Olbrich, F. Mark, D. Schulz*, and *R. Wagner*, Z. Naturforsch. *27b*, 392 (1972); *A. de Cian* and *R. Weiss*, Chem. Commun. *1968*, 348; Acta Crystallogr. *B28*, 3273 (1972); *H. Kühr* and *E. Weiss*, personal communication.

cis-Trithiatris-σ-homobenzene (*cis*-"Benzene Trisulfide")[**]

By *Shinzo Kagabu* and *Horst Prinzbach*[*]

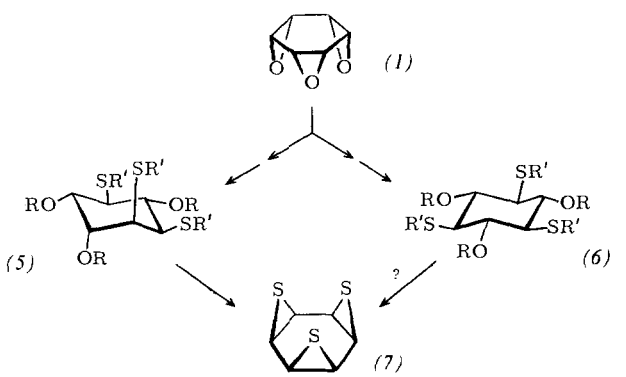
cis-Trioxatris-σ-homobenzene *(1)* and *cis*-triazatris-σ-homobenzene *(2)*[1] have gained significance as synthetic intermediates. Thus thermolysis affords the heterocyclic systems *(3)* and *(4)*[2] and substitution reactions give numerous inositol derivatives which were formerly accessible only *via* more complicated routes, if at all. A very simple and productive synthesis of streptamine may be cited as example[3]. The *cis*-trithiatris-σ-homobenzene (*cis*-"benzene trisulfide") *(7)* should open up further preparative possibilities, while $3\sigma \rightarrow 3\pi$ isomerization to 1,4,7-trithiacyclononatriene *(8)* appeared unlikely from the outset[4].



(1), X = O — *(3)*, X = O
(2), X = NR — *(4)*, X = NR

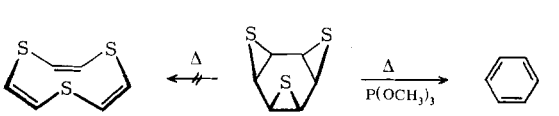
An obvious synthetic route to *(7)*, which has proved its value in the case of the *cis*-triimine *(2)*, started from *(1)* and proceeded *via* the threefold-cleavage products *(5)* with *chiro* configuration. The *scyllo* derivatives *(6)*, having an all-equatorial arrangement of substituents, which, in principle, are also possible alongside *(5)*, should not be suitable for cyclization. We therefore first established whether the selectivity [>90% *(5a)*; triacetate *(5b)*: m.p. 92°C] observed for thiobenzyl alcohol (methanol, sodium methoxide, 60°C) is retained with other S-nucleophiles[5] that can be utilized for episulfide formation. Compound *(1)* reacts quantitatively with an excess of thioacetic acid at 60°C (24 h). Chromatography (silica gel/chloroform) of the oily reaction product, which was immediately esterified with acetic anhydride because of the known tendency of 2-hydroxythioacetates to undergo rearrangement, affords a mixture of *chiro (5c)* and *scyllo*-trithiohexaacetate *(6c)* (40%; *ca.* 1:1). Reaction with an excess of KSCN (methanol, 20°C) or HSCN (methanol/ether, 20°C) is complicated and poorly understood, probably due in part to the instability of the 2-hydroxythiocyanates and the *trans* diaxial eliminations occurring in the 1,2-disubstituted intermediates and in *(5a)* as a result of the relatively high basicity of the medium.

High yields and the desired stereoselectivity are achieved with an excess of thiourea in the presence of concentrated sulfuric acid. A trisisothiouronium salt is obtained [m.p. 161 to 162°C (dec.), yield >90%] which is shown by spectral comparison with *(5a)*–*(5c)*, and particularly by the ^{13}C data [δ = 171.9; 170.5; 168.6 ppm ($\overset{\oplus}{C}(NH_2)_2$); 72.6; 72.4; 68.7 (C—OH); 55.9; 51.9; 51.1 (C—SR); dioxane/water] to be the *chiro* product *(5e)*. The pathway *via (5e)* has the additional advantage that very mild conditions suffice for the liberation of *(7)*. Thus sodium carbonate is added to an aqueous solution (pH *ca.* 8) of *(5e)*, and the emulsion immediately extracted with chloroform. After recrystallization of the chloroform residue from tetrahydrofuran (−20°C), compound *(7)* can be isolated as fine colorless needles (40%). The *cis* orientation of the three episulfide rings deduced from the stereochemistry of the epoxide → episulfide transformation is confirmed by the ^1H [sharp signal at τ = 6.28 ($CDCl_3$), 6.90 (C_6H_6)] and ^{13}C data [δ = 35.7 ppm ($CDCl_3$)].



(a), R = H, R' = CH_2-C_6H_5
(b), R = $COCH_3$, R' = CH_2-C_6H_5
(c), R = R' = $COCH_3$
(d), R = H, R' = CN
(e), R = H, R' = $\overset{\oplus}{C}(NH_2)_2\ HSO_4^{\ominus}$

The thermal properties of *(7)* are characterized by a pronounced trend to undergo polymerization in the solid state and in solution. In the crystalline state, decomposition with yellow coloration starts slowly as low as 20°C and proceeds rapidly above 100°C. In highly dilute $CHCl_3$ solution, *(7)* remains unchanged for some time; on heating to 100°C it decomposes with liberation of benzene (up to 70%). It follows from the concentration dependence of benzene formation, however, that intermolecular processes are involved. In accord with earlier findings[4], $3\sigma \rightarrow 3\pi$ isomerization of *(7)* to *(8)* is consequently unattainable. Sulfur elimination with



(8) *(7)*

[*] Prof. Dr. H. Prinzbach and Dipl.-Chem. S. Kagabu
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

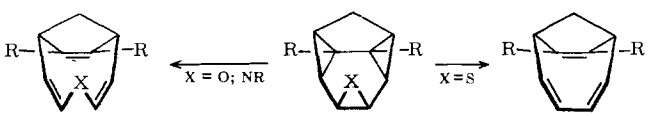
trimethyl phosphite (in THF) to form benzene is fast at 20 °C; nevertheless, neither the disulfide nor the monosulfide can be identified as intermediates (^{1}H-NMR) under a variety of conditions (*e.g.* equimolar ratio; 20 °C). Apparently, elimination of the first sulfur atom has the highest activation energy[6].

The difference between trioxide *(1)*/triimine *(2)* and trisulfide *(7)* apparent from the course of thermolysis is also clear from the mass spectrum: the peaks (inlet temp. 50—70 °C) at *m/e* 174 (M^+), 141 ($M^+ - SH$), 110 ($M^+ - 2S$), 78 ($M^+ - 3S$, 100 %), 64 (S_2) are typical of the fragmentation pattern arising because of preferential loss of sulfur.

Received: December 6, 1974 [Z 146a IE]
German version: Angew. Chem. *87*, 248 (1975)

CAS Registry numbers:
(1), 39078-11-0; *(5a)*, 52911-81-6; *(5b)*, 54657-75-9; *(5c)*, 54657-76-0; *(5d)*, 54657-77-1; *(5e)*, 54657-74-8; *(6c)*, 54657-78-2; *(7)*, 54307-97-0

[1] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *85*, 1107 (1973); Angew. Chem. internat. Edit. *12*, 989 (1973); and earlier literature cited therein.
[2] *H. Prinzbach, R. Schwesinger, M. Breuninger, B. Gallenkamp*, and *D. Hunkler*, Angew. Chem., in press.
[3] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem., in press.
[4] In the model series of bridged *cis*-monoheterotris-σ-homobenzenes *(12)*, the oxa- and aza derivatives isomerize to the trienes *(13)* (140—160 °C)



(13) *(12)* *(14)*
R = CF_3

whereas the thia compound loses sulfur above 100 °C to form *(14)* (*S. Kagabu* and *H. Prinzbach*, Tetrahedron. Lett. *1975*, 29).

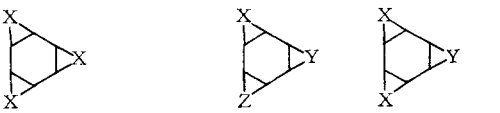
[5] *M. Sander*, Chem. Rev. *66*, 297 (1966).
[6] Accordingly, the disulfide recently synthesized by *Vogel et al.* (Angew. Chem. *86*, 818 (1974); Angew. Chem. internat. Edit. *13*, 736 (1974)) rapidly eliminates sulfur at 20 °C to form benzene. We are indebted to Prof. *Vogel* for informing us prior to publication.

Chemistry of *cis*-Trioxatris-σ-homobenzene. α,α-Dioxa-β-thia- and β-Oxa-α,α-dithiatris-σ-homobenzene[**]

By *Horst Prinzbach, Clemens Kaiser*, and *Hans Fritz*[*]

Our work on the chemistry of *cis*- and *trans*-trisheterotris-σ-homobenzenes *(1a)*–*(1c)*[1] has raised various questions concerned, for example, with the rates and stereochemistries of the individual substitution steps, which have prompted us to undertake comparative studies on systems with differing combinations of hetero atoms, as in *(2)*. We shall now report the preparation of α,α-dioxa-β-thia- *(8)* and β-oxa-α,α-dithiatris-σ-homobenzene *(9)* (the first representatives of the X,X,Y type *(3)*) from *cis*-"benzene trioxide" *(1a)*[2].

The basic problem posed by the synthesis of *(8)* and *(9)* from *(1a)* lay in the synthesis of mono- *(4)* or di-substituted



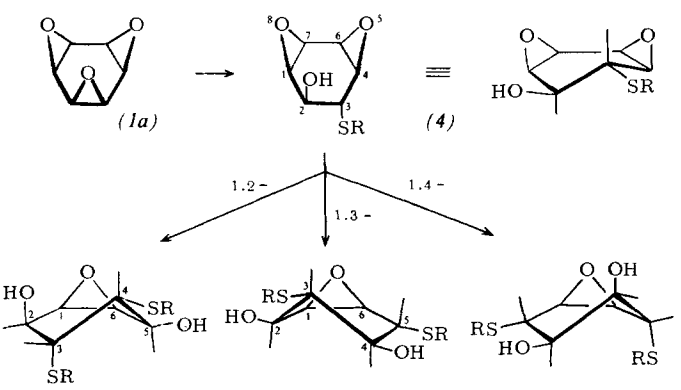
(1) *(2)* *(3)*

(a), X = O
(b), X = NR
(c), X = S

X, Y, Z = O, NR, S, PR

products *(5)* or *(6)* suitable for directed episulfide formation; previous experience with the *cis*-trisulfide *(1c)*[1] indicated the potential usefulness of isothiouronium salts *(4a)* and *(5a)*–*(7a)*.

Under conditions for the opening of one oxirane ring (equimolar proportions, 20 °C), no detectable amounts of *(4a)* can be found alongside residual *(1a)* and the bisadduct *(5a)* after reaction of *(1a)* with thiourea/sulfuric acid. This kinetic advantage of the second substitution is also observed on use of thioacetic acid; opening of the second oxirane ring is again faster than that of the first, and the yield of *(4b)* (colorless crystals, m.p. 99—100 °C) correspondingly low (5—10%)[3]. The desired selectivity [>75% *(4c)*, colorless crystals, m.p. 80 °C] can be achieved with thiobenzyl alcohol in methanol (sodium methoxide); however, *(4c)* is unsuitable for episulfide formation. These difficulties can be circumvented by use of KSCN: at a 1:1 molar ratio (20 °C, methanol, 30% conversion) *ca.* 95% of the dioxathia product *(8)* are formed alongside polymeric material *via* the unstable compound *(4d)*. Product *(8)*, which is freed from *(1a)* by addition of $LiClO_4$ (1:2 complex insoluble in benzene[4]) and from traces of *(9)* by recrystallization from benzene, is obtained as colorless needles, m.p. 140—141 °C (subliming above 120 °C) which can be kept for some time at −20 °C [^{1}H-NMR: τ = 6.58 (br. s) ($CDCl_3$); 7.15 (br. s 5(6)-H); 7.05—7.25 (AA', 1(4)−H); 7.25—7.45 (BB', 2(3)−H) (C_6D_6); ^{13}C-NMR ($CDCl_3$): δ = 48.4 ppm (1(4)−C), 47.3 (2(3)−C), 32.6 (5(6)−C); MS: *m/e* = 142 (M^+), 113 ($M^+ - CHO$), 97 ($M^+ - CHS$), 68 ($M^+ - CHO, -CHS$), 45 (CHS, 100%)]. The α,α,β arrangement of the hetero three-membered rings established by the synthetic pathway leading



(1a) *(4)*

(5) *(6)* *(7)*

(a), R = $\overset{\oplus}{C}(NH_2)_2\ HSO_4^{\ominus}$
(b), R = $COCH_3$
(c), R = CH_2-C_6H_5
(d), R = CN

to *(8)* is confirmed by the small coupling constant $J_{1,6} = J_{4,5} < 2$ Hz (dihedral angle *ca.* 80°), which is comparable with those of other *trans*-heterotris-σ-homobenzenes.

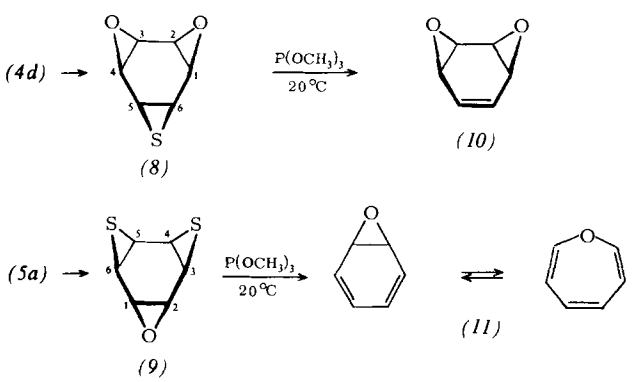
[*] Prof. Dr. H. Prinzbach and Dipl.-Chem. C. Kaiser
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)
Dr. H. Fritz
Ciba-Geigy AG, Basel (Switzerland)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are also indebted to Prof. Dr. *H. Achenbach* for recording some of the mass spectra.

The KSCN method cannot be used for the synthesis of *(9)*. Even under a variety of conditions only very small amounts of *(9)* are detected alongside *(8)* (up to 30%) by spectroscopy of the complex reaction mixture. The method of choice is the reaction with thiourea/sulfuric acid which has proved its value in the case of *(1c)*. Under controlled conditions (1:2 molar ratio, water/2 eq. H_2SO_4, 10d, 20°C) the yield of the 1,2-bisisothiouronium salt *(5a)* [colorless powder, >160°C (dec.)] amounts to *ca.* 80%; residual *(1a)*, *chiro*-tris-isothiouronium salt[1]—small concentrations of *(6a)* and/or *(7a)* cannot be excluded—are removed by reprecipitation in ethanol/water. This regioselectivity of disubstitution[5] also observed with other nucleophiles, likewise applies, albeit less markedly, to the reaction with thiobenzyl alcohol. With a 1:2 molar mixture (methanol/sodium methoxide, 60°C, 2h) mono- *(4c)* and *chiro* tris-adduct[5] are accompanied by *ca.* 30% of *(5c)* (colorless crystals, m.p. 142°C), *ca.* 20% of *(6c)* (colorless crystals, m.p. 107—108°C), and *ca.* 5% of *(7c)*.

Compound *(9)* is obtained in proven manner (addition of Na_2CO_3 to aqueous solution up to pH 8)[1] from *(5a)* in addition to polymeric components; colorless needles [THF, 50—60%, m.p. 119°C (dec.)] which can be sublimed at 60°C/0.01 torr but gradually decompose on standing (−20°C) [^{1}H-NMR: τ = 6.40 (br. s, 1(2)−H); 6.35—6.55 (AA', 3(6)−H); 6.55—6.75 (BB', 4(5)−H) ($CDCl_3$); 6.85—7.05 (AA', 3(6)−H); 7.15—7.35 (BB', 4(5)−H); 7.23 (br. s, 1(2)−H) (C_6D_6); ^{13}C-NMR ($CDCl_3$): δ = 53.1 ppm (1(2)−C), 33.2; 30.6 (3(6)−C), 4(5)−C; MS: *m/e* = 158 (M^+), 129 (M^+−CHO), 94 (M^+-S_2, 100%), 78 (M^+-S_2, −O), 66 (M^+-S_2, −CO), 45 (CHS); metastable peaks at 56.2 (158→94) and 46.5 (94→66)].

As for *(8)* the *trans* arrangements of episulfide and epoxide rings are shown by very small values of the vicinal coupling constants, $J_{1,6} = J_{2,3} < 2$ Hz. Being incapable of 3σ→3π isomerization as *trans*-tris-σ-homobenzenes[6], *(8)* and *(9)* undergo rapid decomposition by an obscure route above 160°C and *ca.* 120°C, respectively. Elimination of sulfur with trimethyl phosphite (20°C) to give benzene dioxide *(10)*[7] and benzene oxide/oxepin *(11)*[8] proceeds readily in both cases. In connection with the differing fragmentation patterns of *cis*-trioxide *(1a)* and *cis*-trisulfide *(1c)*[1] in the mass spectrometer the metastable peak at *m/e* = 56.2 recorded for *(9)*, possibly indicative of S_2 elimination, warrants attention.



The structural elucidation of substitution products *(4)*–*(7)* based on elemental analysis and spectral comparison (IR, ^{1}H-, ^{13}C-NMR, MS) was considerably facilitated by the fact that the ^{1}H-NMR spectra recorded at 270 or 360 MHz could be extensively analyzed. With regard to the conformational properties, the coupling constants for *(4a)*–*(4c)* [*e.g. (4c)*: $J_{1,2} = J_{2,3} = 5$; $J_{3,4} = J_{4,6} = 3$; $J_{2,OH} = 10$ Hz] evidence an equilibrium between the quasi-e,e and the quasi-a,a conformers, and the coupling constants for *(5)*, *(6)*, and *(7)* [*e.g. (5c)*: $J_{1,6} + J_{1,5} = 3$; $J_{2,3} + J_{3,5} = 5$; $J_{2,OH} = 7$ Hz; *(6c)*: $J_{1,2} = 1.5$; $J_{1,6} = 4$; $J_{2,3} = J_{3,4} = 10$; $J_{4,5} = 9$; $J_{2,OH} = J_{4,OH} = 2$ Hz] the expected quasi-a,a,e,e and e,e,e,e preferred conformations.

Received: December 6, 1974 [Z 146b IE]
German version: Angew. Chem. 87, 249 (1975)

CAS Registry numbers:
(1a), 39078-11-0; *(1c)*, 54307-97-0; *(4b)*, 54307-98-1; *(4c)*, 54307-99-2; *(4d)*, 54383-92-5; *(5a)*, 54308-01-9; *(5c)*, 54308-02-0; *(6c)*, 54308-03-1; *(7c)*, 54308-04-2; *(8)*, 54308-05-3; *(9)*, 54308-06-4

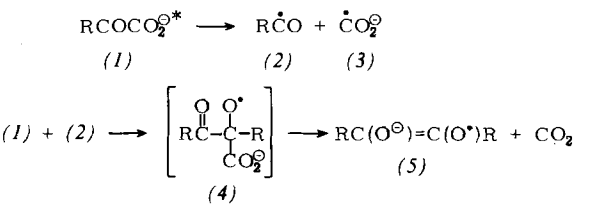
[1] *S. Kagabu* and *H. Prinzbach*, Angew. Chem. *87*, 248 (1975); Angew. Chem. internat. Edit. *14*, 252 (1975), and earlier references cited therein.
[2] In naming the tris-σ-homobenzene compounds we regard them as cyclohexane derivatives and the three-membered rings as divalent substituents, the arrangement of the latter being denoted by α (above), β (below), where the side having two rings is taken as the upper side.
[3] *S. Kagabu*, Dissertation, Universität Freiburg, scheduled for 1975.
[4] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. internat. Edit. *11*, 942 (1972).
[5] *R. Schwesinger*, *H. Fritz*, and *H. Prinzbach*, Angew. Chem. *85*, 1110 (1973); Angew. Chem. internat. Edit. *12*, 993 (1973).
[6] *H. Prinzbach* and *D. Stusche*, Helv. Chim. Acta *54*, 985 (1971).
[7] *H.-J. Altenbach* and *E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. internat. Edit. *11*, 937 (1972).
[8] *E. Vogel* and *H. Günther*, Angew. Chem. *79*, 429 (1967); Angew. Chem. internat. Edit. *6*, 385 (1967).

Formation of *cis*- and *trans*-Semidione Radical Anions by Addition of Acyl Radicals to α-Oxo Carboxylic Acids

By *Steen Steenken* and *Dietrich Schulte-Frohlinde*[*]

During *in situ* EPR photolysis[1] of aqueous solutions of α-oxo carboxylic acids $RCOCO_2H$ above pH 5 we have observed *cis* and *trans* isomers of semidione radical anions of type *(5)*. On simultaneous photolysis of two different α-oxo carboxylic acids $RCOCO_2H$ and $R'COCO_2H$ "mixed" radicals *(6)* containing both R and R' were detected in addition. The stationary concentration of the radicals *(6)* was often found to exceed that of *(5)*.

We explain these results by assuming that in the absence of H donors the electronically excited α-oxocarboxylates *(1)* undergo α-cleavage to yield acyl radicals *(2)* and the carboxyl radical *(3)*. It is suggested that the acyl radicals *(2)* are scavenged by *(1) via* addition of *(2)* to the C=O bond of *(1)* followed by decarboxylation of the intermediate adduct *(4)*. CO_2, which was identified by gas chromatography, could be isolated from photolyzed solutions of *(1)*.



$RC(O^{\ominus})=C(O^{\bullet})R'$ *(6)*

R = H, CH_3, C_2H_5, $(CH_3)_2CHCH_2$, $HO_2CCH_2CH_2$

This mechanism was tested by producing acyl radicals *(2)* independently and reacting them with α-oxo carboxylic acids.

According to *Paul* and *Fischer*[2] electronically excited ketones R'COR", where R" designates the bulkier substituent,

[*] Dr. S. Steenken and Prof. Dr. D. Schulte-Frohlinde
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
433 Mülheim (Ruhr), Stiftstrasse 34—36 (Germany)

fragment to yield acyl radicals ($R'\dot{C}O$) and alkyl radicals ($\dot{R}''$). On photolysis of ketones of this type in the presence of glyoxylic acid ($HCOCO_2H$) in aqueous solution at pH 7 under conditions where more than 99% of the light was absorbed by the ketones, only the "mixed" semidione radical anions $R'C(O^{\ominus})=C(O^{\bullet})H$ were found, in agreement with the proposed mechanism. With acetone, on the other hand, $HC(O^{\ominus})=C(O^{\bullet})H$ was formed. This finding is rationalized in terms of energy transfer from electronically excited acetone to nonhydrated glyoxylic acid followed by its decomposition according to the scheme *(1)*→→*(5)*. In the case of acetone this energy transfer can be observed since acetone undergoes α-cleavage with much lower yield than the ketones R'COR"[2].

The expected "mixed" semidione radical anions $R'C(O^{\bullet})=C(O^{\ominus})R$ were also formed predominantly when the ketones R'COR" were photolyzed in the presence of the acids $RCOCO_2H$ ($R=CH_3$, CH_3CH_2, $HO_2CCH_2CH_2$), provided the molar ratio [R'COR"]/[$RCOCO_2H$] was not lower than ≈50:1.

The mechanism presented is similar to the reactions proposed[3, 4] to account for the production of the semidione of biacetyl observed on free-radical H-abstraction from acetaldehyde. However, *Paul* and *Fischer*[2] were able to show that in this case the semidione is produced by reduction of biacetyl formed by combination of acetyl radicals.

Received: December 12, 1974 [Z 154 IE]
German version: Angew. Chem. 87, 250(1975)

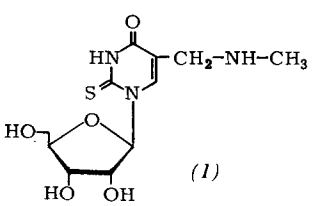
CAS Registry numbers:
(1) (R = H), 298-12-4; *(1)* ($R=CH_3$), 127-17-3;
(1) ($R=C_2H_5$), 600-18-0; *(1)* ($R=(CH_3)_2CHCH_2$), 816-66-0;
(1) ($R=HO_2CCH_2CH_2$), 328-50-7; *(2)* (R = H), 2597-44-6;
(2) ($R=CH_3$), 3170-69-2; *(2)* ($R=C_2H_5$), 15843-24-0;
(2) ($R=(CH_3)_2CHCH_2$), 31304-46-8; *(2)* ($R=HO_2CCH_2CH_2$), 52026-35-4; *(5)* (R = H), 34518-01-9; *(5)* ($R=CH_3$), 12169-49-2;
(5) ($R=C_2H_5$), 54073-26-6; *(5)* ($R=(CH_3)_2CHCH_2$), 54073-28-8;
(5) ($R=HO_2CCH_2CH_2$), 54424-14-5

[1] *R. Livingston* and *H. Zeldes*, J. Chem. Phys. *44*, 1245 (1966).
[2] *H. Paul* and *H. Fischer*, Helv. Chim. Acta *56*, 1575 (1973).
[3] *H. Zeldes* and *R. Livingston*, J. Chem. Phys. *47*, 1465 (1967).
[4] *J. R. Steven* and *J. C. Ward*, Chem. Commun. *1965*, 273.

Synthesis of 5-Methylaminomethyl-2-thiouridine, a Rare Nucleoside from t-RNA[1]

By *Helmut Vorbrüggen* and *Konrad Krolikiewicz*[*]

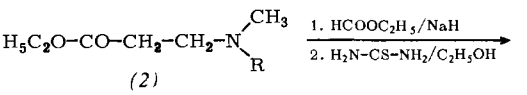
Carbon[2] isolated 5-methylaminomethyl-2-thiouridine *(1)* from *E. coli*-t-RNA and elucidated its structure, while *Nishimura*[3] detected *(1)* in the anticodon of *E. coli*-t-RNA^{Glu} We have now accomplished the first synthesis of *(1)*.



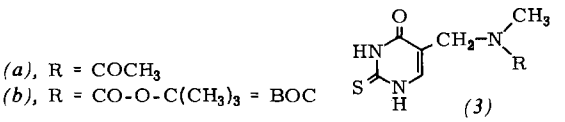
(1)

[*] Dr. H. Vorbrüggen and K. Krolikiewicz
Forschungslaboratorien der Schering AG, Berlin/Bergkamen
1 Berlin 65, Müllerstrasse 170—178 (Germany)

Acylation of ethyl 3-methylaminopropionate[4] with acetic anhydride/pyridine or with *tert*-butoxycarbonyl azide/pyridine gave *(2a)* and *(2b)* in practically quantitative yield. Formylation with ethyl formate/NaH in 1,2-dimethoxyethane and subsequent condensation *in situ* with thiourea and ethanol[5] afforded the thiouracils *(3a)*, m.p. 274—276 °C, and *(3b)*, m.p. 192—194 °C, in 55—60% yield.



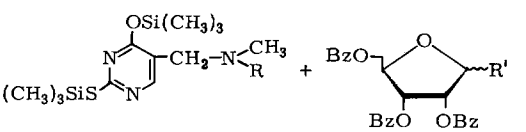
(2)



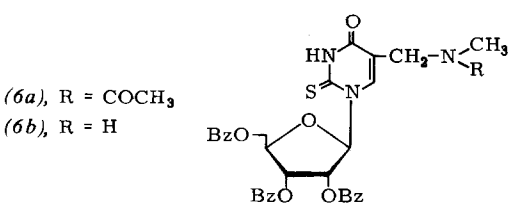
(3)

Silylation of *(3a)* and *(3b)* with hexamethyldisilazane gave the bis-silylated 2-thiouracils *(4a)* and *(4b)* almost quantitatively.

On reaction of *(4a)* with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose *(5a)*/$SnCl_4$[6] in 1,2-dichloroethane a *ca.* 70% yield of the protected nucleoside *(6a)* was obtained. However, the *N*-acetyl group in *(6a)* could not be removed by subsequent treatment with either CH_3OH/NH_3 and $NaOCH_3/CH_3OH$[5] or with 2 N HCl at 80 °C[7].



(4a), R = $COCH_3$ *(5a)*, R' = β-OAc
(4b), R = BOC *(5b)*, R' = Cl



Reaction of *(4b)* with *(5a)*/$SnCl_4$ in 1,2-dichloroethane as well as *(5b)*/$AgClO_4$[5] in benzene resulted in a *ca.* 70% yield of *(6b)* (m.p. 171—173 °C) with concomitant loss[8] of the *tert*-butoxycarbonyl group. After the reaction of *(4b)* with *(5b)*/$AgClO_4$, *(6b)* was isolated after removal of AgCl by filtration as amorphous, ether-insoluble perchlorate.

Saponification of *(6b)* with CH_3OH/NH_3 gave a 80% yield of the desired nucleoside *(1)*, which crystallized from CH_3OH/5% H_2O; m.p. 137—139 °C. $[\alpha]_D = +26.1°$ ($c=1$; H_2O); NMR (D_5-pyridine): $\delta = 2.34$ ($NH—CH_3$); 7.38 (H^1, $J = 1.5$ Hz).

On TLC comparison *(1)* was identical with an authentic sample[2, 9] in i-PrOH/NH_3/H_2O = 7:1:2 ($R_f = 0.67$) as well as in *n*-BuOH/AcOH/H_2O = 5:1:4 (upper phase, $R_f = 0.37$) on cellulose plates (F, Merck Darmstadt).

Received: December 19, 1974 [Z 155 IE]
German version: Angew. Chem. 87, 251 (1975)

CAS Registry numbers:
(1), 32860-54-1; *(2a)*, 26387-58-6; *(2b)*, 54424-07-6; *(3a)*, 54424-08-7; *(3b)*, 54424-09-8; *(4a)*, 54424-10-1; *(4b)*, 54424-11-2; *(5a)*, 6974-32-9; *(5b)*, 29706-90-9; *(6a)*, 54424-12-3; *(6b)*, 54424-13-4; ethyl 3-methylaminopropionate, 2213-08-3; *tert*-butoxycarbonyl azide, 1070-19-5; ethyl formate, 109-94-4; thiourea, 62-56-6; hexamethyldisilazane, 999-97-3; acetic anhydride, 108-24-1

[1] Synthesis of Nucleosides, Part 15. Presented on October 29, 1974 at the meeting "Nucléosides et activités biologiques" in Montpellier.—Part 14: *H. Vorbrüggen, K. Krolikiewicz,* and *U. Niedballa*, Liebigs Ann. Chem., in press.

[2] *J. Carbon, H. David,* and *M. H. Studier*, Science *161*, 1146 (1968).

[3] *Z. Ohashi, F. Harada,* and *S. Nishimura*, FEBS-Lett. *20*, 239 (1972).

[4] Obtained by addition of CH_3NH_2/EtOH to ethyl acrylate at −20 °C.

[5] *H. Vorbrüggen* and *P. Strehlke*, Chem. Ber. *106*, 3039 (1973).

[6] *U. Niedballa* and *H. Vorbrüggen*, Angew. Chem. *82*, 449 (1970); Angew. Chem. internat. Edit. *9*, 461 (1970); *U. Niedballa* and *H. Vorbrüggen*, J. Org. Chem. *39*, 3654, 3660, 3664, 3668, 3672 (1974).

[7] *Z. Ohashi, M. Maeda, J. A. McCloskey,* and *S. Nishimura*, Biochemistry *13*, 2620 (1974).

[8] The acidic properties of trimethylsilylperchlorate [*R. Wannagat* and *W. Liehr*, Angew. Chem. *69*, 783 (1957)] as well as trimethylsilyl trifluoromethanesulfonate [*H. C. Marsmann* and *H.-G. Horn*, Z. Naturforsch. *27b*, 1448 (1972)] will be discussed elsewhere.

[9] We thank Prof. *Carbon* for the authentic sample.

Synthesis of Sulfinato-*O,S* Complexes of Palladium(II)[**]

By *Ingo-Peter Lorenz, Ekkehard Lindner* and *Wolfgang Reuther*[*]

Because of their typical ambivalence, sulfinato complexes are particularly suitable as model substances for detection of various isomerization phenomena[1]. Bonding through one O (sulfinato-*O*) or one S atom (sulfinato-*S*) as well as through two O atoms (sulfinato-*O,O'*) has already been recorded[2]. There has not previously been any unambiguously proved example for the fourth type of bonding in which oxygen and sulfur are simultaneously coordinated (sulfinato-*O,S*)[3].

We have now succeeded in the first directed synthesis of sulfinato-*O,S* complexes *(2)*, by removing water from aquo complexes of palladium(II) *(1)*[4] by means of 2,2-dimethoxypropane.

$$(RS(O)_2)_2Pd(OH_2)_2 \rightleftharpoons (R(O)OS)_2Pd + 2\ H_2O \qquad (1)$$

(1)

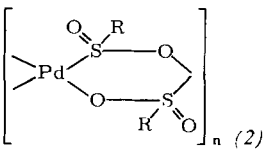
(2a), R = C_6H_5

(2b), R = p-$CH_3C_6H_4$

The compounds *(2a)* and *(2b)* form golden-yellow *diamagnetic* crystals that decompose at 90 and 120 °C, respectively; their composition and structure are proved by elemental analysis and their mass and IR spectra. The mass spectra of the hygroscopic crystals, which decompose even under nitrogen at room temperature, provide R^+, SO_2^+ and SO^+ as the relevant fission products.

In the region between 1220 and 970 cm^{-1} the IR spectra (in Nujol) show two intense absorptions (as doublets), which correspond to ν(SO) and the pseudoasymmetric SOPd stretching vibration: *(2a)*: ν(SO) = 1214 vs, 1203 vs; ν_{as}(SOPd) = 992 vs, 978 sh; *(2b)*: ν(SO) = 1212 vs, 1203 vs; ν_{as}(SOPd) = 994 vs, 975 sh. A striking feature is the unusually large frequency difference, which excludes coordination only through sulfur *or* oxygen[1a] and is characteristic of simultaneous O,S bonding.

A monomeric structure is excluded for *(2)* because the very strained three-membered ring would be unavoidable in that case. The IR spectrum and chemical behavior indicate a polymeric structure.



(2)

The RSO_2^- ligand is always bonded through sulfur to noble metals such as palladium(II) because of their "soft" character[4, 5]. If, for example, the coordinately bound water is removed from the complexes *(1)*, the coordination number 4 favored by Pd^{2+} can be achieved only if an additional Pd—O bond is provided. This is naturally very weak, as is shown in particular by the behavior of the complexes *(2)* with polar solvents. Thus reaction *(1)* is reversible and *(2)* also readily undergoes reversible addition of methanol or acetonitrile with fission of the Pd—O bond; the complexes $(RS(O)_2)_2PdL_2$ with L = CH_3OH or CH_3CN cannot be isolated, but the IR spectra, in solution, show the bands characteristic of a sulfinato-*S* linkage (*e.g.* L = CH_3CN, R = C_6H_5: $\nu_{as}(SO_2) = 1243$, $\nu_s(SO_2) = 1057\ cm^{-1}$). The Pd—O bond in *(2a)* and *(2b)* can be cleaved irreversibly by uni- or bi-dentate ligands such as $P(C_6H_5)_3$, pyridine or 2,2'-bipyridyl, with formation of the known compounds $(RS(O)_2)_2PdL_n$ (n = 1 or 2)[4].

In general, formation of sulfinato-*O,S* complexes is to be expected only in cases when a preponderatingly "soft" central atom is present which favors sulfinato-*S* bonding but undergoes an additional O-bonding in order to reach its favored coordination number (in this case 4) in the absence of a competing ligand.

Experimental:

(1a) or *(1b)* (1 mmol) is stirred with 2,2-dimethoxypropane (3 ml) and acetylacetone (3 ml) at 20 °C for 10 min under N_2, light petroleum (30 ml) is added and the crystalline product is filtered off (D3), washed with ether and dried in a vacuum. Yield: 93% of *(2a)* or 98% of *(2b)*.

Received: October 18, 1974 [Z 157 IE]
revised: November 8
German version: Angew. Chem. *87*, 251 (1975)

CAS Registry numbers:
(1a), 54515-74-1; *(1b)*, 54460-79-6; *(2a)*, 54460-76-3; *(2b)*, 54460-78-5; $(C_6H_5S(O)_2)_2Pd(CH_3CN)_2$, 54460-80-9; CH_3OH, 67-56-1; CH_3CN, 75-05-8; $P(C_6H_5)_3$, 603-35-0; pyridine, 110-86-1; 2,2'-bipyridyl, 366-18-7

[*] Prof. Dr. E. Lindner, Dr. I.-P. Lorenz, and Dipl.-Ing. W. Reuther
Lehrstuhl für Anorganische Chemie II der Universität
74 Tübingen 1, Auf der Morgenstelle (Germany)

[**] Directed Synthesis of Sulfinato-*O* and -*S* Complexes of Some Transition Metals, Part 13. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 12: [4].

[1] a) *G. Vitzthum* and *E. Lindner*, Angew. Chem. *83*, 315 (1971); Angew. Chem. internat. Edit. *10*, 315 (1971); and literature cited therein; b) *A. Wojcicki*, Accounts Chem. Res. *4*, 344 (1971); Advan. Organometal. Chem. *12*, 32 (1974), and literature cited therein.

[2] *E. Lindner, I.-P. Lorenz,* and *G. Vitzthum*, Angew. Chem. *83*, 213 (1971); Angew. Chem. internat. Edit. *10*, 193 (1971); *E. Lindner* and *I.-P. Lorenz*, Chem. Ber. *105*, 1032 (1972); *E. Lindner, I.-P. Lorenz,* and *G. Vitzthum, ibid. 106*, 211 (1973); *S. E. Jacobson* and *A. Wojcicki*, J. Organometal. Chem. *72*, 113 (1974); and literature cited therein.

[3] *J. Chatt* and *D. M. P. Mingos*, J. Chem. Soc. *A 1969*, 1770.

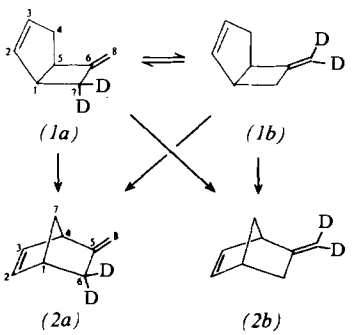
[4] *I.-P. Lorenz, E. Lindner,* and *W. Reuther*, Z. Anorg. Allg. Chem., in press.

[5] *B. Chiswell* and *L. M. Venanzi*, J. Chem. Soc. *A 1966*, 1246; *C. W. Dudley* and *C. Oldham*, Inorg. Chim. Acta *3*, 3 (1969).

Non-equilibrating Diradicals[1]: Stereochemistry of the Thermal Reorganization of Methyl-substituted 6-Methylenebicyclo[3.2.0]hept-2-enes

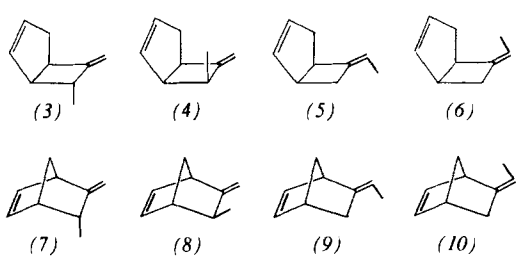
By *Dieter Hasselmann*[*]

Sigmatropic carbon migrations in bisallylic systems are the subject of intense mechanistic investigations[2]. Thermolysis of specifically deuteriated 6-methylenebicyclo[3.2.0]hept-2-enes leads, alongside a relatively slow automerization *(1a)*⇌*(1b)*, to the 5-methylenebicyclo[2.2.1]hept-2-enes *(2a)* and *(2b)*, the product of a formal [1,3]-sigmatropic rearrangement always preponderating slightly[1]. Automerization of the rearrangement products *(2a)*⇌*(2b)* occurs only at appreciably higher temperature[3].



(1a) *(1b)* *(2a)* *(2b)*

The experiments thus far performed, however, do not permit any statement with regard to the stereochemistry of the migrating carbon C^7 (or C^8). The report below concerns the thermal rearrangement of the specifically *methyl*-substituted hydrocarbons *(3)* to *(6)*.



(3) *(4)* *(5)* *(6)*

(7) *(8)* *(9)* *(10)*

At *ca.* 190°C the isomers *(3)* to *(6)* rearrange, both in solution and in the gas phase[4], in each case into one another and into the four methylated 5-methylenebicyclo[2.2.1]hept-2-enes *(7)* to *(10)*[5]. *(7)* to *(10)* can be regarded as stable under the reaction conditions since they rearrange at least 65 times more slowly than the starting material that has the lowest rearrangement rate. The isomerization rates of *(3)* to *(6)* and the product compositions in the gas phase were independent of pressure in the range studied (0.5–6 torr). Added propene or allene exerted no influence on the reaction. At any one temperature the proportions of the stable reaction products proved largely independent of time, although a change in the temperature of thermolysis did effect a change in these product ratios. These results are consistent with the assumption of a set of concurrent, uncatalyzed, unimolecular rearrangements.

Because of the interrelated rearrangements of the starting materials *(3)* to *(6)* the thermolyses follow a complex kinetic scheme of first-order reactions, which can, however, be solved numerically. Starting in each case from pure *(3)*, *(4)*, *(5)*, or *(6)* and using low conversions, we determined approximate values for all the rate constants according to the law for irreversible first-order reactions. These values were improved by extrapolation to zero time. By using these k values educt and product concentrations were calculated with numerical integration by the *Runge-Kutta* method[6] and agreed well with the concentrations found experimentally, so that even a small variation in the experimental k values led to excellent agreement. Table 1 reproduces the rate constants after improvement in this way.

For interpretation of the results three mechanistic alternatives in particular must be taken into account: 1. Competing concerted [3,3]-(Cope) and [1,3]-sigmatropic rearrangements; 2. A two-step mechanism with participation of equilibrated diradicals as intermediates; 3. A course involving non-equilibrating diradicals or diradical transition states of comparable energy ("continuous diradical"[7]).

Table 1. Rate constants [a] of thermolysis of *(3)* to *(6)* (gas phase, 189.0°C).

Educt \ Product	*(3)*	*(4)*	*(5)*	*(6)*	*(7)*	*(8)*	*(9)*	*(10)*
(3)	535.7 [b]	18.3	15.8	0.67	44.7	334.0	120.0	2.20
(4)	16.5	188.9 [b]	10.2	0.48	11.1	16.9	133.0	0.75
(5)	6.7	4.6	59.7 [b]	≈0	6.4	4.8	37.2	≈0
(6)	0.50	0.72	≈0	45.1 [b]	0.20	0.14	≈0	43.5

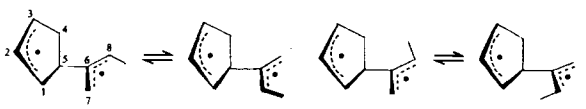
[a] $k \times 10^7 [s^{-1}]$; [b] Total decrease of the educt.

Since stereospecificity cannot be considered as a sufficient criterion[8] for orbital symmetry control[9] of a reaction, an energy gain by resonance stabilization of the aromatic transition state[10] must be demanded in addition as an essential factor. The activation energies for the decrease in amounts of *(3)* to *(6)* can be estimated from the k values (Table 1) with $\lg A = 13.5$—14 to 38—41 kcal/mol (exp. *(1)*→*(2)*: $\lg A = 13.7$, $E_a = 39.6$ kcal/mol[3]). For a hypothetical diradical process a comparable activation energy would be expected[11]. Therefore, according to this model, orbital symmetry controlled energetic assistance can be to a large extent excluded both in the framework of the Frontier Orbital Theory of *Woodward* and *Hoffman*[9] and of the *Berson-Salem* concept[14] of a "subjacent orbital" participation.

Even for thermolysis of *(1)* a significant participation of the [3,3]-sigmatropic (Cope) rearrangement could be excluded on geometrical grounds (C^3—C^8 separation >4 Å)[1]. This prediction is confirmed in this work by the finding that *(9)* is formed at comparable rates from *(3)* and *(4)*; only the reaction *(4)*→*(9)* follows formally the stereochemical course of a Cope rearrangement; and further it is precisely in the case of *(4)*, in contrast to *(3)*, *(5)* and *(6)*, that the *endo*-methyl group should make the transition state for the Cope rearrangement more difficult to reach.

[*] Dr. D. Hasselmann
Abteilung für Chemie der Universität
463 Bochum, Postfach 2148 (Germany)

The sigmatropic [1,3]-migrations *(3)*→*(7)*+*(8)*, and *(4)*→*(7)*+*(8)*, do not occur stereospecifically. This too contraindicates worthwhile resonance stabilization of an aromatic transition state in the [1,3]-rearrangement. The formally orbital symmetry forbidden product *(8)* is actually formed from *(4)* faster than is the allowed product *(7)*[15].



(11a) *(11b)* *(12a)* *(12b)*

The epimerization *(3)*⇌*(4)* requires, in one phase of the reaction, an orthogonal non-bonding relation between C^1 and C^7 and can therefore be regarded as non-concerted. Formal cleavage of the C^1—C^7 bond in *(3)* to *(6)* leads to the resonance-stabilized *cis*- and *trans*-substituted bisallyl diradicals *(11)* and *(12)*. From the product ratio *(7)*/*(8)*, as an example, one can test whether *(11a)*⇌*(11b)* and *(12a)*⇌*(12b)* are equilibrated intermediates: *(5)*→*(7)*/*(8)* = 1.33; *(6)*→*(7)*/*(8)* = 1.43. Then, independently of whatever the *cis*/*trans* ratio *(11)*/*(12)* may be, the values for *(7)*/*(8)* from *(3)* and *(4)* should be found to be between 1.33 and 1.43; however: *(3)*→*(7)*/*(8)* = 0.134; *(4)*→*(7)*/*(8)* = 0.657. The discrepancy between these product ratios is in conflict with equilibrated diradicals as intermediates, in spite of the high energetic stabilization in *(11)* and *(12)*.

Non-equilibrating diradicals offer an explanation for the experimental findings. Even in our more complex system such diradicals appear to behave as individual transition states in the sense of the "continuous diradicals" postulated by *Doering* and *Sachdev*[7]. The hypothesis is supported by the individual rate constants of the rearrangements of *(3)* to *(6)*. The diradical character of the transition states is supported by extensive utilization of the resonance stabilization of both allyl triads and by the gradual change of the rate constants for the total decrease of *(3)* to *(6)*, which reflects only a substituent effect of the methyl group (cf. Table 1). The methyl-free compound *(1)*, with $k_{-(1)} = 100.8 \times 10^{-7}\,s^{-1}$[3] fits in the middle of the series. An alternative that cannot be excluded is the existence of intermediates in flat energy troughs, where product formation competes successfully with rotation around the C^5—C^6 bond in *(11)* and *(12)*. Since the stereochemical course of the rearrangements of *(3)* to *(6)* appears to be severely influenced by the methyl substituents, investigations are in progress with substrates that a) exclude this steric factor and b) increase the flexibility of the system by ring expansion.

Received: November 13, 1974 [Z 158 IE]
German version: Angew. Chem. 87, 252 (1975)

CAS Registry numbers:
(3), 54739-12-7; *(4)*, 54774-07-1; *(5)*, 54739-13-8; *(6)*, 54739-14-9; *(7)*, 54739-15-0; *(8)*, 54739-16-1; *(9)*, 28304-67-8; *(10)*, 28304-66-7

[1] Part 2. This work was supported by the Deutsche Forschungsgemeinschaft. Part 1: *D. Hasselmann*, Tetrahedron Lett. *1973*, 3739.

[2] a) *J. A. Berson*, *T. Miyashi*, and *G. Jones*, J. Amer. Chem. Soc. *96*, 3468 (1974); b) *J. J. Gajewski*, *L. K. Hoffman*, and *C. N. Shih*, *ibid.* *96*, 3705 (1974); c) *F.-G. Klärner*, Angew. Chem. *86*, 270 (1974); Angew. Chem. internat. Edit. *13*, 268 (1974).

[3] *D. Hasselmann*, Tetrahedron Lett. *1972*, 3465.

[4] Thermolyses in solution were carried out in *n*-heptane, those in the gas phase in a 20-l Pyrex round-bottomed flask (temperature constancy better than 0.1 °C) at *ca.* 1 torr.

[5] *(3)* to *(10)* were unambiguously characterized by synthesis, elemental analysis and MS, IR, ^{1}H-NMR and FT-^{13}C-NMR spectroscopy.

[6] Cf.: *R. Zurmühl*: Praktische Mathematik für Ingenieure und Physiker (Practical Mathematics for Engineers and Physicists), 4th Edit., p. 407. Springer, Berlin 1963. I wish to thank Prof. *M. Saunders* for making his computer program available

[7] *W. von E. Doering* and *K. Sachdev*, J. Amer. Chem. Soc. *96*, 1168 (1974).

[8] Cf., *e.g.* [2c].

[9] *R. B. Woodward* and *R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).

[10] *M. J. S. Dewar*, Tetrahedron Suppl. *8*, 75 (1966); Angew. Chem. *83*, 859 (1971); Angew. Chem. internat. Edit. *10*, 761 (1971).

[11] An estimate can be made from 49.5 kcal/mol (E_a for the degenerate methylenecyclobutane rearrangement [12]) minus 12—13 kcal/mol [13] (for the allyl resonance energy of $C^1C^2C^3$).

[12] *W. von E. Doering* and *J. C. Gilbert*, Tetrahedron Suppl. 7, 397 (1966).

[13] *W. von E. Doering* and *G. H. Beasley*, Tetrahedron *29*, 2231 (1973); *W. R. Roth*, *G. Ruf*, and *P. W. Ford*, Chem. Ber. *107*, 48 (1974).

[14] *J. A. Berson* and *L. Salem*, J. Amer. Chem. Soc. *94*, 8917 (1972).

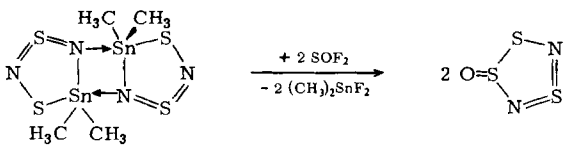
[15] The [1,3]-rearrangement of the analogous 6-acetate gives a similar result: *J. A. Berson* and *G. N. Nelson*, J. Amer. Chem. Soc. *92*, 1096 (1970).

N_2S_3O—The First Oxide of a Five-Membered Sulfur-Nitrogen Ring[**]

By *Herbert W. Roesky* and *Hartmut Wiezer*[*]

The recent synthesis of $N_4S_4O_4$[1] has raised the question whether oxides of cyclic SN compounds containing less than six ring members can be prepared.

$(CH_3)_4Sn_2N_4S_4$ *(1)*[2,4], prepared from S_4N_4 and $[(CH_3)_3Sn]_3N$ by reaction in a molar ratio of 1:1, reacts with SOF_2 with elimination of $(CH_3)_2SnF_2$ according to



(1) *(2)*

The reaction product having the composition N_2S_3O *(2)* is isolated as a red liquid which can be vacuum-distilled without decomposition (b.p. 50 °C/0.01 torr); it does not wet glass. No signs of decomposition were observed, even after storage for several weeks at room temperature. In contrast, the previously known isomer formulated as $(S{=}N)_2SO$ is readily decomposable[4].

The structure of the new compound was elucidated by elemental analysis, IR spectrum, and mass spectrum.

The molecular ion is observed at *m/e* 140 with a relative intensity of 11%, accompanied by the following fragments *m/e* 94 NS_2O (4%), 92 N_2S_2 (4%), 80 S_2O (10%), 78 S_2N (28%), 76 N_2SO (12%), 64 $S_2(SO_2)$ (50%), 60 N_2S (8%), 48 SO (46%), and 46 NS (100%).

In the IR spectrum (cm^{-1}) the band at 1125 vs could be assigned to the SO stretching mode, and those at 981 s, 910 s, and 734 s to the ring skeleton. Further absorptions were registered at 1181 m, 663 s, and 583 m.

Procedure:

An excess of SOF_2 is passed into a suspension of *(1)* (9.9 g) in CH_2Cl_2 (600 ml). The mixture is then stirred for 3 h, the

[*] Prof. Dr. H. W. Roesky and Dr. H. Wiezer
Anorganisch-chemisches Institut I der Universität
6 Frankfurt am Main 50, Niederurseler Hang (Germany)

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

insoluble $(CH_3)_2SnF_2$ filtered off, the solvent removed *in vacuo*, and the residue distilled. Yield: 4.1 g (70%) of *(2)*.

Received: October 15, 1974;
revised: November 14, 1974 [Z 159 IE]
German version: Angew. Chem. *87*, 254 (1975)

CAS Registry numbers:
(1), 54517-19-0; *(2)*, 54460-74-1; SOF_2, 7783-42-8

[1] *H. W. Roesky* and *O. Petersen*, Angew. Chem. *84*, 946 (1972); Angew. Chem. internat. Edit. *11*, 918 (1972).

[2] According to structural studies by *B. Krebs*, Bielefeld, the compound has an almost planar cyclic skeleton with Sn—N distances of 2.135 and 2.316 Å; the Sn—S distance of 2.603 Å is remarkably long. *(1)* is the first SnN four-membered ring whose structure has been determined by X-ray methods [3].

[3] Cf. *D. Hänssgen* and *I. Pohl*, Angew. Chem. *86*, 676 (1974); Angew. Chem. internat. Edit. *13*, 607 (1974).

[4] *A. Meuwsen* and *M. Lösel*, Z. Anorg. Allg. Chem. *271*, 220 (1953).

Vinyllithium and 1,4-Dilithiobutane from Ethylene and Lithium

By *Valentin Rautenstrauch*[*]

Procedure:

A solution of biphenyl (70 mg, 0.45 mmol) and naphthalene (10 mg, 0.08 mmol) in dimethoxymethane (DMM) (2 ml) is stirred at room temperature (RT) in a Schlenk tube under argon with lithium pieces (*ca.* 500 mg, 72 mmol) until the solution turns dark brown (2—10 min). The stirred mixture (RT) is then diluted with DMM (18 ml) over a period of *ca.* 1 h, and stirring is continued for another 30 min. A 2 l flask containing ethylene (normal pressure, *ca.* 90 mmol) is fitted to the Schlenk tube, ethylene is condensed into the solution by cooling it to *ca.* −110 °C, and the system is brought to normal pressure by introduction of argon. The solution is then stirred with the lithium for *ca.* 20 h at −10 °C. The Schlenk tube and the 2 l flask form a closed system; the gas mixture over the cooled solution remains at RT. The solution then contains 3.0 mmol of vinyllithium *(3)*, 1.2 mmol of 1,4-dilithiobutane *(5)*, 0.04 mmol of 1,6-dilithiohexane *(6)*, 0.04 mmol of 3-butenyllithium *(7)*, 0.07 mmol of butyllithium *(8)*, and probably at least 3.3 mmol of lithium hydride *(4)* (along with biphenyl, naphthalene, products derived therefrom, and unreacted lithium).

None of these products is formed at lower temperatures (below −30 °C); *(5)* is not stable at higher temperatures (RT and above).

The organolithium compounds were identified by the usual derivatizations, with ketones, CO_2, and chlorosilanes. Definite proof for the presence of lithium hydride *(4)* is still lacking. After reaction with phenyldimethylchlorosilane *(9)*, phenyldimethylsilane *(10)* can be isolated; *(10)* is probably formed by reaction of *(4)* with *(9)*[1].

Interpretation and Discussion:

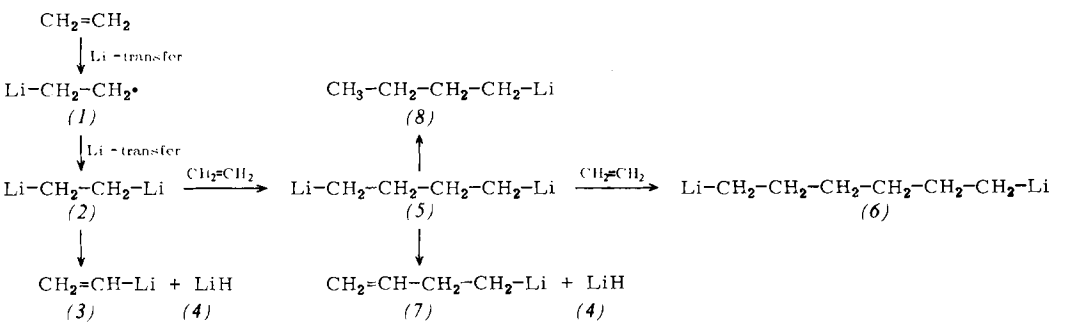
A transfer of lithium to ethylene takes place. This leads to the formation of one or several reactive short-lived intermediates. These react to give vinyllithium *(3)*, lithium hydride *(4)*, and 1,4-dilithiobutane *(5)*. Two parallel overall reactions (1) and (2) can be formulated.

$$\underset{}{CH_2{=}CH_2} + 2\,Li \longrightarrow \underset{(3)}{CH_2{=}CH{-}Li} + \underset{(4)}{LiH} \qquad (1)$$

$$2\,CH_2{=}CH_2 + 2\,Li \longrightarrow \underset{(5)}{Li{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}Li} \qquad (2)$$

The structures and mechanisms which play a role in these reactions are largely unknown. In particular, it is not known in what way the system biphenyl/naphthalene/lithium is involved in the transfer process[2].

Transfer of lithium to ethylene should lead to an "ethylene anion radical with lithium cation as the counterion" *(1)*[3] and perhaps also to a "1,2-dilithioethane" *(2)*[3]. An obvious hypothesis is that *(1)* and/or *(2)* are intermediates in our reactions (see scheme). It is striking that both a decomposition[4] of *(2)* into vinyllithium *(3)* and lithium hydride *(4)* and an addition of ethylene[5] to *(2)*, which would give 1,4-dilithiobutane *(5)*, would have direct analogies in the behavior of "normal" alkyllithium compounds. Both reactions would bring about a separation of the neighboring charges in *(2)*, and would therefore be especially favored.



Precisely this "normal" behavior is observed in the slow further reactions of 1,4-dilithiobutane *(5)* (scheme). Addition of ethylene leads to the next higher homolog[6], 1,6-dilithiohexane *(6)*, and loss of lithium hydride gives 3-butenyllithium *(7)*; in addition, *(5)* metalates the solvent with formation of butyllithium *(8)*.

To our knowledge, compounds of type *(1)* are unknown, and compounds of type *(2)* have not been identified conclusively[7]; no theoretical studies have been carried out on *(1)* and *(2)*. The overall reaction (1) has parallels in known reactions[8]; reaction (2) is novel.

The postulated formation of *(1)* and *(2)* is plausible. Lithium is a very powerful reducing agent in donor solvents and can form electron-deficient multicenter bonds with carbon; *(2)* would entail two bonds to primary carbon atoms.

[*] Dr. V. Rautenstrauch
Firmenich SA, Research Laboratory
CH-1211 Genève 8, B. P. 239 (Switzerland)

Received: November 17, 1974;
revised: January 13, 1975 [Z 160 IE]
German version: Angew. Chem. *87*, 254 (1975)

CAS Registry numbers:
$CH_2{=}CH_2$, 74-85-1; Li, 7439-93-2; *(2)*, 13067-82-8; *(3)*, 917-57-7; *(5)*, 2123-72-0; *(6)*, 2223-57-6; *(7)*, 14660-39-0; *(8)*, 109-72-8

[1] Authentic *(4)*, which is certainly less finely divided and covered by a hydroxide layer, does not react with *(9)* under these conditions.

[2] Biphenyl *(11)* appears to be the active "carrier". The reactions described proceed approximately as fast in the presence of *(11)* alone under otherwise identical conditions; however, reaction of lithium with *(11)* alone does not start easily in DMM. They also seem to occur in the presence of naphthalene alone, but are then much slower (small amounts of stable *(3)* can be detected). In the absence of *(11)* and of naphthalene no detectable reaction takes place. Action of Li on *(11)* in aprotic donor solvents such as DMM affords solutions containing equilibrium mixtures of biphenyllithium *(12)*, and possibly also biphenyldilithium *(13)* with *(11)* and lithium. [Reviews: *V. Kalyanaraman* and *M. V. George*, J. Organometal. Chem. *47*, 225 (1973); *N. L. Holy*, Chem. Rev. *74*, 243 (1974); see also: *D. F. Lindow*, *C. N. Cortez*, and *R. G. Harvey*, J. Amer. Chem. Soc. *94*, 5406 (1972)]. At present we consider two mechanisms (formulated for *(11)* as the carrier): 1) *(12)* and/or *(13)* transfer electrons and lithium cations to ethylene [see *M. Szwarc*: Carbanions, Living Polymers, and Electron Transfer Processes. Wiley-Interscience, New York 1968]. 2) Lithium which reacts directly with ethylene is formed (surface activation, transport into solution) in the reaction system $2\,Li + (11) \rightleftarrows Li + (12) \rightleftarrows (13)$. Transfer activity of the carriers [*(11)* is active, naphthalene weakly active, anthracene inactive] and the energy of their lowest antibonding molecular orbital [see *A. Streitwieser*, Jr.: Molecular Orbital Theory for Organic Chemists. Wiley-Interscience, New York 1968, p. 425] would seem to be related.

[3] As usual in this field we use names and formulas which symbolize the true structures, all of which are unknown. In the case of *(1)* the choice is particularly arbitrary. Possible structures are: *(1)*: ion pair, 2-lithioethyl radical and aggregated structures derived from both; *(2)*: monomeric covalent *(2)* and a cluster structure; *(5)*: cluster structure.

[4] *K. Ziegler* and *H.-G. Gellert*, Liebigs Ann. Chem. *567*, 179 (1950); *R. A. Finnegan* and *H. W. Kutta*, J. Org. Chem. *30*, 4138 (1965).

[5] *P. D. Bartlett*, *C. V. Goebel*, and *W. P. Weber*, J. Amer. Chem. Soc. *91*, 7425 (1969); *A. Maercker* and *W. Theysohn*, Liebigs Ann. Chem. *747*, 70 (1971).

[6] We have indications that higher homologs are also formed in decreasing amounts, *i. e.* we observe the initial steps of a "polymerization" of ethylene [see *K. Clusius* and *H. Mollet*, Helv. Chim. Acta *39*, 363 (1956)]. The first insertion $(2) \rightarrow (5)$ is faster than subsequent ones: the homologs undergo partial decomposition by loss of lithium hydride and by reaction with the solvent (scheme).

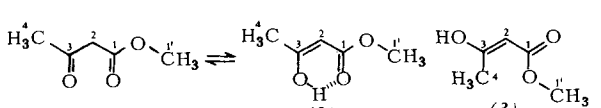
[7] *H. Kuus*, Uch. Zap. Tartu Gos. Univ. *1966*, 133 [Chem. Abstr. *69*, 67443 (1968)]; *1968*, 245 [Chem. Abstr. *71*, 49155 (1969)].

[8] In the absence of solvent certain 1-alkenes react at 20—120 °C with lithium suspension to form *(4)* and the corresponding 1-lithio-1-alkynes and 1-lithio-1-alkenes can be detected as unstable intermediates: *D. L. Skinner*, *D. J. Peterson*, and *T. J. Logan*, J. Org. Chem. *32*, 105 (1967).

Detection of the *trans*-Enol in Methyl Acetoacetate by ^1H- and ^{13}C-NMR Spectroscopy

By *Rudolf Matusch*[*]

The keto-enol tautomerism of methyl acetoacetate $(1) \rightleftarrows (2)$ has been thoroughly studied and the position of the equilibrium determined in numerous ways[1]. However, the *trans*-enol form *(3)*, which should exist alongside the keto form *(1)* and the hydrogen-bonded *cis*-enol form *(2)*, has not hitherto been detected. Since energy values of up to 10 kcal/mol are reported[2] for the hydrogen bond in *(2)*, the form *(3)* would appear to be at a considerable disadvantage.



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

Nevertheless, *(3)* can be enriched in yields of up to 15% very simply by distillation of acetoacetic ester at normal pressure; the rest of the distillate consists of *(1)* and *(2)*. If distillation is performed at reduced pressure no *trans*-enol *(3)* can be detected. Attempted photochemical *cis-trans* isomerization of *(2)* to *(3)* was unsuccessful.

Form *(3)* can be detected by neither UV nor IR spectroscopy[4]. Even with the aid of ^1H-NMR spectroscopy *(3)* can only be recognized on use of anisotropic solvents (Table 1).

Table 1. ^1H-NMR data (δ(TMS) = 0 ppm, coupling constants in Hz), [5] and ^{13}C-NMR data (TMS = 0 ppm) [7] of acetoacetic ester *(1)*, the *cis*-enol form *(2)*, and the *trans*-enol form *(3)*.

	^1H-NMR				
	CH_3	CH_2	OCH_3	Vinyl-H	OH
(1)	1.93 t $J = 0.50$	3.16 m	3.46 t $J = 0.18$		
(2)	1.69 d $J = 0.74$		3.49 s	4.91 q $J = 0.74$	12.60 s
(3)	2.28 d $J = 0.60$		3.26 d $J = 0.46$	4.99 qq $J = 0.60$, $J = 0.46$	
	^{13}C-NMR				
	C-1	C-2	C-3	C-4	C-1′
(1)	167.89	49.72	200.25	29.70	51.91
(2)	173.19	89.73	176.33	20.89	55.29
(3)	168.11	91.03	173.46	18.78	50.52

Support for the conformation proposed for *(3)* comes from a comparison of the coupling constants in *(2)* and *(3)*. The decrease in the allyl coupling constant can be regarded as indicative of isomerization about the double bond; the increase in the coupling constant between the ester methyl group and the vinylic proton from an unmeasurable value to 0.46 Hz can be explained by the W arrangement of the bonds involved in the coupling in form *(3)*.

Unequivocal confirmation of the existence of forms *(1)*, *(2)*, and *(3)*[6] is further provided by the ^{13}C-NMR spectrum[7] (Table 1).

Since changes in the charge density at the carbon atom are known from experience to cause marked shifts of the ^{13}C resonance frequencies, we have here a particularly impressive demonstration of the difference in the electron-withdrawing effect of the hydroxy group with [*(2)*] and without [*(3)*] hydrogen bonding.

Received: January 9, 1975 [Z 167 IE]
German version: Angew. Chem. *87*, 283 (1975)

CAS Registry numbers:
(1), 105-45-3; *(2)*, 4525-25-1; *(3)*, 4525-24-0

[1] a) *H. Grossmann*, Z. Phys. Chem. *109*, 305 (1924); b) *C. Giessner-Prettre*, C. R. Acad. Sci. *250*, 2547 (1960); c) *J. L. Burdett* and *M. T. Rogers*, J. Amer. Chem. Soc. *86*, 2105 (1964).

[2] *M. A. Dollivier*, *T. L. Gresham*, *G. B. Kistiakowsky*, *E. A. Smith*, and *W. E. Vaughan*, J. Amer. Chem. Soc. *60*, 440 (1938).

[3] "Spaltrohr" column HMS 500, Fischer Bonn-Bad Godesberg.

[4] This applies to the IR spectrum of a capillary film. A series of dilutions has not yet been measured.

[5] 60 MHz spectrum, Varian A-60A, 30% in D_8-toluene; δ(TMS internal) = 0.00 ppm, measuring temp. 40 °C.

[6] The expression "tautomeric forms" has been purposely avoided here since only *(1)* and *(2)* are tautomers in the usual sense: *R. Matusch*, to be published.

[7] 20 MHz spectrum, noise decoupled; Varian CFT-20, 30% in D_6-benzene.

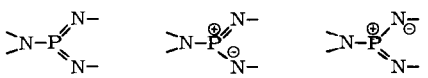
[*] Dr. R. Matusch
Fachbereich Pharmazie und Lebensmittelchemie der Universität
355 Marburg, Marbacher Weg 6 (Germany)

Phosphorus(V) Having Trigonal Planar Coordination

By *Siegfried Pohl, Edgar Niecke*, and *Bernt Krebs*[*]

The σ-bond skeletons of four- to six-coordinate phosphorus can generally be described with the aid of tetrahedra, trigonal bipyramids, and octahedra[1]. Occupation of only three coordination sites leading to planar coordination has hitherto only been postulated for unstable intermediates on the basis of stereochemical and kinetic studies[2].

The synthesis[3] of a phosphorus(V) derivative stabilized by $p_\pi-p_\pi$ bonds and having the composition $(R_3Si)_2NP(NSiR_3)_2$ with $R=CH_3$ has now provided an opportunity to establish, by complete X-ray structural analysis, whether trigonal planar coordination of phosphorus exists in a stable compound. We also wished to examine to what extent the polar resonance structures *(2a)* and *(2b)* should feature alongside *(1)* in descriptions of the bonding in aminodiiminophosphorane.



(1) *(2a)* *(2b)*

Bis(trimethylsilyl)aminobis(trimethylsilylimino)phosphorane[3], m.p. 46 °C, forms monoclinic crystals of space group C2/c having the lattice constants (at 18 °C) $a=17.905$, $b=10.654$, $c=13.236$ Å; $\beta=109.27°$; $V=2383$ Å^3; $Z=4$.

The structure was solved from diffractometer data by the direct method of symbolic addition. Least squares refinement with the structure factors of 1045 reflections observed at 18 °C converged to an R value of 4.3%.

In the solid state the molecule has C2 symmetry. The central phosphorus atom exhibits a planar threefold coordination to nitrogen atoms. The uncorrected P—N bond lengths are 1.503 and 1.646 Å (Fig. 1). The P—N_{imine} distances, which

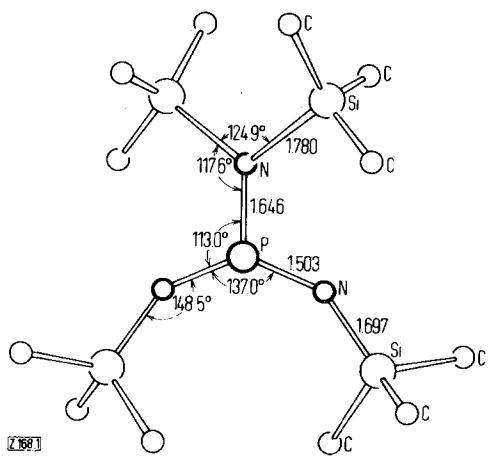


Fig. 1. Molecular structure of bis(trimethylsilyl)aminobis(trimethylsilylimino)-phosphorane in the crystal (bond lenghts in Å).

correspond formally to double bonds, lie at the lower limit of all known values for PN bonds[4]. Apparently, planarity favors particularly strong π bonds which probably also contribute to the stabilization of the coordinatively unsaturated phosphorus. Thus any significant weight of the polar resonance structures can be ruled out.

The P—N_{amine} bond is significantly shorter than a single bond (1.77 Å in $NaPO_3NH_3$[5]). The strengthening of this bond can be explained by $d_\pi-p_\pi$ interaction between phosphorus and amine nitrogen. Although the $N(SiR_3)_2$ group is twisted by about 32° out of the PN_3 plane the participation of d orbitals still permits this kind of overlapping. Similar effects are probably responsible for the shortening of the Si—N_{imine} bonds (1.697 Å) whereas the amine nitrogen is linked to silicon by a normal single bond (1.780 Å). The strengthening of the Si—N_{imine} π bond is in accord with the increase in the PNSi angle to 148.5°.

The Si—C bond lengths average about 1.871 Å. Successful localization of all the H atoms shows that the methyl groups are sterically fixed.

A supplementary low temperature study is in progress.

Received: November 27, 1974 [Z 168 IE]
German version: Angew. Chem. 87, 284 (1975)

CAS Registry numbers:
Bis(trimethylsilyl)aminobis(trimethylsilylimino)phosphorane, 52111-28-1

[1] A square pyramidal geometry has also been observed for pentacoordinate phosphorus in a spirocyclic structure: *J. A. Howard, D. R. Russell*, and *S. Trippett*, J. C. S. Chem. Comm. *1973*, 856.
[2] *J. Wiseman* and *F. H. Westheimer*, J. Amer. Chem. Soc. *96*, 4262 (1974); and references cited therein.
[3] *E. Niecke* and *W. Flick*, Angew. Chem. *86*, 128 (1974); Angew. Chem. internat. Edit. *13*, 134 (1974); *O. J. Scherer* and *N. Kuhn*, Chem. Ber. *107*, 2123 (1974).
[4] *H. R. Allcock:* Phosphorus-Nitrogen Compounds. Academic Press, New York 1972.
[5] *D. W. J. Cruickshank*, Acta Crystallogr. *17*, 671 (1964).

Lithium Tetraphenyl- and Tetramethylniccolate(II)

By *Rudolf Taube* and *Gerd Honymus*[*]

Simple binary σ-organylnickel(II) compounds NiR_2 generally display pronounced thermal lability. Thus $Ni(CH_3)_2$ already decomposes below −100 °C[1]. The only stable compounds capable of isolation have so far proved to be those containing bulky carbanions devoid of β-hydrogens, such as $Ni[C(C_6H_5)_3]_2$[2] and $Ni[C_6H_2(CH_3)_3]_2$[3].

A considerable stabilization, regardless of the organyl group, is known to occur on complexation, and numerous σ-organyl complexes of the general type NiR_2L_n, $NiR(X)L_n$, and $cpNiRL_n$ have been described[4].

Our attempts to prepare chelate complex-stabilized monoorganylnickel compounds led us to the tetraorganyl complexes $Li_2[Ni(C_2C_6H_5)_4]\cdot 4$ THF *(1)*, $Li_2[Ni(C_6H_5)_4]\cdot 4$ THF *(2)*, and $Li_2[Ni(CH_3)_4]\cdot 2$ THF *(3)*, of which *(2)* and *(3)* represent the hitherto unisolable pure phenyl- and methylnickel(II) combinations stabilized by "ate" complex formation.

For their synthesis, $Ni(dpi)_2$[5] (dpi = anion of 1,3-bis(2-pyridylimino)isoindoline) was added at −78 °C to a solution of $LiC_2C_6H_5$ in THF/hexane or of LiC_6H_5 or $LiCH_3$ in THF/ether and the mixture shaken with warming to room temperature until reaction was complete (*ca.* 1—2 h). Compounds *(1)*, *(2)*, and *(3)* are deposited as small lustrous crystals from the brown solutions; they are filtered off, washed, and recrystallized from THF/hexane [*(1)*] or from THF [*(2)* and *(3)*] by hot extraction[8]. Yield: *(1)*, 65%; *(2)*, 60%; and *(3)*, 56%.

[*] Prof. Dr. B. Krebs and Dr. S. Pohl
Fakultät für Chemie der Universität
48 Bielefeld, Universitätsstrasse (Germany)
Dr. E. Niecke
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstrasse 4 (Germany)

[*] Prof. Dr. R. Taube and Dipl.-Chem. G. Honymus
Sektion Verfahrenschemie der Technischen Hochschule "Carl Schorlemmer" Leuna-Merseburg
DDR—42 Merseburg, Geusaer Strasse (German Democratic Republic)

Properties of *(1)*: beige crystals, decomposition with dark discoloration above 90 °C, soluble in THF. *(2)*: yellowish crystals, decomposition at 102—103 °C, moderately soluble in THF. Protolysis with cyclohexanol affords (alongside THF) benzene and biphenyl, and reaction with iodine in THF, with consumption of 4.15 I/Ni, exclusively biphenyl. *(3)*: golden-yellow lustrous crystals, decomposition at 129—130 °C, soluble in ether, more so in THF. Protolysis with butanol affords CH_4 (94%). Reaction with iodine in THF with consumption of 4.1 I/Ni gives CH_4 (35%), C_2H_6 (64%), and C_2H_4 (1%).

The strongly air- and moisture-sensitive new complexes are diamagnetic and therefore have planar coordination. Compared with the previously known solvate-free potassium salt[6], complex *(1)* is characterized by its better solubility and enhanced stability. Complexes *(2)* and *(3)* demonstrate that planar NiC_4 coordination can be achieved not only with sp but also with sp^2 and sp^3 hybridized carbon. The relatively high thermal stability, particularly of the methyl compound, contradicts the frequently cited Chatt-Shaw "π-bonding effect"[7], whose significance for the stability of the transition metal-carbon bond is frequently overestimated. The choice of a suitable nickel(II) chelate complex as starting compound is of essential importance in the preparation of *(2)* and *(3)*. When $NiBr_2 \cdot 2$ THF was used only about 2% of *(3)* could be isolated alongside metallic nickel. This demonstrates the great importance of the synthetic pathway for organo-transition-metallic compounds, the success of the present method apparently resting upon adequate complex-chemical stabilization of the nickel-carbon bond in all the intermediates of organylation.

Received: November 28, 1974 [Z 169 IE]
German version: Angew. Chem. 87, 291 (1975)

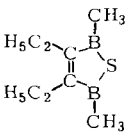
CAS Registry numbers:
(1), 54712-91-3; *(2)*, 54688-82-3; *(3)*, 54688-83-4;
$Ni(dpi)_2$, 15134-62-0; $LiC_2C_6H_5$, 4440-01-1; LiC_6H_5, 591-51-5;
$LiCH_3$, 917-54-4

[1] *K. Fischer, K. Jonas, P. Misbach, R. Stabba*, and *G. Wilke*, Angew. Chem. *85*, 1002 (1973); Angew. Chem. internat. Edit. *12*, 943 (1973).
[2] *G. Wilke* and *H. Schott*, Angew. Chem. *78*, 592 (1966); Angew. Chem. internat. Edit. *5*, 581 (1966).
[3] *G. Wilke*, Pure Appl. Chem. *17*, 179 (1968).
[4] *D. R. Fahey*, Organometal. Chem. Rev. *7*, 245 (1972).
[5] *M. A. Robinson, S. I. Trotz*, and *T. J. Hurley*, Inorg. Chem. *6*, 392 (1967).
[6] *R. Nast*, Angew. Chem. *72*, 26 (1960).
[7] *J. Chatt* and *B. L. Shaw*, J. Chem. Soc. *1960*, 1718.
[8] *(2)* at reduced pressure.

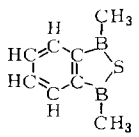
1-5-η-Benzothiadiborolenetricarbonyliron—A Complex Having a Fixed π-Electron System in the Benzene Ring[1]

By *Walter Siebert, Gunther Augustin, Roland Full, Carl Krüger*, and *Yi-Hung Tsay*[*]

1,2,5-Thiadiborolenes have both Lewis-acid and Lewis-base character. *(1)*[2] and *(2)*[3] react with $Fe_2(CO)_9$ and $Fe_3(CO)_{12}$ to give red thiadiborolenecarbonyliron complexes formulated as tricarbonyl derivatives *(1)*·$Fe(CO)_3$ and *(2)*·$Fe(CO)_3$ on the basis of analytical and mass-spectrometric data. However, for *(2)*·$Fe(CO)_3$ this implies that the "aromatic" acts as an unusual two-electron donor, which should lead to a loss of π-electron delocalization and fixation of the π bonds in the annelated benzene ring.



(1)



(2)

Spectroscopic findings (Table 1) confirm the participation of two π electrons of the benzene ring in complexation. It follows from the marked upfield shift of the ^{11}B-NMR signal by 51 ppm that the boron atoms interact with the $Fe(CO)_3$ group to a greater extent than in the previously known thiaborane-metal complexes $B(SCH_3)_3 \cdot Cr(CO)_3$ (41 ppm)[4] and $(CH_3)_2BSCH_3 \cdot Cr(CO)_5$ (21 ppm)[5].

Table 1. Spectroscopic data of *(1)* and *(1)*·$Fe(CO)_3$, and *(2)* and *(2)*·$Fe(CO)_3$.

(1)	*(1)*·$Fe(CO)_3$	*(2)*	*(2)*·$Fe(CO)_3$
^{1}H-NMR, δ [ppm] rel. to TMS			
(in CCl_4)		(in $CDCl_3$)	
−0.95 (s, 6)	−0.83 (s, 6)	−1.31 (s, 6)	−1.14 (s, 6)
−0.90 (tr, 6)	−1.17 (tr, 6)	−7.46 (m, 2)	−7.12 (m, 2)
−2.20 (qu, 4)	−2.10 (m, 4)	−7.63 (m, 2)	−7.33 (m, 2)
(J = 7.6 Hz)	(J = 7.6 Hz)		
^{11}B-NMR, δ [ppm] rel. to $(C_2H_5)_2O \cdot BF_3$			
(in CCl_4)		(in $CDCl_3$)	
−66.2	−27.8	−77.2	−26.4
IR, ν(CO) [cm^{-1}] in CCl_4			
	2060 (s)		2060 (s)
	1990 (vs)		1990 (vs)

The IR spectra show two bands for the $Fe(CO)_3$ group in the ν(CO) region, and changes in the region of C=C vibrations, on going from the free ligand to the complex. In the ^{1}H-NMR spectrum all signals are shifted upfield, thus indicating an enhanced electron density on boron and a weakening of the aromatic character of the benzene ring. Owing to relaxation effects, the two C atoms engaged in complex bonding and the CH_3—B group cannot be observed in the ^{13}C-NMR spectrum. The remaining signals undergo a slight upfield shift; the ^{13}C resonances coincide to give just one signal: −211.1 and −210.4 ppm for *(2)*·$Fe(CO)_3$ and *(1)*·$Fe(CO)_3$ respectively (relative to TMS in $CDCl_3$).

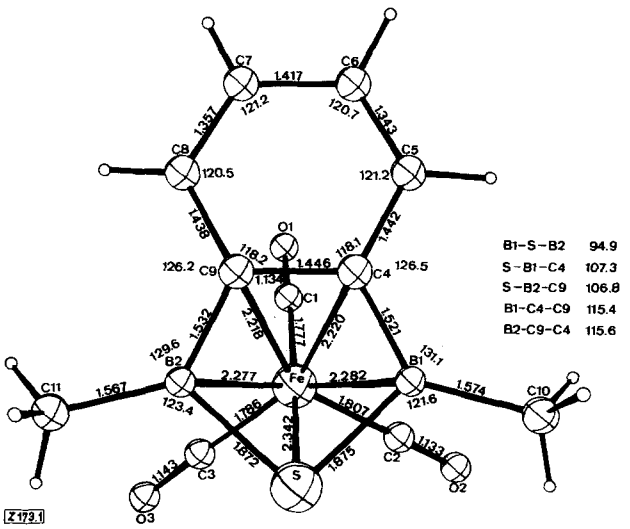
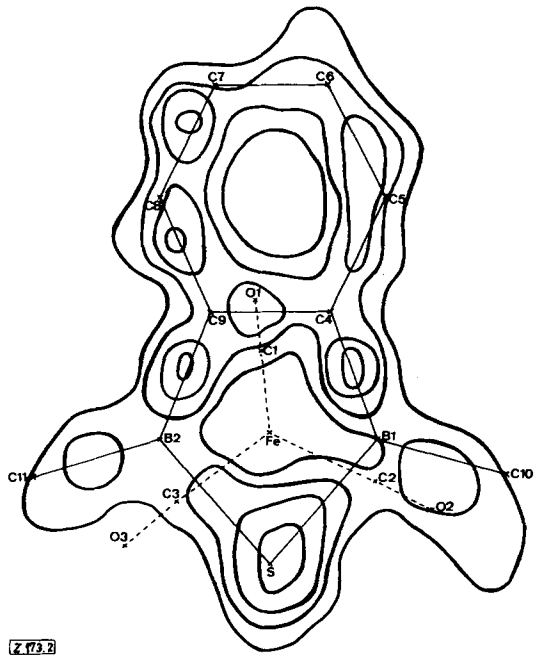


Fig. 1. Molecular structure of benzo-1,2,5-thiadiborolenetricarbonyliron. Maximum error ± 0.004 Å and ± 0.02°.

[*] Prof. Dr. W. Siebert, Dipl.-Chem. G. Augustin, and R. Full
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)
Dr. C. Krüger and Dr. Y.-H. Tsay
Max-Planck-Institut für Kohlenforschung
433 Mülheim-Ruhr, Lembkestrasse 5 (Germany)

The structure of a *pentahapto*-thiadiborolenetricarbonyliron complex deduced from the spectroscopic data is confirmed by X-ray structure analysis of *(2)*·$Fe(CO)_3$ (Fig. 1).

Crystal data: $a=9.221(3)$, $b=9.322(2)$, $c=9.529(2)$ Å; $\alpha=69.66(2)$, $\beta=72.08(2)$, $\gamma=60.71(3)°$; $Z=2$; $d_{calc}=1.507$ g cm^{-3}; space group $P\bar{1}$. Refined from 2848 measured structural amplitudes (763 unobserved; Nonius CAD 4 diffractometer) including hydrogen atoms to an R value of 0.0262 ($R_w=0.0364$)[6].



Z 173.2

Fig. 2. π-Electron density in benzo-1,2,5-thiadiborolenetricarbonyliron. Contours in 0.1 e Å^{-3}.

The bond lengths in the ring system unequivocally establish the fixation of the π-electron system as cyclohexatriene with formation of a long π bond to the iron. Figure 2 shows a difference Fourier synthesis through the best plane (±0.02 Å) of the thiadiborolene ring; the Fourier coefficients were obtained on refinement of all atoms except hydrogen with 1468 reflections ($\sin\theta/\lambda=0.5$, $R=0.0305$, $\lambda_{Mo}=0.71069$ Å) The π-electron densities accord with the bond lengths found. The appearance of π-electron density in the B1—C4 and B2—C9 bonds warrants particular attention. The relatively long B—S bonds (1.874 Å) exceed those in trithiaborolanes[7] (1.803 Å) and thiaborins[8] (1.807 Å). Expectedly, a CO group on the iron is positioned *trans* to the sulfur.

Procedure:

Compound *(2)* is reacted with dodecacarbonyltriiron (molar ratio 1:1) in boiling toluene (1.5 h). After removal of solvent the dark red product is sublimed at 50 °C/0.01 torr and recrystallized from pentane at −10 °C. Yield 67%, m. p. 82—84 °C (dec.).

Received: December 2, 1974;
revised: December 20, 1974 [Z 173 IE]
German version: Angew. Chem. 87, 286 (1975)

CAS Registry numbers:
(1), 54677-51-9; *(2)*, 51926-30-8; *(1)*-$Fe(CO)_3$, 54688-79-8; *(2)*-$Fe(CO)_3$, 54688-80-1

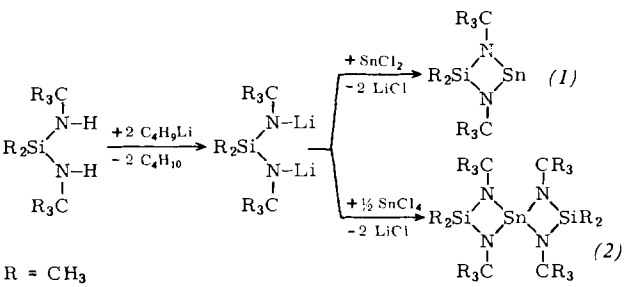
[1] Diboron Compounds as Ligands in Metal Complexes, Part 1.
[2] *W. Siebert* and *R. Full*, to be published; *W. Siebert*, Chem. Ztg. Chem. App. *98*, 479 (1974).
[3] *B. Asgarouladi, R. Full, K.-J. Schaper*, and *W. Siebert*, Chem. Ber. *107*, 34 (1974).
[4] *H. Nöth* and *U. Schuchardt*, J. Organometal. Chem. *24*, 435 (1970).
[5] *U. Schuchardt*, Dissertation, Universität München 1973; *W. Erl* and *H. Vahrenkamp*, Chem. Ber. *103*, 3563 (1970).
[6] For measurement and calculation techniques see *C. Krüger*, Angew. Chem. *84*, 412 (1972); Angew. Chem. internat. Edit. *11*, 387 (1972); *D. J. Brauer, C. Krüger, P. J. Roberts*, and *Y.-H. Tsay*, Chem. Ber. *107*, 3706 (1974).
[7] *H. M. Seip, R. Seip*, and *W. Siebert*, Acta Chem. Scand. *27*, 15 (1973); *A. Almenningen, H. M. Seip*, and *P. Vassbotn*, *ibid.* *27*, 21 (1973).
[8] *W. Schwarz, H. D. Hausen, H. Hess, M. Mandt, W. Schmelzer*, and *B. Krebs*, Acta Crystallogr. *B 29*, 2029 (1973).

Cyclic Nitrogen Derivatives of Tetra- and Divalent Tin

By *Michael Veith*[*]

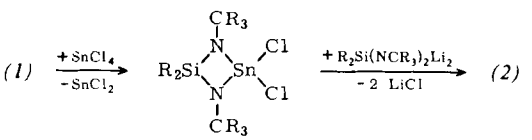
Whereas four-membered silicon-nitrogen rings (cyclodisilazanes) have been known for some time[1,2], corresponding tin-nitrogen rings (cyclodistannazanes) were synthesized only recently[3]. The present communication reports the preparation and characterization of four-membered heterocycles containing tin atoms having a valency of 4 or 2, in addition to silicon and nitrogen atoms. In the latter case the product constitutes the first cyclic nitrogen derivative of a Group IVB element in the divalent state[7].

Preparation of 1,3-di-*tert*-butyl-2,2-dimethyl-1,3,2,4λ^2-diazasilastannetidine *(1)* and the spiro compound *(2)* is accomplished by reaction of dimethyl-*N*,*N'*-bis(*tert*-butyl)silazane[4] according to the following reaction scheme:



The structure of the resulting heterocycles follows from the ^{1}H-NMR spectra, which contain only two signals each in the intensity ratio 3:1 for *(1)* and *(2)*, from the physical data, and from the molecular weights and molecular formulas determined by high-resolution mass spectrometry (Table 1).

Of the many possible *reactions*, that leading to *(2)* is cited as chemical proof for compound *(1)*.



The reaction affords *(2)* almost quantitatively, and also offers the opportunity of preparing spiro compounds of type *(2)* having different kinds of ligands.

X-Ray structure analysis of compound *(2)*[5] confirms the spiro structure expected from chemical arguments. In the crystal the molecule has $2(C_2)$ symmetry; in addition it also

[*] Dr. M. Veith
Institut für Anorganische Chemie der Universität
75 Karlsruhe 1, Englerstrasse 11 (Germany)

Table 1. Physical data for compounds *(1)* and *(2)*.

	(1)	*(2)*
	red liquid	colorless crystals
Phase transitions	b.p. 55—57 °C/0.1 torr	b.p. 110 °C/0.01 torr
	m.p. 5 °C	m.p. 162 °C
^{1}H-NMR in benzene,	−22.0 Hz (1.0);	−23.5 Hz (1.0);
TMS internal ref.	−72.5 Hz (3.0)	−80.0 Hz (3.0)
(integrations in parentheses)		
High resolution	$^{28}SiN_2C_9H_{21}$ ^{120}Sn $(M-CH_3)$	$^{28}Si_2N_4C_{20}H_{48}$ ^{120}Sn (M)
mass spectrometry	exp. 305.0482	exp. 520.2431
(PKF as standard)	calc. 305.0496	calc. 520.2439
MW (cryoscopic in benzene)	324	515

possesses approximate 4 2 m (D_{2d}) symmetry. The four-membered rings are oriented perpendicular to each other, the rings themselves being largely planar. The N—C bonds are inclined only slightly to the ring planes so that the nitrogen has a planar environment. A remarkable feature of the bond lengths and angles (a selection is given in Table 2) is the very small angle at the tin atom. The NSiN′ and SiNSn angles are consequently larger than in the comparable structure of tetramethyl-*N*,*N*′-bis(trimethylsilyl)cyclodisilazane[6] (∢ NSiN′ = 88°, ∢ SiNSi = 92°).

Table 2. Characteristic bond lengths and angles in the molecule *(2)* (the values given are the average values of chemically equivalent bond lengths, the deviations listed in parentheses are in units of the last decimal place).

Sn—N	2.033 (5) Å	∢ SiNSn	95.2°
Si—N	1.727 (7) Å	∢ NSiN	93.4°
C—N	1.469 (7) Å	∢ NSnN	76.3°

Procedure:

A solution of the dilithium salt of dimethyl-*N*,*N*′-bis(*tert*-butyl)silazane (0.05 mol) in hexane is added dropwise over 1 h to a suspension of $SnCl_2$ (0.05 mol) or a solution of $SnCl_4$ (0.025 mol), prepared with cooling, in diethyl ether (50 ml). The mixture warms up slightly and turns red ($SnCl_2$) or yellowish ($SnCl_4$). After 4 hours' stirring the LiCl is filtered off and the solvents removed under reduced pressure. In the case of compound *(1)* the residue is fractionally distilled, and for isolation of compound *(2)* the residue is taken up in ether and crystallized out at −20 °C. Yields: *(1)* 12.0 g (74%), *(2)* 9.9 g (76%).

Received: December 23, 1974 [Z 174 IE]
German version: Angew. Chem. *87*, 287 (1975)

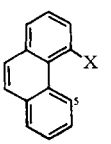
CAS Registry numbers:
(1), 54724-62-8; *(2)*, 54677-67-7; $(CH_3)_3CNLiSi(CH_3)_2NLiC(CH_3)_3$, 54677-64-4; $SnCl_2$, 7772-99-8; $SnCl_4$, 7646-78-8

[1] *W. Fink*, Chem. Ber. *96*, 1071 (1963).
[2] *K. Lienhard* and *E. G. Rochow*, Z. Anorg. Allg. Chem. *331*, 316 (1964).
[3] *D. Hänssgen* and *I. Pohl*, Angew. Chem. *86*, 676 (1974); Angew. Chem. internat. Edit. *13*, 607 (1974).
[4] *W. Fink*, Helv. Chim. Acta *47*, 498 (1964).
[5] *M. Veith*, unpublished results. X-Ray diffraction, single crystal. Space group C2/c; *Z* = 4, 1804 reflections; *R* value, 5.0%.
[6] *P. J. Wheatley*, J. Chem. Soc. *1962*, 1721.
[7] *Note added in proof* (March 14, 1975): Five- to seven-membered heterocycles with divalent tin have recently been reported by *C. D. Schaeffer* and *J. J. Zuckerman*, J. Amer. Chem. Soc. *96*, 7160 (1974).

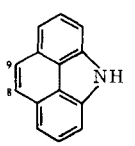
A New Route to 4*H*-Benzo[*def*]carbazole[1]

By *Richard Kreher* and *Wilfried Köhler*[*]

4*H*-Benzo[*def*]carbazole *(2)*, as a tetracyclic hetarene with an integrated isoindole system, exhibits remarkable thermal stability[3]. A versatile synthetic method has been developed[4] in order to facilitate a systematic study of the chemical properties and structure of the homologous [*def*]-annelated carbazoles.



(1)



(2)

Table 1. Prepared compounds *(1a)*—*(1d)* and *(2)*.

(1a), X = CN: m.p. 106—108 °C (methanol); yield 70%; ^{1}H-NMR ($CDCl_3$): τ = 0.1—0.5 (*m*, H^5), 1.9—2.8 (*m*, 8 aromat. H); cf. [6]

(1b), X = $CONH_2$: m.p. 266—267 °C (ethanol); yield 95%; ^{1}H-NMR (hexadeuteriodimethyl sulfoxide): τ = 1.0—1.3 (m, H^5), 1.7—2.7 (aromat. H and NH_2)

(1c), X = NH_2: m. p. 64—65 °C (petroleum ether); yield 70%; ^{1}H-NMR (CS_2): τ = 0.8—1.2 (m, H^5), 2.0—3.0 (m, 7 aromat. H), 3.2—3.6 (m, 1 aromat. H), 6.02 (s, NH_2); cf. [7]

(1d), X = N_3: m.p. 95—96 °C (*n*-hexane); yield 66%; ^{1}H-NMR (CS_2): τ = 0.5—0.9 (m, H^5), 2.4—3.3 (m, 8 aromat. H); MS (70 eV/20 °C): M^+ 219 (18%), $[M-N_2]^+$ 191 (100%), $[M-N_2H]^+$ 190 (48%)

(2): m.p. 174—175 °C (sublimation) ([3]: 173—174 °C); yield 63%; ^{1}H-NMR (hexadeuteriodimethyl sulfoxide): τ = −1.38 (s, NH), 1.9 (s, H^8, H^9), 2.1—2.5 (m, 6 aromat. H); UV (*n*-hexane): λ_{max} = 234 nm (log ε = 4.80), 270 (4.35), 327 (4.11); MS (70 eV/50 °C): $[M+H]^+$ 192 (16%), M^+ 191 (100%), $[M-H]^+$ 190 (30%), $[M-HCN]^+$ 164 (7%)

The essential step consists in the synthesis of the carbazole ring by cyclization[5] of 4-azidophenanthrene *(1d)*, which is obtained from 4-phenanthrenecarbonitrile *(1a)* (Table 1). This is readily and conveniently accessible from 1-naphthylacetonitrile and 1,3-bis(dimethylamino)trimethinium perchlorate by condensation and electrocyclic rearrangement[6]. Under optimized reaction conditions (25 h/80 °C and 110 h/220—225 °C) yields of up to 70% are achieved on a preparative scale. The partial hydrolysis of the carbonitrile *(1a)* to the 4-phenanthrenecarboxamide *(1b)* with conc. KOH solution and glycol monomethyl ether (2.5 h/120 °C) is almost quantitative.

Hofmann degradation to 4-aminophenanthrene *(1c)* cannot be achieved under the usual conditions. This was successfully carried out by reaction with excess hypochlorite solution and dioxane; optimal yields are obtained only with gradual temperature adjustment (5 h/45 °C and 2.5 h/80 °C).

The primary amine *(1c)*[7] is diazotized with sodium nitrite and dilute hydrochloric acid (2 h/0 °C) in a dioxane suspension, and after addition of urea is subsequently converted by reaction with excess sodium azide solution into *(1d)*, which can be isolated by adsorptive filtration.

Of the known ring closing reactions[5, 8], thermolysis of the azide *(1d)* in diphenyl ether (20 min/240 °C) proved to be the best. While the thermally induced N_2-elimination under

[*] Prof. Dr. R. Kreher and Dipl.-Ing. W. Köhler
Institut für Organische Chemie der Technischen Hochschule
61 Darmstadt, Petersenstrasse 15 (Germany)

these conditions does in fact lead to the 4*H*-benzo[*def*]carbazole *(2)*, formation of *(1c)* by hydrogen abstraction predominates (yield 71%) in xylene. N_2-elimination also occurs under mass spectrometric conditions. The molecular peak is accompanied by the same fragmentation pattern as observed in the case of *(2)*, but with different distribution of intensities.

The above synthetic method might be generally suited for the synthesis of [*def*]-annelated carbazoles and thus extend the scope of bifunctional cyclization of 4,5-disubstituted carbazoles[9].

Received: January 20, 1975 [Z 176 IE]
German version: Angew. Chem. 87, 288 (1975)

CAS Registry numbers:
(1a), 37044-95-4; *(1b)*, 54677-81-5; *(1c)*, 17423-48-2; *(1d)*, 54677-82-6; *(2)*, 203-65-6; 1-naphthylacetonitrile, 132-75-2; 1,3-bis(dimethylamino)trimethinium perchlorate, 54677-84-8

[1] Structure and reactivity of iso-annelated heterocyclic systems with $4n\pi$ and $(4n+2)\pi$ electrons, Part 3.—This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.—Part 2: [2].

[2] *R. Kreher* and *G. Vogt*, Angew. Chem. *82*, 958 (1970); Angew. Chem. internat. Edit. *9*, 955 (1970).

[3] *(2)* was first isolated from the last-runnings of the pyrene fraction (b.p. 400—423 °C) in the distillation of coal-tar; cf. *O. Kruber* and *G. Grigoleit*, Chem. Ber. *87*, 1895 (1954).—Electrophilic substitution reactions, see *M. Zander* and *H. Franke*, *ibid. 99*, 1279 (1966); *H. Hoellinger*, *N. P. Buu-Hoi*, and *Ph. Mabille*, J. Heterocycl. Chem. *6*, 409 (1959).

[4] The older methods are preparatively time consuming and less attractive; cf. Ref. [3] and *J. W. Cook* and *J. S. Moffatt*, J. Chem. Soc. *1951*, 2487.

[5] For cyclization *via* nitrene intermediates cf. *J. Sauer* and *J. Engels*, Tetrahedron Lett. *1969*, 5175 and references cited therein. For a review see: *R. A. Abramovitch*, Advan. Free Radical Chem. *2*, 128 (1967).

[6] *C. Jutz* and *R. M. Wagner*, Angew. Chem. *84*, 299 (1972); Angew. Chem. internat. Edit. *11*, 315 (1972); we thank these authors for providing full details of the experimental procedure.

[7] Despite experimental modifications the isolation of *(1c)* involves considerable preparative effort.—*M. J. S. Dewar* and *W. H. Poesche*, J. Org. Chem. *29*, 1757 (1964); *F. M. Beringer*, *L. L. Chang*, *A. N. Fenster*, and *R. R. Rossi*, Tetrahedron *25*, 4339 (1969).

[8] For a review of the chemistry of carbazoles see: *R. Livingstone* in: Rodd's Chemistry of Carbon Compounds: Heterocyclic Compounds, 2nd Edit., Elsevier, Amsterdam 1965, Vol. IV A, pp. 486ff.

[9] *W. Gerhardt*, Diplomarbeit, Technische Hochschule Darmstadt 1974.

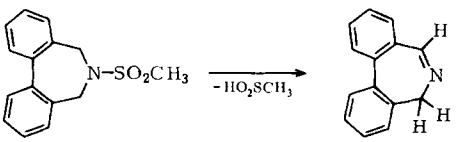
Synthesis of 5*H*-Dibenz[*c*,*e*]azepine by Elimination of Methanesulfinic Acid[1]

By *Richard Kreher* and *Werner Gerhardt*[*]

Heterocycles containing a cyclic CN double bond are generally prepared by cyclization of α,ω-bifunctional compounds[3]. An attractive alternative is the introduction of the cyclic CN double bond by elimination[4]. In this way halogen-substituted 2*H*-isoindoles are accessible in good yields from *N*-methanesulfonylisoindolines by base-catalyzed cleavage of methanesulfinic acid[2].

We have found a further preparatively interesting application of this method, namely the synthesis of the 5*H*-dibenz[*c*,*e*]azepine *(2)*[5]. The *N*-methanesulfonyl-6,7-dihydro-5*H*-dibenz[*c*,*e*]azepine *(1)*[6] required as starting compound is readily accessible from 2,2-bis(bromomethyl)biphenyl and methanesulfonamide. In the reaction with potassium *tert*-butoxide/dimethyl sulfoxide, methanesulfinic acid is eliminated under mild conditions and the cyclic azomethine *(2)* is obtained in remarkably good yields.

[*] Prof. Dr. R. Kreher and Dipl.-Ing. W. Gerhardt
Institut für Organische Chemie der Technischen Hochschule
61 Darmstadt, Petersenstrasse 15 (Germany)



(1) *(2)*

Analytical and spectroscopic findings substantiate the existence of the cyclic azomethine structure *(2)*. Further supporting evidence is provided by the formation of cyclic imonium salts on reaction of *(2)* with methyl iodide or trimethyloxonium tetrafluoroborate. Reaction with 2 N sodium hydroxide solution does not result in deprotonation to give *N*-methyl-6*H*-dibenz[*c*,*e*]azepine but in nucleophilic addition of the hydroxide ion to the positively charged CN double bond[7].

Isomerization of the 5*H*-dibenz[*c*,*e*]azepine *(2)* to the tautomeric 6*H*-dibenz[*c*,*e*]azepine with *o*-quinonoid structure has not been observed, either spectroscopically or chemically. A similar behavior is exhibited by the thermally stable 5*H*-dibenz[*c*,*e*]azepine *N*-oxide, which likewise shows no tendency to rearrange[8].

5*H*-Dibenz[*c*,*e*]azepine *(2)*

A mixture of *(1)* (50 mmol) in anhydrous dimethyl sulfoxide (160 ml) and potassium *tert*-butoxide (165 mmol) is stirred for 45 min at room temperature under N_2. More alkoxide (25 mmol) is added to the mixture and stirring is continued for a further 45 min. The final mixture is subjected to two-phase solvolysis with water/ether. The ethereal layer, after separation, drying over calcium chloride, and concentration by evaporation yields an oil, which on distillation (b.p. 124 to 126 °C/0.01 torr) affords *(2)* as colorless crystals (m.p. 83 to 85 °C) in 85% yield [m.p. after sublimation (70 °C/0.2 torr) 84–85 °C]: ^{1}H-NMR ($CDCl_3$): $\tau = 1.62$ (s, H^7); 2.21–2.73 (m, 8 aromat. H); 5.66 (s, CH_2); ^{1}H-NMR (trifluoroacetic acid): $\tau = 0.93$ (d, $J = 9.5$ Hz, H^7); 1.82–2.46 (m, 8 aromat. H); 5.24 (d, $J = 5.5$ Hz, CH_2); ^{1}H-NMR (deuteriotrifluoroacetic acid): $\tau = 0.85$ (s, H^7); 1.77–2.39 (m, 8 aromat. H); 5.18 (s, CH_2).— ^{13}C-NMR ($CDCl_3$): $\delta_{TMS} = 161.9$ (C^7), 139.5, 139.1, 137.4, 132.8, 129.6, 129.0, 128.3, 128.0, 127.7, 127.6, 126.9, 55.0 (C^5).

Received: February 6, 1975 [Z 177 IE]
German version: Angew. Chem. 87, 289 (1975)

CAS Registry numbers:
(1), 42060-47-9; *(2)*, 316-31-4; methanesulfinic acid, 1796-73-0

[1] Oxidative Elimination Reactions, Part 2.—This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.—Part 1: Ref. [2].

[2] *R. Kreher* and *K. J. Herd*, Angew. Chem. *86*, 782 (1974); Angew. Chem. internat. Edit. *13*, 739 (1974).

[3] The preparative limitation in the cyclization condensation of α,ω-aminoaldehydes and in the reductive cyclization of α,ω-nitro or α,ω-cyanaldehydes lies both in the accessibility of the starting substance and the choice of reaction conditions; cf. *J. Mathieu*, *A. Allais*, and *J. Valls*, Cah. Syn. Org. *9*, 95, 201 (1962); for an overview see: *R. Livingstone* in: Rodd's Chemistry of Carbon Compounds: Heterocyclic Compounds, 2nd Edit., Elsevier, Amsterdam 1973, Vol. IV A, pp. 368ff.

[4] *S. Dayagi* and *Y. Degani* in *S. Patai*: The Chemistry of the Carbon-Nitrogen Double Bond. Interscience, New York 1970, pp. 61ff.

[5] The cyclic azomethine is formed as an oil in a complex series of reactions in the pyrolysis of 2,2'-bis(azidomethyl)biphenyl; cf. *B. Coffin* and *R. F. Robbins*, J. Chem. Soc. *1965*, 1252.

[6] A multi-step synthesis is described by *J. L. Huppatz*, Aust. J. Chem. *26*, 1307 (1973); cf. Chem. Abstr. *79*, 31827k (1973).

[7] *G. Use* and *H. Hennige*, unpublished.

[8] *R. Kreher* and *H. Pawelczyk*, Z. Naturforsch. *29b*, 425 (1974).

Reviews

Abstracts of selected progress reports and review articles

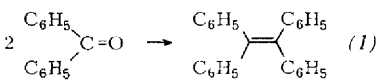
Induced autoimmune diseases are reviewed in an article by *E. M. Tan*. Several drugs (hydralazine, procainamide) generate an autoimmune disease similar to Lupus erythematosus but apparently *via* a different mechanism than the spontaneously occurring disease. It could be shown that a hydralazine-DNA-protein complex is formed *in vitro* whose antigenicity is more stable toward trypsin than that of the original nucleoprotein. *In vivo*, the immunological potential of the nucleoprotein is possibly increased by complex formation. Furthermore, the appearance of the disease is coupled with a decrease in the acetyl transferase level. [Drug-Induced Autoimmune Disease. Fed. Proc. *33*, 1894—1897 (1974); 13 references]

[Rd 763 IE—R]

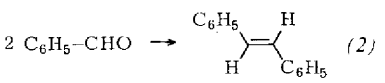
Vibrational spectra of transition metal chalcogen compounds are the subject of a review by *K. H. Schmidt* and *A. Müller*. Especially highly symmetrical molecules and ions are reviewed with spectra that can be totally assigned. Furthermore, the paper contains data of transition metal chalcogen compounds measured with special methods (intensities and band contours, Resonance Raman Effect, matrix spectra). It is shown how conclusions can be drawn from vibrational spectra about the nature of M—O, M—S, and M—Se bonds. [Schwingungsspektren von Übergangsmetall-Chalkogen-Verbindungen. Coord. Chem. Rev. *14*, 115—179 (1974); 326 references]

[Rd 765 IE—H]

The use of low-valent titanium compounds in organic chemistry is discussed in a report by *J. E. McMurry*. Thus in aqueous solution $TiCl_3$ is a versatile reducing agent, which, depending on the reaction conditions, can convert *e.g.* oximes into imines, haloketones into ketones, and nitro compounds into ketones. Noteworthy is the reductive coupling of carbonyl



(1)

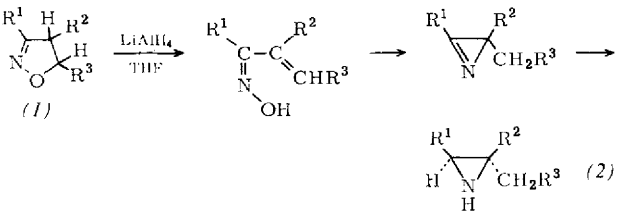


(2)

compounds such as benzophenone or benzaldehyde to tetraphenylethylene *(1)* and *trans*-stilbene *(2)*, respectively, by $LiAlH_4$—$TiCl_3$. Of special interest is the use of $TiCl_3$ for the deoxygenation of sulfoxides and for the reduction of enedicarbonyl compounds. [Organic Chemistry of Low-Valent Titanium. Accounts Chem. Res. *7*, 281—286 (1974); 29 references]

[Rd 768 IE—L]

The synthesis of heterocycles by ring transformation reactions of isooxazoles is reviewed by *T. Nishiwaki*. Aziridines *(2)* and azirines can be obtained by reduction of 2,5-dihydroisooxazoles *(1)* and by thermolysis and photolysis of isoxazoles, respectively. While there are only a few examples for the transformation to four-membered ring azetidines, numerous cases can be cited for the preparation of pyrrole, indole, isothiazole, and pyrazole derivatives thermally or by hydrogenation.



(1) *(2)*

Pyridine, quinoline, isoquinoline, acridine, and pyran derivatives can be prepared by reduction, photolysis or cycloaddition. Diazine, oxazine, and triazine rings can likewise be synthesized by hydrogenation, treatment with alkali or photolysis of the corresponding isoxazole. Seven- and eight-membered heterocycles can be obtained from isoxazoles by hydrogenation or by photolysis. [Synthesis of Heterocycles by Means of the Ring Transformation Reactions of Monocyclic and Condensed 1,2-Oxazoles (Isoxazoles); Synthesis *1975*, 20—37; 115 references]

[Rd 769 IE—M]

Applications of diffuse reflectance spectroscopy to the chemistry of transition metal coordination compounds are reviewed by *E. L. Simmons*. Theories of diffuse reflectance and the problems encountered in reflectance measurements are outlined. The method has been applied to studies of, *e.g.*, thermal decompositions of ammine, oxalate, halogen, and aquo complexes and solid state photochemical reactions. Quantitative analysis is also possible. [The Application of Diffuse Reflectance Spectroscopy to the Chemistry of Transition Metal Coordination Compounds. Coord. Chem. Rev. *14*, 181—196 (1974); 81 references]

[Rd 766 IE—H]

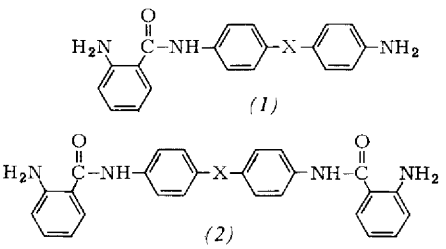
Selected highlights in immunological research in the last decade is the title of a review article by *M. Sela*. During this period the structure and conformation of antibodies have been elucidated and the constant and variable regions of their protein chains have been discovered. Further important progress has been made in the elucidation of antigenicity on a molecular level, of the relation between antibodies, their synthesis and immunologically active cells, as well as of the genetic control of the immune response. Immunology is playing an ever-increasing role as an experimental technique in other branches of science. [Selected Highlights in Immunological Research in the Last Decade. FEBS Lett. *40*, 85—97 (1974); 237 references]

[Rd 762 IE—R]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Polyamidimides with elastic properties, suitable as foils, fibers, and varnishes, are prepared by polycondensation of diamides



(1)

(2)

X = $-CH_2-$, $-O-$, $-CO-$, $-NH-$, $-S-$, $-SO_2-$, $-C(CH_3)_2-$

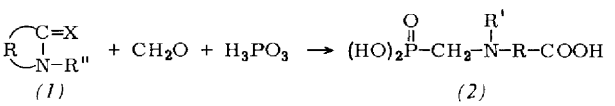
of type *(1)* or *(2)* with, *e.g.* benzophenonetetracarboxylic dianhydride in *e.g.*, methylpyrrolidone. [DOS 2230121; BASF AG, Ludwigshafen (Germany)]

[PR 253 IE—W]

Development of smoke from burning polyvinyl chloride or polyurethanes can be diminished by the addition of a dicyclopentadienyliron compound. In the examples, ferrocene is added in amounts of 0.25 to about 0.5 wt-%. [DOS 2307387; Syntex Corp., Panama]

[PR 251 IE—W]

***N*-Phosphonomethylaminocarboxylic acids** *(2)* with good metal ion-sequestering action are obtained by heating a cyclic amide *(1)* with formaldehyde and phosphorous acid (or PCl_3



(1) *(2)*

R = organic group; X = O, S; R′ = organic group, $-CH_2PO_3H_2$; R″ = H, organic residue

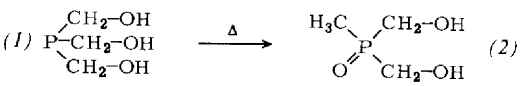
and water) in water. [DOS 2423881; Monsanto Co., St. Louis (USA)]

[PR 259 IE—D]

Low-molecular polymers containing terminal hydroxy groups, suitable for the preparation of polyurethanes, are obtained by the polymerization of conjugated dienes with hydrogen peroxide as catalyst in a liquid multiphase reaction system. The preferred reaction medium is a mixture of isopropanol and water containing 70—88% of the alcohol. [DOS 2326677; Atlantic Richfield Co., Los Angeles (USA)]

[PR 261 IE—D]

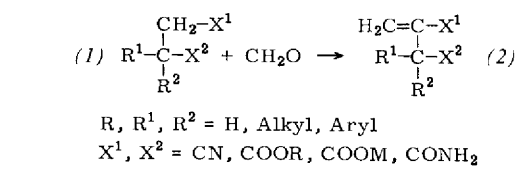
Bis(hydroxymethyl)methylphosphane oxide *(2)* is formed in an exothermic reaction by rearrangement of tris(hydroxymethyl)phosphane *(1)* at 80—150 °C in an inert diluent. *(2)* is used as an intermediate in the synthesis of flame retardants. [DOS 2313307; Farbwerke Hoechst AG, Frankfurt/M. (Germany)]



(1) *(2)*

[PR 262 IE—D]

Itaconic acid and its derivatives *(2)* are obtained in a good yield by a base-catalyzed condensation of formaldehyde with



(1) *(2)*

R, R^1, R^2 = H, Alkyl, Aryl

X^1, X^2 = CN, COOR, COOM, $CONH_2$

succinic acid derivatives *(1)*. [DOS 2422375; Snam Progetti S.p.A., Milan (Italy)]

[PR 264 IE—D]

BOOK REVIEWS

Atlas der Kunststoff-Analyse (Atlas of Plastics Analysis). By *D. O. Hummel* and *P. Scholl*. Vol. II Zusatzstoffe und Verarbeitungshilfsmittel (Additives and Processing Aids). Carl Hanser Verlag, Munich and Verlag Chemie GmbH, Weinheim 1973. 1st Edit., xix, 663 pp., 30 figs. 86 tables and 1151 spectra, bound, DM 268.—

This volume deals with the isolation and determination of admixtures and processing aids for plastics. It provides the long-expected supplement to the first volume[*] which dealt with the identification of high polymers and resins and has meanwhile proved its value.

The present volume begins with an outline of the most important experimental analytical methods, which could be kept quite short in view of the explanations in the first volume; finding the experimental details for a given case is made easier by the large number of references to the extensive literature. Then follows a description of the methods of detection of additives and processing aids: solvents, softeners, antiaging materials, stabilizers, vulcanization agents, fillers, pigments, antioxidants, antistatics, biocides, and flame-retardants are considered.

[*] Cf. Angew. Chem. internat. Edit. *10*, 204 (1971).

The following spectral section forms the largest part of the book. In some 1100 IR and 50 UV spectra the user has at his disposal an invaluable store of comparative material on the above-mentioned auxiliary additives. The excellent graphical presentation, linear in wave number, permits unambiguous comparison with his own spectra.

It should also be mentioned that, besides the extensive spectral section, there are abundant data on thin-layer chromatography, gas chromatography, and mass spectrography, as well as information about solvents and an extensive bibliography.

This second volume of the Atlas is an aid for the analytically active polymer chemist and, after short use, will become indispensible.

Wolfgang Brendlein [NB 248 IE]

Ullmanns Encyklopädie der Technischen Chemie (Ullmann's Encyclopedia of Technical Chemistry). Editorial board: *E. Bartholomé, E. Biekert, H. Hellmann*, and *H. Ley* (deceased). Vol. 8: Antimon und Antimon-Verbindungen bis Brot und andere Backwaren (Antimony and Antimony Compounds to Bread and Bakery Products). Verlag Chemie GmbH, Weinheim 1974, 4th Edit., XVI, 730 pp., 160 figures, 294 tables, subscription price DM 345.—; final price *ca.* DM 385.—.

The present volume 8 of the new edition of "Ullmann"[*] is the second in the alphabetical part which, treating the whole field of technical chemistry under alphabetically arranged keywords, forms the major part of the encyclopedia. Here are found not only inorganic and organic starting materials, intermediates and chemicals, raw materials, metals, and polymers, but also application-oriented areas such as dyestuffs, fibers, pharmaceuticals, cosmetics, pesticides, and foodstuffs.

An impression of the range of materials covered by Ullmann can be obtained from a brief look at the more important keywords in the present volume: from inorganic chemistry there are the elements antimony, arsenic, barium, beryllium, lead (Blei), boron, bromine, and their industrially interesting compounds; from the field of organic intermediates there are ethanol, aliphatic ethers, ethylene and several of its derivatives such as ethylene oxide, ethylene glycol, ethylene chlorohydrin, ethanolamine, and ethyleneimine, as well as benzene and some of its derivatives; to these must be added the keywords for materials with special applications, namely antioxidants, asbestos, building materials, bitumen, bleaches, and dyes of the azine and azo series; finally, in the range of biological products and processes we have the keywords biotechnology, bread and other bakery products, beer, and blood—blood needed in medicine not only in the fresh or preserved state for transfusions but also as a raw material for the proteins that are fractionated out of it for special therapeutic applications.

The entry on ethanol also includes drinks obtained by distillation from the products of alcoholic fermentation. Of general interest under this keyword is the section "Physiology and Toxicology": there we learn, *inter alia*, that in flying accidents with a lethal outcome 35—40% of the pilots were ethanol-positive, and that alcohol increases, and sometimes even potentiates, the action of all the old and new depressant psychopharmaceuticals, especially barbiturates.

The entry on biotechnology deserves special attention. Its inclusion shows that the present state of knowledge is kept in mind not only in the content of the entries but also in the conception of the work as a whole. This entry shows particularly well how clarity in subdivision and presentation, in places by tabulated reviews, can lead to a compressed but nevertheless very easily apprehended summary of an extensive subarea of chemical technology. Here as elsewhere in Ullmann, the large number of references to important literature sources contributes to the large content of information.

Summarizing, it remains only to state that in its new form too Ullmann is an essential source of information for all concerned with chemical-industrial problems. In addition, the work will be a valuable tool for the scientist engaged in pure research, for instance when he is interested in the purity and composition of industrial products or in their toxicity.

Ulfert Onken [NB 249 IE]

[*] Cf. Angew. Chem. internat. Edit. *14*, 73 (1975).

Methods of Enzymatic Analysis. Edited by *H. U. Bergmeyer*. 4 Volumes. Verlag Chemie GmbH, Weinheim/Academic Press, New York 1974. 2nd English Edition. Total of 2626 pp., numerous figures and tables. Individual price $ 56 per volume. Set price $ 198 for all four volumes.

Eleven years after the first English edition we have the second edition of "Methods of Enzymatic Analysis" by *H. U. Bergmeyer*, this time in collaboration with *K. Gawehn*. This reference book with its participation of 240 authors has long since become the standard work, and the editor has used the opportunity provided by the need for a new edition to bring it completely up to date. The general subdivision of the book and the clear presentation of its contents remain unchanged. The introduction of additional chapters has increased its size, but not very greatly; tautening the text in many places and omission of outdated material have prevented unnecessary bulk. The expansion of the references listed, almost throughout the work and including publications of very recent date, is most welcome.

The general introduction to the fundamentals of enzyme analysis has been considerably expanded and improved. There are new chapters on reaction kinetics in general and on the kinetics of enzymatic reactions in particular, as well as a chapter on methods of determining Michaelis and inhibitor constants. The text has been kept concise and is very well suited for recapitulation by the advanced student and as an introduction to practical work by the beginner. Moreover, the "Experimental" chapter in the general introduction has been revised and somewhat expanded. New experimental directions, description of a rapid automatic analyser, and new values for the extinction coefficients of reduced pyridine nucleotides (they are a few percent higher then previously) are examples of careful work performed by the authors and editors.

Section B of the book, devoted to biochemical reagents, has been rearranged. It begins with a new chapter in which the nomenclature and problems of standardization, concepts of quality of biochemical reagents, and their sources of supply, are discussed; these are followed by descriptions of enzymes, coenzymes, and substrates and by final collation of the reagents in the approved way.

Section C is concerned with methods of measuring enzyme activities and Section D deals with methods of determining metabolites. These two are only slightly altered, for example by transposing individual enzymes so that they correspond to the new arrangement in the IUB Enzyme Catalog 1973, or by replacing some old methods of determination by improved processes.

Summarizing, it can be stated that in its present form the book needs hardly any fundamental improvement, only that it maintain its high quality.

Dieter Oesterhelt [NB 250 IE]

Magnetochemie. Grundlagen und Anwendungen. (Magnetochemistry. Fundamentals and Applications). By *A. Weiss* and *H. Witte*. Verlag Chemie GmbH, Weinheim 1973. 1st

Edit., ix, 281 pp., 120 figs., 78 tables, bound, DM 59.—.

Thirty-six years after the appearance of *Wilhelm Klemm*'s monograph now comes the first further book on magnetochemistry in the German language. In plan it corresponds largely to its predecessor. The authors first direct their attention to chemists, using simple mathematical formulations. After a short chapter on physical fundamentals the methods of measurement are described, including that for single crystals. Not only the well-known procedures based on field forces but also susceptibility measurements by induction methods and those with the aid of nuclear magnetic resonance are discussed. There follows a chapter on diamagnetism, which treats classical theory and the results of quantum mechanics, the semiempirical and the incremental methods, as well as ion-diamagnetism. The chapter on "Paramagnetism" contains sections on the magnetic properties of free atoms and ions, influences of ligands, spin-path coupling, *Van Vleck*'s paramagnetism, complexes with 4d- and 5d-metal ions, and rare-earth compounds. The conclusion is provided by cooperative effects (antiferromagnetism, ferrimagnetism, and ferromagnetism, electrons in metals and alloys) and examples of the use of magnetochemistry in chemical problems. The dimensions and units for electrical and magnetic magnitudes are collected in an Appendix.

The book is intended as an introduction to the performance and interpretation of magnetic measurements, and its value lies in its first part. Thus, the methods of measurement, their physical foundations, and the sources of error (in particular ferromagnetic impurities) and methods of overcoming them are described simply and clearly. The theory of transition-metal compounds, the chief of interest to the magnetochemist, is important for the interpretation of the experimental data, and this part, as also the presentation of cooperative effects (except for the section on "Electrons in Metals and Alloys") is kept too short. Important concepts, like the Jahn-Teller effect and metamagnetism, are missing and the tables are incomplete (pages 182, 187). In contrast, in many places the authors could have been more concise: thus, *Pauling*'s views on the structure of complexes are now of only historical interest; the incremental methods of determining diamagnetic susceptibility could have been restricted to the *Haberditzl* method. There are also some repetitions (derivation of the Van Vleck formula, magnetic properties of closed electron shells).

If one disregards these shortcomings, the book provides much useful practical information for the magnetochemist by virtue of its extensive bibliography and the numerous examples of applications.

Heiko Lucken [NB 251 IE]

Methoden der Analytischen Chemie (Methods of Analytical Chemistry). Vol. 1. Trennungsmethoden (Methods of Separation). By *R. Bock*. Verlag Chemie GmbH, Weinheim 1974. 362 pp., 236 figs., 79 tables, bound, DM 42.—.

The task of presenting the confusing multiplicity of separation methods used in today's analytical chemistry clearly and systematically is as necessary as it is difficult. It is therefore very pleasing to find that an author as competent as *Rudolph Bock* has undertaken this task in the first volume of his monograph series "Methoden der Analytischen Chemie".

The division of separation methods adopted here, essentially into two large groups (separations by different distributions between two immiscible phases and separations by different migration rates in one phase) at first appears disconcerting, but becomes intelligible on closer attention to the book. Nevertheless, it would have been better to designate the first group as "Separation by establishment of different phase equilibria" (cf. *B. L. Karger, L. R. Snyder*, and *C. Horvath*: An Introduction to Separation Science, Wiley, New York 1973), since natural incorporation of processes such as distillation and sublimation is then possible. Unfortunately, strict adherence to the system resulting from the author's classification leads here and there to statements that could be misunderstood; these arise mainly from insufficient differentiation between separation principles (such as distribution), physical phenomena (such as adsorption), and experimental techniques (such as chromatography).

In a few matters of detail the reviewer does not agree with the author's views. For example, isotope dilution analysis is treated relatively extensively, whereas for detectors in gas chromatography, the reader is referred to Volume 2 of this series; a distribution ratio (in extractions involving the establishment of chemical equilibria) is called a distribution coefficient (in the sense of a Nernst distribution); the term "extraction" is reserved exclusively for dissolution of specific substances out of a solid mixture, whereas the widely used liquid-liquid extraction is referred to as "shaking out".

Nevertheless, the volume as a whole can be regarded as a successful review of methods of separation and thus as a valuable source of information. The didactically skilful method of presentation, which characterizes the experienced college lecturer, makes it easy to become familiar with the problems discussed, and the large number of carefully chosen and collected references makes it easy to search deeper into the material. The keyword subdivisions placed at the head of individual chapters provide rapid information on the contents and are very helpful for tracing detail; this method of presenting material should find increasing application in textbooks.

Dieter Klockow [NB 253 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Practical Electrophoresis. By *G. J. Moody* and *J. D. R. Thomas*. Merrow Publishing Co. Ltd., Watford 1975. VII, 104 pp., stitched, £ 2.50.

Chemistry and Biochemistry of Amino Acids, Peptides, and Proteins. A Survey of Recent Developments. Edited by *J. Weinstein*. Marcel Dekker, Inc., New York 1974. Vol. 2: XI, 380 pp., bound, $ 27.50; Vol. 3: XI, 324 pp., bound, $ 2 .50

Physical Properties of Inorganic Compounds. SI Units. By *A. L. Horvath*. Edward Arnold, London 1974. XIII, 466 pp., bound, £ 22.50.

Chemical and Biochemical Reactivity. Proceedings of an International Symposium held in Jerusalem, 9—13 April 1973 (The Jerusalem Symposia on Quantum Chemistry and Biochemistry, VI). Edited by *E. D. Bergmann* and *B. Pullman*. The Israel Academy of Sciences and Humanities, Jerusalem 1974. 580 pp., bound, $ 39.00.

Spectroscopic Properties of Inorganic and Organometallic Compounds, Vol. 7. Senior Reporter: *N. N. Greenwood*. The Chemical Society, London 1974. XII, 699 pp., bound, £ 24.00.—A volume in the series "Specialist Periodical Reports".

Higher Excited States of Polyatomic Molecules, Vol. II. By *M. B. Robin.* Academic Press, New York 1975. X, 418 pp., bound. $ 39.50.

Investigation of Rates and Mechanisms of Reactions. Part I: General Considerations and Reactions at Conventional Rates. Edited by *E. S. Lewis.* Volume VI of the series "Techniques of Chemistry". Edited by *A. Weissberger.* John Wiley & Sons, New York 1975. 3rd Edit., XIII, 838 pp., bound, £ 21.00.

Arrégé de Chimie. Vol. 1: Chimie Generale. By *G. Germain, R. Mari,* and *D. Burnel.* From the series "Comprendre et Appliquer". Edited by *G. Germain.* Masson & Cie., Paris 1975. XII, 274 pp., stitched, 36 F.

Thermal Vibrations in Crystallography. By *B. T. M. Willis* and *A. W. Pryor.* Cambridge University Press, Cambridge 1975. XVI. 280 pp., bound, £ 9.50.

Les Grandes Réactions de la Synthese Organique. By *J. Mathieu, R. Panico,* and *J. Weill-Raynal.* From the series "Actualités Scientifiques et Industrielles". Hermann, Paris 1975. XIV, 340 pp., stitched, 76 F.

Techniques and Applications of Plasma Chemistry. Edited by *J. R. Hollahan* and *A. T. Bell.* John Wiley & Sons, New York 1974. VIII, 403 pp., bound, £ 12.00.

Structure and Bonding, Vol. 20. Edited by *J. D. Dunitz, P. Hemmerich, R. H. Holm, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Springer-Verlag, Berlin 1974. IV, 167 pp., bound, DM 66.—.

Organic Electronic Spectral Data, Vol. X, 1968. Edited by *J. P. Phillips, H. Feuer,* and *B. S. Thyagarajan.* John Wiley & Sons, New York 1974. XIII, 1034 pp bound, £ 18.00.

Einführung in die Mikrobiologie. By *J. F. Wilkinson.* "taschentext", Band 26. Verlag Chemie/Physik Verlag, Weinheim 1974. VIII, 162 pp., stitched, DM 13.80.

Forschung in Deutschland. Bilanz und Analyse. Edited by *V. von Hagen.* Hase & Koehler Verlag, Mainz 1974. 284 pp., bound, DM 25.—.

Struktur. Stoff. Reaktion. Allgemeine und anorganische Chemie, Sekundarstufe I. By *H. R. Christen.* Diesterweg Salle, Frankfurt/Verlag Sauerländer, Aarau 1974. XI, 344 pp., bound, DM 19.80.

Protein-Metal Interactions. Edited by *M. Friedman.* Volume 48 of the series "Advances in Experimental Medicine and Biology". Edited by *N. Back, N. R. di Luzio, B. Halpern, E. Katchalski, D. Kritchevsky, A. Lajtha,* and *R. Paoletti.* Plenum Press, New York 1974. X, 692 S. bound, $ 47.40.

Medicinal Chemistry IV. Proceedings of the 5th International Symposium on Medicinal Chemistry, Noordwijkerhout, September 9—13, 1974. Edited by *J. Maas.* Elsevier Publishing Co., Amsterdam 1974. VIII, 376 pp., bound, Dfl. 90.00.

Systemtechnik—Grundlagen und Anwendung. Edited by *G. Ropohl.* Carl Hanser Verlag, München 1975. XVI, 356 pp., stitched, DM 64.—.

Correlation Tables for the Structural Determination of Organic Compounds by Ultraviolet Light Absorptiometry. By *M. Pestemer.* Verlag Chemie, Weinheim 1974. 157 pp., DM 98.—.

Methods of Enzymatic Analysis, Vols. 1—4. Edited by *H. U. Bergmeyer.* Verlag Chemie, Weinheim/Academic Press, New York 1974. 2. English Edit., Vol. 1: General Introduction/Biochemical Reagents. 647 pp., bound, DM 145.—. Vol. 2: Methods for Determination of Enzyme Activity. 639 pp., bound, DM 129.—. Vol. 3: Methods for Determination of Metabolites. 582 pp., bound, DM 129.—. Vol. 4: Proteins, Peptides and Amino Acids/Fatty Acid Metabolites, Lipids and Steroids/Nucleic Acids, Purines, Pyrimidines, Nucleosides, Coenzymes and Related Compounds/Other Substrates and Effectors/Concentration of Metabolites in Animal Tissues. 758 pp., bound, DM 129.—

Methodicum Chimicum, Vols. 1 A and 1 B. By *F. Korte.* Academic Press, New York 1975. Band 1A: X, 628 pp.; Band 1 B: X, 1218 pp., total price, bound, $ 98.00.

Gmelin Handbuch der Anorganischen Chemie. System-Nr. 61: Silber. Teil B5: Silber-Organische Verbindungen. Organische Silbersalze. Springer-Verlag, Berlin 1975. VI, VI, 187 pp., bound, DM 322.—.

Gmelin Handbuch der Anorganischen Chemie. System-Nr. 39: Seltenerdelemente: Sc, Y, La und Lanthanide. Teil C2: Verbindungen mit H+O, Alkalimetall+O, N sowie die zugehörigen Alkalidoppelverbindungen. Springer-Verlag, Berlin 1974. VI, XV, 299 pp., bound, DM 478.—.

Fehlerrechnung. Eine Einführung für Naturwissenschaftler. By *J. Topping.* Band 29 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. VIII, 124 pp., stitched, DM 16.80.

Reagents for Organic Synthesis, Vol. 4. By *M. Fieser* and *L. F. Fieser.* John Wiley & Sons, New York 1974. 660 pp., bound, £ 12.50.

Physical Chemistry. By *F. Daniels* and *R. A. Alberty.* John Wiley & Sons, New York 1975. 4. Edit., XII, 687 pp., bound, £ 7.50.

Gmelin Handbuch der Anorganischen Chemie. System-Nr. 14: Kohlenstoff. Part C4: Ausgewählte C—H—O-Radikale. Ameisensäure. Essigsäure. Oxalsäure. Springer-Verlag, Berlin 1975. 8. Edit., VI, VIII, 236 pp., bound, DM 376.—.

Automatic Chemical Analysis. By *J. K. Foreman* and *P. B. Stockwell.* "Ellis Horwood Series in Analytical Chemistry". Edited by *R. A. Chalmers.* Ellis Horwood, Chichester/John Wiley & Sons, New York 1975. XI, 346 pp., bound, £ 15.00.

Ions and Ion Pairs in Organic Reactions Vol. 2: Role of Ions and Ion Pairs in Chemical Reactions. Edited by *M. Szwarc.* John Wiley & Sons, New York 1974. XIII, 566 pp., bound, £ 13.65.

Römpps Chemie-Lexikon, Band 4: M—Pk. By *O.-A. Neumüller.* Franckh'sche Verlagshandlung, Suttgart 1974. 7., completely new and revised Edition, 689 pp., bound, DM 160.—.

Compendium of Organic Synthetic Methods, Vol. 2. By *I. T. Harrison* and *S. Harrison.* John Wiley & Sons, New York 1974. XVIII, 437 pp., bound, £ 7.50.

Technique of Electroorganic Synthesis, Part I. Edited by *N. L. Weinberg.* Band V of the series "Techniques of Chemistry". Edited by *A. Weissberger.* John Wiley & Sons, New York 1974. X, 917 pp., bound, £ 20.00.

Gmelin Handbuch der Anorganischen Chemie. Supplement to 8. Edit. Band 17: Nickel-Organische Verbindungen. Part 2: Einkernige Verbindungen (Fortsetzung). Mehrkernige Verbindungen. Springer-Verlag, Berlin 1974. VI, X, 402 pp., bound, DM 618.—.

Energy. Vol. I: Demands, Resources, Impact, Technology, and Policy. By *S. S. Penner* and *L. Icerman*. Addison-Wesley Company, Reading 1974. XX, 373 pp., bound, $ 14.50/ stitched, $ 8.50.

Photodegradation, Photo-oxidation and Photostabilization of Polymers. Principles and Applications. By *B. Ranby* and *J. F. Rabek*. John Wiley & Sons, London 1975. XV, 573 pp., bound, £ 16.50.

Electroanalytical Chemistry. Series editor *H. W. Nürnberg*. From the series "Advances in Analytical Chemistry and Instrumentation". Edited by *Ch. N. Reilley* and *R. W. Murray*. John Wiley & Sons, London 1975. XI, 609 pp., bound, £ 18.50.

Elektrosorptionsanalyse mit der Wechselstrompolarographie. By *H. Jehring*. Akademie-Verlag, Berlin 1974. XV, 456 pp., bound, *ca.* DM 98.—.

Advances in Photochemistry, Vol. 9. Edited by *J. N. Pitts, Jr., G. S. Hammond*, and *K. Gollnick*. John Wiley & Sons, New York 1974. 566 pp., bound, £ 12.00.

Gmelin Handbuch der Anorganischen Chemie. System-Nr. 46: Zinn. Teil C2: Verbindungen von Zinn und Schwefel bis Zinn und Wismut. Springer-Verlag, Berlin 1975. VI, XVI pp., bound, DM 477.—.

Progress in Bioorganic Chemistry, Vol. 3. Edited by *E. T. Kaiser* and *F. J. Kézdy*. John Wiley & Sons, New York 1974. XIII, 274 pp., bound, £ 10.75.

Dispersion Polymerization in Organic Media. Edited by *K. E. J. Barrett*. John Wiley & Sons, London 1975. XV, 322 pp., bound, £ 9.50.

The Chemistry of Diacetylenes. By *M. F. Shostakovskii* and *A. V. Bogdanova*. John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1974. XVII, 493 pp., bound, £ 18.15.

Structural Effects on Equilibria in Organic Chemistry. By *J. Hine*. John Wiley & Sons, New York 1975. XII, 347 pp., bound, £ 9.45.

Environmental Chemistry, Vol. 1. Senior Reporter: *G. Eglinton*. The Chemical Society, London 1975. XII, 199 pp., bound, £ 7.00.—A volume in the series "Specialist Periodical Reports".

Molecular Structure by Diffraction Methods, Vol. 2. Senior Reporters: *G. A. Sim* and *L. E. Sutton*. The Chemical Society, London 1974. XIII, 513 pp., bound, £ 17.50.—A volume in the series "Specialist Periodical Reports".

Reaction Kinetics, Vol. 1. Senior Reporter: *P. G. Ashmore*. The Chemical Society, London 1975. XI, 396 pp., bound, £ 13.50.—A volume in the series "Specialist Periodical Reports".

Handbook of Moisture Determination and Control. Principles, Techniques, Applications. Vol. 2. By *A. Pande*. Marcel Dekker, New Yorl 1975. XI, 584 pp., bound, $ 33.50.

The Structure and Function of Chromatin. Ciba Foundation Symposium 28 (new series). Elsevier/Excerpta Medica/North-Holland, Amsterdam 1975. IX, 368 pp., bound, $ 23.50.

Molecular Behaviour and the Development of Polymeric Materials. Edited by *A. Ledwith* and *A. M. North*. Chapman and Hall, London 1975. 553 pp., bound. £ 12.00.

Dielectric and Related Molecular Processes, Vol. 2. Senior Reporter: *M. Davies*. The Chemical Society, London 1975. XI, 291 pp., bound, £ 12.00.—A volume in the series "Specialist Periodical Reports".

Synthetic Production and Utilization of Amino Acids. Edited by *T. Kaneko, Y. Izumi, I. Chibata*, and *T. Itoh*. Kodansha, Tokyo/John Wiley & Sons, New York 1975. XII, 312 pp., bound, $ 12.15.

Applications of High-speed Liquid Chromatography. By *J. N. Done, J. H. Knox* and *J. Loheac*. John Wiley & Sons, London 1975. VII, 238 pp., bound, £ 6.50

Essential Aspects of Mass Spectrometry. By *A. Frigerio*. Spectrum Publications, Flushing 1974, X, 121 pp., bound, £ 4.30.

Topics in Carbon-13 NMR Spectroscopy, Vol. 1. Edited by *G. C. Levy*. John Wiley & Sons, New York 1974. X, 292 pp., bound, $ 9.45.

Bonded Stationary Phases in Chromatography. By *E. Grushka*. Ann Arbor Science Publishers, Ann Arbor 1975. IX, 237 pp., bound, £ 9.20.

Encyclopedia of Electrochemistry of the Elements, Vol. III: Co, Ni, P. Edited by *A. J. Bard*. Marcel Dekker, New York 1975. XII, 432 pp., bound, $ 60.00 (Subscr.-price to all volumes: 15% discount).

Physical Chemistry. An Advanced Treatise. Vol. XI A: Mathematical Methods. Edited by *H. Eyring, D. Henderson*, and *W. Jost*. Academic Press, New York 1975. XXIV, 564 pp., bound, $ 45.00.

Pyridine and its Derivatives, Supplement Part I. Edited by *R. A. Abramovitch*. Vol. 14 of the series "The Chemistry of Heterocyclic Compounds". Edited by *A. Weissberger* and *E. C. Taylor*. John Wiley & Sons, New York 1975. XV, 451 pp., bound, £ 21.00.

Reviews in Macromolecular Chemistry, Vol. 12. Edited by *G. B. Butler, K. F. O'Driscoll*, and *M. Shen*. Marcel Dekker, New York 1975. XII, 390 pp., bound, $ 29.50.

Comprehensive Analytical Chemistry. Edited by *G. Svehla*. Vol. III: Elemental Analysis with Minute Samples; Standards and Standardization; Separations by Liquid Amalgams; Vacuum Fusion Analysis of Gases in Metals; Electroanalysis in Molten Salts. Elsevier Publishing Company, Amsterdam 1975. XVI, 399 pp., bound, $ 51.95.

Comprehensive Analytical Chemistry. Edited by *G. Svehla*. Vol. IV: Instrumentation for Spectroscopy; Atomic Absorp-

tion and Fluorescence Spectroscopy; Diffuse Reflectance Spectroscopy. Elsevier Publishing Company, Amsterdam 1975. XVIII, 374 pp., bound, $ 47.95

Electrochemical Data. Edited by *L. Meites, P. Zuman*, and others. Part I: Organic, Organometallic, and Biochemical Substances, Vol. A. John Wiley & Sons, New York 1975. XI, 725 pp., bound, £ 17.00.

Biochemie der Pflanzen. Ein Lehrbuch. By *H. Kindl* and *G. Wöber*. Springer-Verlag, Berlin 1975. IX, 364 pp., bound, DM 78.—.

Ramanspektren von Molekülen und Kristallen. By *M. M. Suschtschinskij*. Edited by *H. Kriegsmann*. Heyden & Son GmbH, Rheine 1974. XI, 437 pp., bound, DM 98.—.

Einführung in die Theoretische Chemie. Band 1. Quantenmechanische Grundlagen. By *W. Kutzelnigg*. Verlag Chemie, Weinheim 1975. XXIII, 297 pp., bound, DM 68.—.

Molecular Reaction Dynamics. By *R. D. Levine* and *R. B. Bernstein*. Oxford University Press, New York 1974. VI, 250 pp., bound, £ 5.00.

Advances in Catalysis. Vol. 24. Edited by *D. D. Eley, H. Pines*, and *P. B. Weisz*. Academic Press, New York 1975. XVI, 427 pp., bound, $ 38.50.

Inhibitors of Nucleic Acid Synthesis. Biophysical and Biochemical Aspects. By *H. Kersten* and *W. Kersten*. Vol. 18 of the series "Molecular Biology, Biochemistry and Biophysics". Edited by *A. Kleinzeller, G. F. Springer*, and *H. G. Wittmann*. Springer-Verlag, Berlin 1974. IX, 184 pp., bound, DM 68.—.

Entropy-Driven Processes in Biology. Polymerization of Tobacco Mosaic Virus Protein and Similar Reactions. By *M. A. Lauffer*. Vol. 20 of the series "Molecular Biology, Biochemistry and Biophysics". Edited by *A. Kleinzeller, G. F. Springer*, and *H. G. Wittmann*. Springer-Verlag, Berlin 1975. X, 264 pp., bound, DM 73

The Hydrogen Bond and Other Intermolecular Forces. By *J. Clare Speakman*. "Monographs for Teachers", No. 27. The Chemical Society, London 1975. 37 pp., stitched, 60 p.

Peptides, Polypeptides, and Proteins. Proceedings of the Rehovot Symposium on Poly(Amino Acids), Polypeptides, and Proteins and their Biological Implications, Israel, May 1974. Edited by *E. R. Blout, F. A. Bovey, M. Goodman*, and *N. Lotan*. John Wiley & Sons, New York 1975. XII, 644 pp., bound, £ 12.25.

La Réaction Chimique. Lecons de Chimie, III. By *P. Laszlo*. Vol. 23 of the "Collection Enseignement des Sciences". Hermann, Paris 1974. XIII, 178 pp., bound, 58 F.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 4036, ⟨14036⟩, 4037, ⟨14037⟩. Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim. Pappelallee 3. P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 4031, ⟨14031⟩ Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 5
May 1975
Pages 273–374

Synthetic Reactions of Metal Atoms at Temperatures of 10 to 273 °K[**]

By Peter L. Timms[*]

Metal atoms, easily formed by vaporizing metals at high temperatures under vacuum, are reacted with inorganic and organic compounds in solution at 80 to 273 °K or by co-condensing the atoms and substrate vapors at 10 to 80 °K. Gram quantities of products containing metals in low valency states can be isolated in many cases, and some of the compounds formed are inaccessible by conventional synthetic routes.

1. Evaporation of Metals

Much is known about the evaporation of metals because of the scientific and commercial importance of forming metal films by condensation of vapors. The wide range of volatilities among metals is shown in Table 1. The temperatures given are those at which the metal has a vapor pressure of 0.01 to 0.1 torr, sufficient to give rapid evaporation under high vacuum.

Table 1. Evaporation temperature of metals under vacuum.

T[°C]	<1000	1000—1400	1400—1700	1700—2000	2000—2500	>2500
ΔH_{vap} [kJ]	<200	200—360	360—430	430—520	520—600	>600
	Li	Be				
	Na Mg	Mn Cu	Cr Fe Co Ni	Ti V		
	K Ca Zn	Ag Sn	Pd		Zr Ru Rh	Nb Mo
	Rb Sr Cd	Au		U	Pt	Hf Ta W Re Os Ir
		Pr, Nd, Gd, Tb,	La, Ce, Lu			
	Sm, Eu	Dy, Ho, Er, Tm				

Main Group metals are more volatile than most transition metals. With the transition metals, volatility usually decreases down the Groups as the binding energy of the metals increases. Although the lanthanoids are chemically very similar, the volatilities of the metals show surprisingly large variations.

The practical difficulties of vaporizing a metal depend partly on how high a temperature is required and partly on the corrosiveness of the liquid metal. A greater variety of evaporation techniques can be used for the volatile metals than for the very refractory ones. We favor two methods of vaporization of metals for atom synthesis on a preparative scale. The first is evaporation from an alumina crucible wound with molybdenum or tungsten wire which is heated resistively. This is very satisfactory for the transition metals Cr, Mn, Fe, Co, Ni, Pd, Cu, Ag, and Au. We use crucibles of varying sizes giving evaporation rates of 1 to 50 g per hour of these metals. For more refractory metals, or metals which attack alumina, we use electron bombardment vaporization. Our electron gun (Fig. 1) has a heated tungsten filament from which electrons flow to the metal charge maintained at a high positive potential.

[*] Prof. Dr. P. L. Timms
School of Chemistry, University of Bristol
Cantock's Close, Bristol, BS8 1TS (England)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

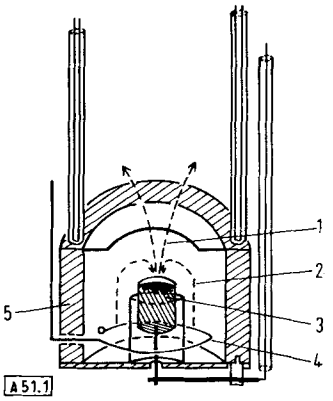


Fig. 1. Electron beam evaporation source. 1, metal vapor; 2, electron beam; 3, crucible (+ve); 4, hot filament (grounded); 5, water-cooled copper block.

This arrangement seems to overcome some of the problems due to stray electrons experienced with electron guns in which the heated charge is at ground potential. Although it is possible to use a water-cooled copper container for the liquid metal, much greater efficiency is achieved by using uncooled tungsten, tantalum, or graphite containers. On a small scale, little contamination of the evaporating metal by the crucible material is observed because the electrons are focused on to the surface of the liquid metal which is thus much hotter than the crucible.

The method of metal atom synthesis requires that the metal vapor is condensed on a cooled surface. The heat radiation which is liberated while a metal is being evaporated has to be absorbed by the refrigerant. The amount of cooling required increases rapidly with the evaporation temperature of the metal. For example, Cr, Mo, and W each vaporize at a rate of 1 g cm^{-2} h^{-1} at a temperature of about 1460, 2760, and 3400 °C respectively. The radiant heat emission from each metal at the given temperature is about 13, 120, and 260 W cm^{-2} h^{-1} respectively. The extra cost of cooling required when vaporizing the refractory metals may be trivial on a laboratory scale, but it will be significant if metal atom syntheses are adopted commercially.

2. Techniques for Reacting Metal Vapors

Much preparative work has been carried out by condensing a metal vapor and the vapors of other compounds on a liquid nitrogen cooled surface under high vacuum[1, 2]. We originally used stainless steel vacuum apparatus[3], and this is undoubtedly very safe and convenient for large scale work. However, largely as a result of success with a glass apparatus built for teaching undergraduates[2], some of our research apparatus is now made of glass and is of a simple and versatile design. Figure 2 shows the type of vessel, set up for vaporization of 2—5 g of a metal from an alumina crucible. The sample inlet system can be heated to aid volatilization of slightly volatile compounds.

After co-condensing the metal vapor with one or more compounds at −196 °C, highly volatile products can be pumped on to the vacuum line when the vessel is warmed. Alternatively, the vessel can be filled with gaseous nitrogen or argon and the furnace and inlet assembly can be lifted out. A variety of fittings can then be put on the top flange of the vessel to facilitate recovery of products by solution techniques in the absence of air and, if necessary, at low temperatures.

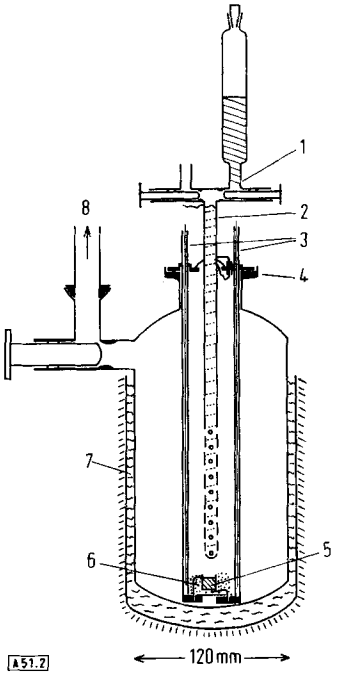


Fig. 2. Apparatus for co-condensation of metal atoms and ligand substrates at −196 °C. 1, inlet for liquids or gases; 2, inlet heating wires; 3, water cooling and electricity; 4, O-ring flange; 5, heated metal; 6, Mo-wire-wound Al_2O_3 crucible; 7, liquid nitrogen; 8, high vacuum.

Recently, we have used a new type of apparatus in which the metal vapor is condensed into a solution of a compound in an inert solvent contained in a rotating evacuated flask (Fig. 3). The solution must be kept at a temperature where its vapor pressure is less than about 10^{-3} torr otherwise the pressure in the flask may be too high to give efficient vaporization of the metal.

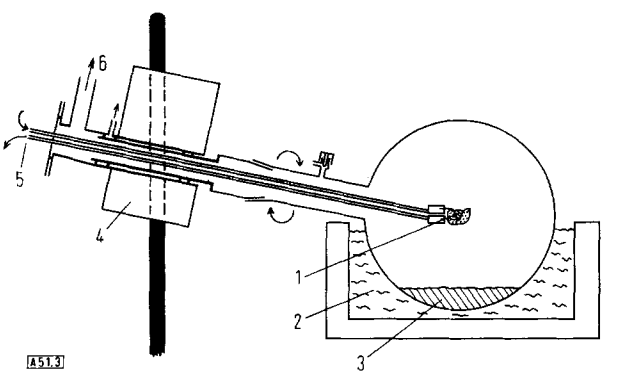


Fig. 3. Rotary apparatus for reacting metal atoms with cooled solutions. 1, evaporating metal; 2, cooling bath; 3, substrate solution; 4, rotary drive mechanism; 5, water and electrical power; 6, high vacuum.

Provided that the solvent and solute are both of low volatility, it is possible to condense metal atoms into solutions at room temperature, although low temperatures are used more commonly to reduce the vapor pressure and to stabilize the reaction products.

In addition to the higher temperature of operation, the procedure has several other advantages over the co-condensation method:

1) Substrates which are too involatile or too unstable to be volatilized can be reacted with metal atoms, provided that they are soluble in an inert solvent.

2) The products are obtained in a convenient form for isolation by conventional solution techniques or for further reaction with other compounds added to the rotary reactor.

3) The apparatus is easily scaled-up or made continuous in operation. For example, a cooled, evacuated, rotating drum 100 cm in diameter and 150 cm long, containing 150 l of a reactant solution, could house one of the metal evaporation sources described by *Reichelt*[14] for producing metal vapor at the rate of 3 kg h^{-1}. On this scale, continuous renewal of the solution and of the metal charge would be practicable.

The main problem with the solution technique is to find an inert solvent which will dissolve at least 2% of the reactant compound at a temperature at which the vapor pressure of the solution is below 10^{-3} torr. Table 2 shows a range of useful solvents and some of their physical properties. The compounds given are not too viscous at their operating temperature to give rapid mixing of the solution as the flask rotates.

Table 2. Solvents for the rotating solution reactor.

Solvent	Operating temp. [a]	M.p. [°C]	B.p. [°C]
Propane	−185	−187	− 42
Isopentane	−145 to −160	−160	+ 28
Methylcyclohexane	−110 to −125	−126	+101
Pet. ether (120—160)	− 80 to − 90	*ca.* −90	
m-Diisopropylbenzene	− 60 to −100	−105	+202
Bis(ethylhexyl) ether	− 10 to − 60	*ca.* −80	+280
Light liquid paraffin	+ 20 to 0	− 20	> +300
Silicone 704 (phenylmethylsiloxane)	+ 50 to − 20	− 20	> +350

[a] Vapor pressure of solution $< 10^{-3}$ torr [°C].

We also have done some work on the reactions of metal atoms with compounds under matrix isolation conditions at 10—40°K. For this, we prefer to form the metal vapors and other high temperature species from tiny alumina tube furnaces with resistively heated tungsten wire windings, but in most respects our apparatus is conventional[4].

3. Results

Much of our most recent work has been on the reactions of transition metal atoms with potential ligands to form complexes containing the metal in a zerovalent or a low valent state. These reactions are conveniently considered according to the number of electrons donated by the ligands. We have also studied dehalogenation reactions of copper, silver, and gold which will be discussed later.

3.1. Reactions with Some 2-Electron Donors

Early work on trifluorophosphane[3] showed that this is a very useful ligand in metal atom co-condensation reactions. It resembles carbon monoxide in its properties as a ligand, but it can be condensed at −196°C unlike carbon monoxide. We have continued to use trifluorophosphane mixed with other ligands in a variety of metal atom reactions.

Trimethylphosphane reacts on condensation with Co, Ni, and Pd atoms to form the known tetrakis(trimethylphosphane)metal(0) complexes in modest yields (5—15%). Iron vapor and trimethylphosphane give the previously unknown $Fe[P(CH_3)_3]_5$, a yellowish-red intensely reactive solid, which can be sublimed at room temperature. The yield of the compound is higher if the trimethylphosphane is diluted with pentane. The co-condensate at −196°C is green-colored, suggesting that $Fe[P(CH_3)_3]_5$ results from secondary reactions on warm-up. Hexane does not have the same effect as pentane and seems to inhibit complex formation. The reason for this striking difference in behavior between two chemically inert diluents is not yet understood.

We have reacted triphenylphosphane with nickel atoms in the rotary apparatus, using a solution in methylcyclohexane at −120°C or a solution in Silicone 704 at 0°C. In both cases, the yield of tetrakis(triphenylphosphane)nickel(0) was very high. Recovery of the pure crystalline solid was easier from the volatile hydrocarbon than from the oily Silicone.

The diatomic molecule PN is generated by heating P_3N_5 at 850°C under high vacuum.

$$P_3N_5 \longrightarrow 3\ PN + N_2 \qquad (1)$$

We have condensed PN and metal atoms with a very large excess of krypton on to a CsI window at 10°K, and we have observed the formation of metal complexes by changes in the infrared spectra on warming the matrix to 20—30°K. With Ni atoms, we see the formation of nickel-N_2 and nickel-PN complexes, and complexes in which both N_2 and PN are coordinated to the nickel. The Ni—N_2 system has been previously studied by *Ozin et al.*[5]. Ag atoms complex preferentially with PN and the species AgPN and $(AgPN)_2$ are formed. Studies with $P^{14}N$ and $P^{15}N$ suggest that PN coordinates through the phosphorus atom to transition metals.

We have attempted to make $Ni(N_2)_4$ by condensing nickel vapor on a surface cooled by liquid nitrogen in the presence of 1 torr pressure of gaseous nitrogen. Subsequent addition of other ligands such as 1,5-cyclooctadiene which would be expected to displace coordinated N_2 and form complexes, gave no evidence that any $Ni(N_2)_4$ was present. In a related experiment, palladium was condensed at −196°C in the presence of 1 torr pressure of CO. Addition of PF_3 did result in the formation of $Pd(PF_3)_4$, suggesting that $Pd(CO)_4$ may have been present on the cold surface. Tetracarbonylpalladium has previously only been prepared in matrix isolation studies by *Ogden et al.*[6]. The matrix isolation method permits the formation of metal complexes which may be endothermic with respect to the solid metal and the ligand. The possibility of obtaining these compounds free of the matrix environment depends critically on their kinetic stability. Our results indicate that $Ni(N_2)_4$ is not kinetically stable at −196°C but that $Pd(CO)_4$ may be stable.

3.2. Reactions with 3-Electron Donors

Apart from work on reactions of nitric oxide with metal atoms[7], our work with 3-electron donors has been confined to studies of allyl compounds. Using tetraallyltin as a source of allyl groups in a co-condensation with Ni atoms at −196 °C gives fair yields (20—30%) of bis(η-allyl)nickel. We could not isolate tris(η-allyl)iron from a similar co-condensation of Fe atoms amd tetraallyltin. However, condensation of Fe atoms with a mixture of tetraallyltin and trifluorophosphane forms $(\eta^3\text{-}C_3H_5)Fe(PF_3)_3$, a paramagnetic, purple compound, stable for short periods at 20 °C. Only a trace of $(\eta^3\text{-}C_3H_5)_2Fe(PF_3)_2$ is formed although this is an 18-electron compound and the observed product is a 17-electron compound.

The reaction of Co atoms with trifluorophosphane and either propene or cycloheptatriene gives an allyl derivative: in each case, the hydrogen loss from the organic reactant must be facilitated by the formation of the tetrakis(trifluorophosphane)cobalt hydride (eq. (2)).

$$\begin{aligned} Co(g) + C_3H_6(g) + PF_3(g) &\xrightarrow[-196\,^\circ C]{\text{condensed}} (\eta^3\text{-}C_3H_5)Co(PF_3)_3 \\ &\quad + HCo(PF_3)_4 \\ Co(g) + C_7H_8(g) + PF_3(g) &\xrightarrow[-196\,^\circ C]{\text{condensed}} (\eta^3\text{-}C_7H_7)Co(PF_3)_3 \\ &\quad + HCo(PF_3)_4 \end{aligned} \qquad (2)$$

3.3. Reactions with 4-Electron Donors

We have prepared bis(1,5-cyclooctadiene)iron(0) by condensing iron vapor into a 10% solution of 1,5-cyclooctadiene in methylcyclohexane at −120 °C in the rotary reactor[15]. This is believed to be the first synthesis of the iron analog of the well-know bis(1,5-COD)nickel(0). Typically, we condensed 2 g to 5 g of iron vapor into 200 ml of the ligand solution in an hour. The product crystallizes from the solution during the preparation and is carried around the rotating flask as a slurry. At the end of the condensation, the compound is dissolved and recrystallized using low temperature solution techniques (yield 30—40%). The pyrophoric, brown crystals decompose with deposition of iron above −40 °C. Green solutions of the compound in hexane quickly deposit an iron mirror above −30 °C, but solutions in 1,5-COD are stable up to 0 °C. Solutions of the compound give no ^{1}H-NMR signal indicating that the compound is paramagnetic, but NMR, ESR, and magnetic balance measurements have all been rendered uncertain by the very facile decomposition of the compound to metallic iron. If the compound is paramagnetic, this would indicate a tetrahedral arrangement of the double bonds in the ligand around the metal, but diamagnetism would indicate a square planar structure.

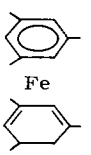
Many other ligands displace cyclooctadiene from $(COD)_2Fe$, including phosphanes, cyclooctatetraene, cycloheptatriene, and butadiene. Since gram quantities of the compound can be made it is a useful reagent for synthesizing other iron compounds. In many cases, it is unnecessary to isolate the pure compound but merely to add a reactant to the crude product in the rotary reactor. Co-condensation of iron vapor and a mixture of cyclooctatetraene and trifluorophosphane at −196 °C gives a low yield of cyclooctatetraene-tris(trifluorophosphane)iron(0). It seems that COT is readily polymerized in metal atom reactions and this accounts for the poor yield of the complex.

3.4. Reactions with 5- and 6-Electron Donors

Nickel vapor reacts on co-condensation with the *closo*-carborane $C_2B_9H_{11}$ to give the known complex $(C_2B_9H_{11})_2Ni$. This compound is a derivative of the *nido*-carborane anion $[C_2B_9H_{11}]^{2-}$. Thus the metal atom forces the carborane to undergo a cage opening reaction from a *closo*- to a *nido*-structure. It is hoped that this will prove to be a general method for making metallo-carborane complexes.

Unlike the neighboring elements in the first transition series, manganese vapor does not react on condensation with cyclopentadiene at −196 °C. However, a mixture of cyclopentadiene and benzene, toluene, or mesitylene condensed with manganese vapor gives a low yield of the corresponding (arene)$Mn(C_5H_5)$ compound. Hydrogen is evolved only on warming the condensate to about −120 °C showing that cyclopentadienyl derivatives are not primary products. The results imply that an arene-manganese complex is better able to coordinate to cyclopentadiene than are manganese atoms. Using different experimental methods, *Koerner von Gustorf*[16] reported similar reactions of manganese vapor.

The formation of arene-iron complexes in co-condensation reactions has already been reported[7–10]. However, we have found that condensation of iron vapor with mesitylene gives modest yields of *(1)* as the only isolable product. It is not clear how one of the diene ligands can gain two additional hydrogen atoms, although the product is then a stable 18-electron compound whereas bis(mesitylene)iron would be a 20-electron compound.



(1)

The reactions of chromium atoms with aromatic compounds has been studied more extensively than any other type of metal atom reaction[2, 8, 10, 11]. We can now report a few additional recent observations: we have prepared two complexes of chromium with hexafluorobenzene, $(C_6F_6)Cr(PF_3)_3$ and $(C_6F_6)Cr(C_6H_6)$ by condensing chromium vapor and C_6F_6 with PF_3 and C_6H_6, respectively. The yields are very poor, 1—2% at the most. The competing reaction seems to be defluorination of the C_6F_6 by chromium. However, each of the C_6F_6 complexes is quite stable in air and can be heated to 100 °C without decomposition.

Work by *Skell et al.*[11] has shown that the yields of arene-chromium complexes from atom reactions are higher for some halobenzenes than for benzene itself. To study this effect further, we took an equimolar mixture of C_6H_6, C_6H_5F, 1,4-$C_6H_4F_2$, 1,3,5-$C_6H_3F_3$, 1,2,3,5-$C_6H_2F_2$, C_6HF_5, and C_6F_6, along with excess trifluorophosphane, and condensed it with chromium vapor. The yield of (arene)$Cr(PF_3)_3$ was a maximum with 1,4-$C_6H_4F_2$ and fell to a minimum with C_6F_6. The decrease in yield from difluoro- to hexafluorobenzene must be due to the increasing tendency for a defluorination reaction to occur. It seems that kinetic factors determine the high

yield of the difluorobenzene complex relative to the benzene complex, as the benzene complex is more stable thermodynamically.

Condensation of Cr atoms with a mixture of pyridine and trifluorophosphane gives two volatile products, $(\sigma\text{-}C_5H_5N)Cr(PF_3)_5$ and $(\pi\text{-}C_5H_5N)Cr(PF_3)_3$. The latter appears to be the first authentic π-pyridine complex. The ^{1}H-NMR spectra of the two molecules are very similar but the resonances in the π-complex are about 2 ppm upfield of those in the σ-complex. Although $(\pi\text{-}C_5H_5N)Cr(PF_3)_3$ is stable in air for short periods, moisture eventually promotes base attack by the pyridine on coordinated trifluorophosphane and an involatile white solid is formed.

3.5. Dehalogenation Reactions of Copper, Silver, and Gold

The dehalogenation of boron trichloride by Cu atoms was the first reaction of a transition metal vapor to be reported[12]. The reaction provides one of the best ways of making diboron tetrachloride or alkyl-substituted diboron chlorides as the yields are high (40—70%) and copper can be vaporized in large quantities. The corresponding reaction of Cu or Ag atoms with phosphorus trichloride gives a 15% yield of diphosphorus tetrachloride, but much of the reduced phosphorus trichloride remains coordinated to the metal halide.

Copper and silver atoms are more selective dehalogenating reagents towards organic compounds than are atoms of the alkali metals. We have condensed Cu and Ag atoms with *R*(−)-*sec*-butyl chloride at −196°C and in each case the product is *S,S*(−)-3,4-dimethylhexane in about 70% optical purity. The reaction of *R*(−)-*sec*-butyl chloride with sodium vapor at −196°C gives an optically inactive 3,4-dimethylhexane.

Gold atoms react on co-condensation with ethyl bromide at −196°C to give butane, ethylene, ethane, and gold(I) bromide. However, ethyl chloride does not react with Au atoms. This observation has important implications. Using available thermodynamic information, it can be calculated that the hypothetical reaction between solid gold and ethyl bromide would be just exothermic, whereas a reaction between solid gold and ethyl chloride would be endothermic. Despite the high heat of formation of Au atoms, it seems that in this case the only advantage in using atomic instead of solid gold is kinetic rather than thermodynamic.

4. Final Comments and Conclusions

Although we have been so successful with a variety of metal atom reactions, not all reactions we attempt go as planned for several reasons. Some metal vapors, notably manganese and tin, are very much less reactive than expected. As discussed by *Ozin*[13], this may be due to more rapid aggregation of these atoms on the cold surface than for other metal atoms. Furthermore, the metal atoms occasionally cause unwanted chemical changes such as dehalogenations, deoxygenations, or catalytic polymerization of organic compounds. Finally, the finely divided metal formed by aggregation of some of the metal atoms sometimes catalyzes the decomposition of the reaction products. We are learning when to expect these types of behavior, but metal atom reactions nevertheless continue to provide surprises.

It must be predicted that many more chemists will soon be using metal atoms in chemical synthesis because useful and exciting compounds can thus be made simply. The apparatus need not be expensive or elaborate to give excellent results. Static apparatus for co-condensations at −196°C and rotary solution apparatus for reactions at higher temperatures should become standard items of equipment to be found in those laboratories synthesizing metal compounds. Probably much more use will be made of the atoms of metals which can be easily vaporized at moderate temperatures on a 2—10 g scale than of the very refractory elements.

The experiments described in this paper have been carried out by Dr. R. Mackenzie, Dr. T. Turney, Dr. R. Middleton, and R. Atkins, and by M. Anthony, M. Baxter, and P. Taylor. R. Porter has given technical assistance and the work has been generously supported by the Science Research Council.

Received: June 27, 1974 [A 51 IE]
German version: Angew. Chem. 87, 295 (1975)

[1] *P. L. Timms*, Advan. Inorg. Chem. Radiochem. *14*, 121 (1972); *P. S. Skell* and *M. J. McGlinchey*, Angew. Chem. *87*, 215 (1975); Angew. Chem. internat. Edit. *14*, 195 (1975).
[2] *P. L. Timms*, J. Chem. Educ. *49*, 782 (1972).
[3] *P. L. Timms*, J. Chem. Soc. *A 1970*, 2526.
[4] *E. V. Hallam*: Vibrational Spectroscopy of Trapped Species. Wiley-Interscience, London 1973.
[5] *H. Huber, E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, J. Amer. Chem. Soc. *95*, 332 (1973).
[6] *J. H. Darling* and *J. S. Ogden*, J. C. S. Dalton *1973*, 1079.
[7] *R. Middleton, J. R. Hull, S. R. Simpson, C. H. Tomlinson*, and *P. L. Timms*, J. C. S. Dalton *1973*, 120.
[8] *P. L. Timms*, Chem. Commun. *1969*, 1033.
[9] *E. Koerner von Gustorf, O. Jaenicke*, and *O. E. Polansky*, Angew. Chem. *84*, 547 (1972); Angew. Chem. internat. Edit. *11*, 532 (1972).
[10] *D. L. William-Smith, L. R. Wolf*, and *P. S. Skell*, J. Amer. Chem. Soc. *94*, 4042 (1972).
[11] *P. S. Skell, D. L. William-Smith*, and *M. J. McGlinchey*, J. Amer. Chem. Soc. *95*, 3337 (1973).
[12] *P. L. Timms*, Chem. Commun. *1968*, 1525; J. C. S. Dalton *1972*, 830.
[13] *E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, Angew. Chem. *87*, 314 (1975); Angew. Chem. internat. Edit. *14*, 293 (1975).
[14] *W. Reichelt*, Angew. Chem. *87*, 239 (1975); Angew. Chem. internat. Edit. *14*, 218 (1975).
[15] *R. Mackenzie* and *P. L. Timms*, J.C.S. Chem. Comm. *1974*, 650.
[16] *E. A. Koerner von Gustorf, O. Jaenicke, O. Wolfbeis*, and *C. R. Eady*, Angew. Chem. *87*, 300 (1975); Angew. Chem. internat. Edit. *14*, 278 (1975).

The Laser-Evaporation of Metals and Its Application to Organometallic Synthesis[**]

By Ernst A. Koerner von Gustorf, Ottmar Jaenicke, Otto Wolfbeis, and Colin R. Eady[*]

1. Introduction

In recent years reactions with metal atoms have become an important synthetic method in the area of inorganic and organometallic chemistry[1-3]. The high reactivity of completely "naked" metal atoms often allows reactions at liquid nitrogen temperatures or even lower as a result of the missing interactions in the metal assembly of the condensed phase. Furthermore, steric shielding is also absent. The differences in reactivity between the isolated atoms and the condensed phase increase with the heat of atom formation[2].

Metal atoms are produced by evaporation of metals in high vacuum[4]. Several procedures exist for metal evaporation: Electrical resistive heating; bombardment with electrons of a few kV; cathodic sputtering; inductive heating; and evaporation by arcing.

The first four of these procedures are industrially applied to the production of thin layers[5]. All procedures have different advantages and disadvantages for chemical synthesis with metal atoms.

Since continuous lasers with high output have become available, and since further developments in this area can be expected, we have investigated the possibilities of metal evaporation with lasers and the application of this method to chemical synthesis[6].

[*] Dr. E. A. Koerner von Gustorf, Dr. O. Jaenicke [***], Dr. O. Wolfbeis [****], and Dr. C. R. Eady [*****]
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
433 Mülheim/Ruhr, Stiftstrasse 34—36 (Germany)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

[***] Present address: Research Laboratories, Eastman Kodak Co., Rochester (USA)

[****] Present address: Institut für Organische Chemie, Universität Graz (Austria)

[*****] Present address: University Chemical Laboratory, Cambridge (England)

2. Laser-Evaporation of Metals

2.1. Selection of Suitable Lasers

Lasers systems currently available are listed in Table 1[7]. It is seen that only gas and solid state lasers can be considered for metal evaporation when operating in the continuous wave mode.

Commercially available high powered lasers are the technically sound CO_2 and YAG lasers. CO_2 lasers can give an output of several kW while a YAG laser can produce several hundred watts. The CO_2 laser functions by transfer of vibrational energy from N_2, excited by gas discharge, to CO_2, the stimulated emission of which is at 10.6 μm. However, to achieve laser action a resonator is needed of at least 3 m in length, and even when folded it still requires a great deal of space. Since the CO_2 laser is very robust and reliable under conditions of continuous operation, it has found many applications in *e.g.* welding and cutting.

Table 1. Laser systems with typical data [7].

Laser system	Active medium	Excitation	Typical lengths [cm]	Output [watt] continuous/pulsed operation	
Gas laser	Noble gases, molecular gases, metal vapors	Gas discharge, chemical excitation	50	10^{-3}—10^{4}	10^{3}—10^{11}
Liquid laser	Organic dyes in solvents	Light from flash or laser	5	10^{-1}	10^{6}
Semiconductor laser	Semiconductor elements doped with Zn or Se	Electric current	0.1	10^{-1}	10^{4}
Solid-state laser	Crystals and glasses doped with metal atoms or rare earths	Flash lamps, continuous gas discharge lamps, tungsten-band lamps.	5	10^{-2}—10^{2}	10^{4}—10^{9}

The YAG laser consists of Yttrium-Aluminum-Garnet doped with Nd^{3+}. On optical excitation, a metastable doublet state of Nd^{3+} is populated which emits at 1.06 μm. A special advantage of a YAG crystal is its high thermal conductivity, allowing large excitational energies. The krypton lamps which are commonly used for the optical excitation have an average life span of 50 hours and can be easily exchanged.

A decision between these two types of lasers should be guided by two points. Firstly, a YAG laser is two to three times more expensive than a CO_2 laser with the same output. Secondly, the wavelength-dependent reflectivity of metals is of special importance. Figure 1 shows the reflectivity of some selected metals as a function of the wavelength[8] and in relation to the emission of a CO_2, a YAG, and a ruby laser.

Iron, for example, is seen to absorb approximately seven times as much energy at 1.06 μm (YAG) as at 10.6 μm (CO_2), which means that in this case preference is to be given to the YAG laser, also in view of the output/price ratio. It further

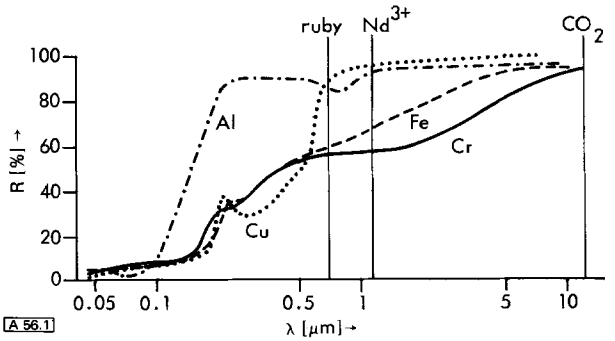


Fig. 1. Reflectivity R of metals as a function of wavelength, λ [8].

becomes clear that highly reflecting metals like aluminum can only be evaporated with great difficulty using an IR laser.

However, two points should be considered in this connection:

a) Many materials absorb like gray bodies[9] in the melting point region, which means that the reflectivity in this temperature range can change to higher energy absorption.

b) As can be seen from Figure 2, the reflectivity at 1.06 μm decreases with increasing energy flux density due to non-linear interaction between light and irradiated material[10]. This effect is significant above 10^8 W/cm^2.

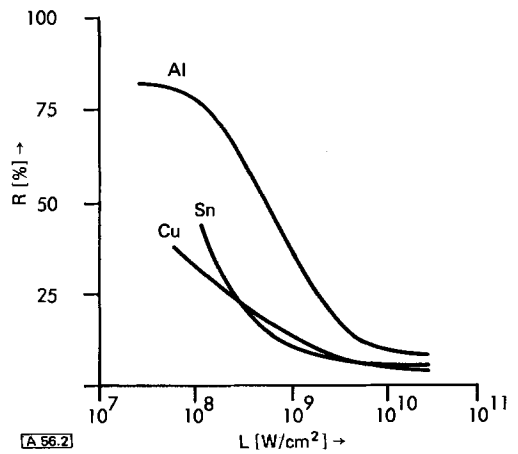


Fig. 2. Reflectivity R at 1.06 μm of aluminum, tin, and copper as a function of energy flux density [10].

Typical values for the diameter of focused laser beams lie in the range of 0.1—2 mm. A 200 W YAG laser in continuous operation and with a beam diameter of approximately 1 mm, produces a power density of 2×10^4 W/cm^2. Hence a region of decreasing reflectivity can only be reached by pulsing (see Table 1).

2.2. The "Window Problem"

While conventional methods of metal evaporation permit location of the energy source inside the high vacuum system, a window is needed when using a laser in order to allow the beam to enter the system from outside. According to our experience[11], germanium is well suited as a window material at 10.6 μm. The window can also be shaped as a lens for the purpose of focusing the beam. Quartz is a suitable window material for 1.06 μm. It is important that the evaporated material does not coat the window. If the window is no longer transparent energy absorption will result in rapid destruction. *Timms*[12] judges this problem as follows: "Heating methods such as a laser beam or focused energy from the sun or from an arc are not easily used for continuous vaporization under vacuum, as vaporized material tends to coat the window through which energy passes into the vacuum system."

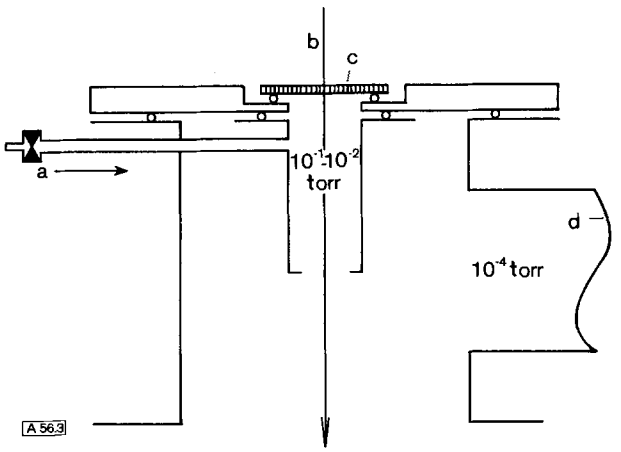


Fig. 3. Principle of a "gas window" which prevents the coating of the laser beam window. a, gas flow control valve; b, laser beam; c, quartz lens; d, vacuum port.

A simple solution of this technical problem is shown in Figure 3. Underneath the quartz lens a gas "window" is mounted on the high vacuum side. This is a piece of tubing into which one can admit gas (*e. g.* argon) through a controlled leak (gas flow control needle valve). Thus the pressure can be increased in this area so that the mean free path is reduced to a few mm. The metal atoms which are moving vertically upwards from the evaporating material are deviated in this chamber by collision. They hit the inner wall of the tubing, remain there, and can therefore no longer reach the window. The window remained completely uncoated when this device was tested by evaporating metals for several hours at a rate of approximately 10 g/h in the apparatus shown in Figures 6 and 7.

Under certain circumstances it is necessary to refocus the laser beam in close proximity to the evaporating material. The lens has to be mounted completely inside the apparatus. Coating of the lens under these conditions can be avoided by using the device depicted in Figure 4.

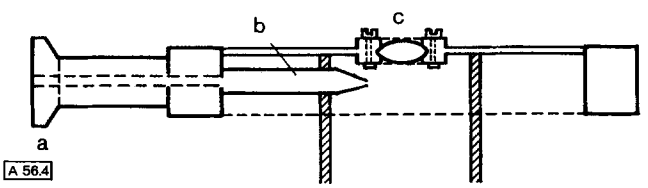


Fig. 4. Ring-shaped lens support with slit jet (to avoid coating of lenses). a, flange for gas flow control valve; b, slit jet; c, lens.

A slit jet is attached to the ring-shaped support of the lens. This slit jet is fed with *e. g.* argon through a gas flow control needle valve. The gas stream flows out of the slit jet across that surface of the lens which has to be kept clear. A sufficient gas dosage will deflect evaporating material away from the lens area. Thus, it can be seen that the "window problem" can easily be controlled in practice.

2.3. Advantages of Laser Application

After a discussion of the problems connected with the application of lasers to metal evaporation, it appears appropriate to point out briefly the specific advantages of this method.

a) No other evaporation method allows the production of comparable energy flux densities. With a focused laser beam it is possible to heat very small areas of material, *e.g.* the tip of a wire. This helps to avoid undesired reactions of extensive hot surfaces with a substrate which is to be co-condensed with the metal atoms. We have developed a device for the continuous evaporation of metal wire using a laser beam. This is depicted in Figure 5.

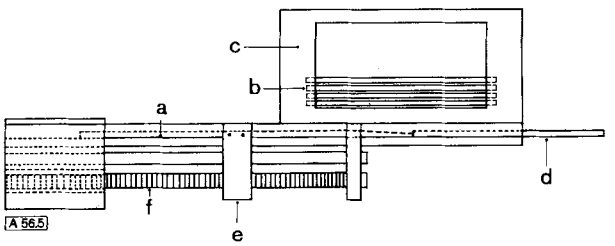


Fig. 5. Device for the automatic feeding of pieces of metal wire into the focal point of a laser beam. a, loading bolt; b, wire cartridge; c, wire magazine; d, cartridge pushed forward; e, threaded guide; f, worm.

Wire pieces of 8 cm length and 1—2 mm diameter are placed in the magazine of the wire feeding mechanism. The lowest wire is pushed forward by a loading bolt out of the magazine into the focal point of the laser beam. The loading bolt is connected by a threaded guide to a worm which is driven by an electric motor. The feed is regulated with a gear box, and adjusted to the speed of melting and evaporation. When the loading bolt is retracted a new piece of wire automatically falls into the slit and is pushed forward with the next forward movement of the bolt.

b) The process of evaporation reacts with little inertia to the switching on and off of the laser, since only small amounts of the material to be evaporated are heated. By fitting a rapid electromechanical shutter into the laser cavity, we are able to chop our YAG laser "mechanically" and thus evaporate metals intermittently.

In principle the possibility of optically deviating the beam allows the alternating evaporation of different metals in the same apparatus.

c) Metal evaporation by the use of laser beams allows the application of the so-called "containerless" method. The metal itself, if necessary cooled from the outside, serves as a container for the molten and evaporating portion. In this way, contamination resulting from a reaction of the container with the molten metal is avoided.

d) The supply of energy by a laser beam from outside provides the possibility of combining several apparatus of different geometry with one laser.

e) There is a special advantage of laser beams in the IR region. Scattered radiation cannot cause any changes of the substrate. This could be of importance for the preparation of radiation-sensitive chemical compounds and is the key problem in the technology of semiconductors for which the application of electron beam evaporation appears to be problematical due to the associated radiation damage.

2.4. Apparatus for Chemical Syntheses with Metal Atoms by Metal Evaporation with a YAG Laser

The aspects discussed in Sections 2.1 to 2.3 have been considered in the construction of the apparatus shown schematically in Figure 6[13]. The reactor, which is 36 cm in diameter and 40 cm high, is made from stainless steel, and can be evacuated to 10^{-4}—10^{-5} torr with a diffusion pump of 1000 l/s suction. The walls of the reactor can be cooled from the outside with liquid nitrogen. The metal to be evaporated is either brought into the focal point of the laser beam using the wire feeding mechanism attached to the side of apparatus, or is put as granules or powder on the bottom of the reactor in a water-cooled copper block to be bombarded there by the laser beam. An alumina crucible which can be heated electrically with a tungsten coil (1.5 mm diameter, 100 A, 10 V) can be placed in this copper block so that our apparatus can also be applied to the evaporation of those metals which cannot be satisfactorily evaporated with a laser beam owing to their high reflectivity. The top of the reactor carries the support for the lens-shaped quartz window, underneath which the gas window described in Figure 3 is located. Attached to the top are also two substrate inlet tubes which can be controlled by magnetic valves. Through these tubes is admitted

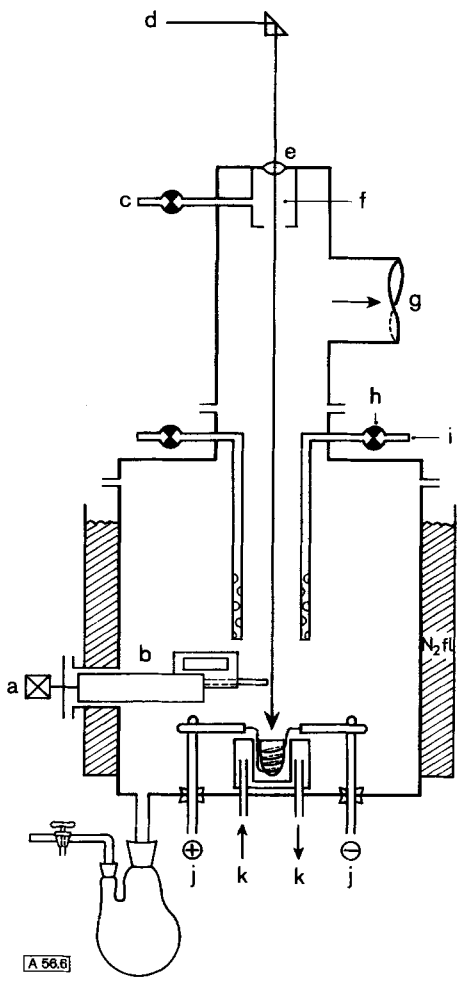


Fig. 6. Diagram of an apparatus for the evaporation (by laser and resistive heating) and co-condensation of metals with organic substrates. a, motor and gearbox; b, wire feeding mechanism; c, gas flow, control valve; d, laser beam; e, lens; f, gas window; g, to vacuum pump; h, magnetic valve; i, substrate inlet; j, current feedthroughs for crucible heating; k, cooling water.—Scale 1 :9 (see Fig. 7). N_2fl = liquid nitrogen.

the material which is to be co-condensed with the metal atoms onto the wall of the reactor. An inspection glass in the top of the reactor allows direct observation of evaporation. Figure 7 shows the apparatus in our laboratory.

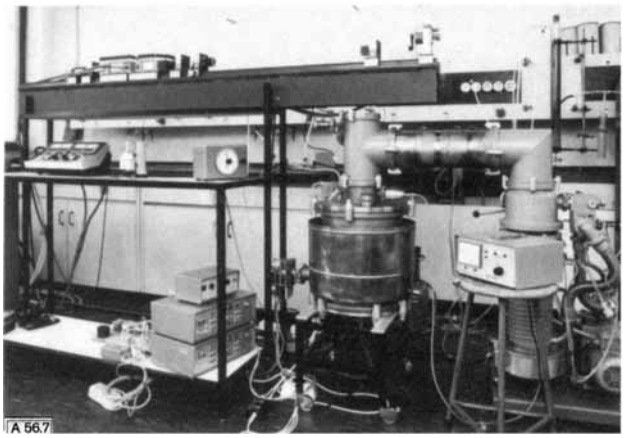


Fig. 7. Apparatus for chemical syntheses with metal atoms in the Mülheim laboratory (see Fig. 6).

The laser used by us is a 200 W cw YAG laser manufactured by Holobeam, and consists of two YAG rods of 7 cm length and 0.7 cm diameter, which are pumped by two krypton lamps each of 5 kW input. The two laser heads together with the mirrors occupy a volume of 60 × 10 × 10 cm, and are mounted on an optical bench. The laser beam is guided by a 90° reflecting prism through the window (lens) into the reactor.

The wire feeding mechanism, the magnetic inlet valves for substrate introduction, and the electromagnetic rapid shutter in the laser cavity, can all be controlled by digital timers.

With the apparatus described we have been able to evaporate chromium, manganese, iron, nickel, copper, erbium, dysprosium, holmium, zinc, tin, lead, and aluminum in amounts of approximately 0.5 to 10 g/h. In the cases of high reflectivity we worked with additional electrical resistive heating. For co-condensation several hundred grams of organic substrate can be used.

Prior to an experiment, the wall of the reactor is first coated with pentane, and thus the co-condensation of metal atoms and reactive substrate takes place on this film. When warming up at the end of an experiment the melting pentane will remove the product mixture from the walls, and everything will be collected in a flask attached to the bottom of the reactor. In many cases it is of advantage to add further reactive compounds during the warming up process. This applies especially to gases which cannot (or only with difficulty) be condensed or frozen at liquid nitrogen temperatures. Reactive primary products can very often be converted into stable compounds by such an after-treatment.

3. Chemical Syntheses with Metal Atoms

The following point of view has been of importance to us for the selection of reactions in order to test the scope and possibilities of our method. Most synthetic procedures in organometallic chemistry can be related *cum grano salis* to the principle of *addition* and *substitution*[14].

Successive addition of ligands to metal atoms allows, in principle, the stepwise formation of a compound:

$$M + xL \rightarrow L_xM \xrightarrow{+yL'} L_xML'_y \quad (1)$$

Complementary to this reaction is the corresponding transformation of a given metal compound by successive steps of substitution:

$$ML_{x+y} \xrightarrow{+yL'} L_xML'_y + yL \quad (2)$$

The photochemical cleavage of the M—L bond is especially suitable[16, 17] for carrying out substitution reactions with dissociative activation[15] according to eq. (3) and (4) (for instance L = CO, PR_3, olefins, dienes).

$$L_nM \xrightarrow{h\nu} L_{n-1}M + L \quad (3)$$

$$L_{n-1}M + L' \rightarrow L_{n-1}ML' \quad (4)$$

Metal atom reactions and photosubstitution can be carried out at very low temperatures, *i.e.* under "extreme" conditions. In many cases they should lead to the same final product (*e.g.* $L_xML'_y$) *via* the same intermediates (*e.g.* L_xM).

Our investigations have been directed towards an analysis of the complementary character of these two methods in order to find out under which circumstances the two methods support each other (*e.g.* for the identification of intermediates), and under which circumstances they supplement each other by showing specific advantages in preparative applications.

3.1. Syntheses of Metal Carbonyls

It was shown by *De Kock*[18] in 1971 that nickel atoms form $Ni(CO)_n$ ($n = 1$—4) in a CO doped argon matrix at 4 K. The stepwise formation of metal carbonyls has also been demonstrated by using matrix spectroscopy in the chromium atom and CO system[19, 20], and for several other metals (see, for instance[3, 21]). With respect to the preparative importance of metal carbonyls which are widely used as starting materials, and considering the relatively high price[22] of current synthetic procedures[23], we have considered the possibility of the synthetic use of the co-condensation of Cr, Mn, and Fe atoms with CO[24]. Since carbon monoxide (m.p. −207 °C) cannot be directly condensed at the temperature of liquid nitrogen and at 10^{-4} torr, we have tried to "getter" it with an excess of tetrahydrofuran. The procedure of warming-up the tetrahydrofuran matrix after finishing the evaporation was also carried out under a CO atmosphere.

As can be seen from Table 2, the yields of $Cr(CO)_6$, $Mn_2(CO)_{10}$, and $Fe(CO)_5$ under these conditions are rather poor. Furthermore, higher evaporation rates did not show any improvement.

According to the work of *Ozin*[25], the binuclear manganese carbonyl results from a diatomic metal species which is formed by the combination of two metal atoms *via* diffusion on the surface of the matrix. In the case of iron it cannot be decided offhand whether a similar mechanism is operative or whether a reactive tetracarbonyl(tetrahydrofuran)iron complex[26] yields $Fe_2(CO)_9$ and $Fe_3(CO)_{12}$ on warming up the matrix. By irradiation of $Fe(CO)_5$ in tetrahydrofuran we have prepared the corresponding complex and submitted it to the same work-up conditions. $Fe_3(CO)_{12}$ is also formed in this case[27].

Table 2. Direct synthesis of metal carbonyls from metal atoms using tetrahydrofuran (THF) as a "getter" system.

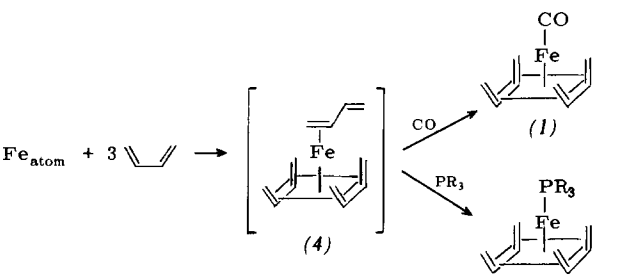
Evaporated metal	[mmol]	THF [ml]	CO [mmol] [a]	Products	Yield [%] [b]
Cr	18	250	45	$Cr(CO)_6$	2.3
Mn	9	140	45	$Mn_2(CO)_{10}$	1.0
Fe	2	220	27	$Fe(CO)_5$	0.4
				$Fe_3(CO)_{12}$	0.2
				$Fe_2(CO)_9$	traces

[a] Addition during evaporation; warming up of the THF matrix in the presence of 3 mol CO.
[b] Yields based on evaporated metal.

3.2. Butadiene Complexes of Iron and Chromium

The smooth photochemical substitution of 4CO groups by 2 butadiene molecules in pentacarbonyliron yielding bis(butadiene)monocarbonyliron *(1)*[28] suggested that we explore the successive addition of butadiene and CO to iron atoms. Co-condensation of butadiene with iron atoms and subsequent warming-up of the matrix under a CO atmosphere, produced *(1)* in a yield of 31%[11]. We suggest that CO interacts with the reactive co-ordinatively saturated intermediate *(4)*. Formation of *(1)* was observed at the same time, and independently of us, by *Skell*[29].

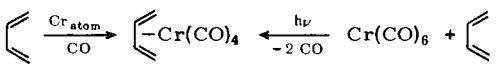
While the photochemical substitution of the last CO in *(1)*, by *e. g.* phosphanes, can only be achieved by irradiation at rather short wavelengths (254 nm)[30], *(2)* can be produced in 17% yield by warming up the *(4)*-containing matrix with PF_3[11]. The corresponding reaction with $P(OCH_3)_3$ gives *(3)*[24].



Bis(butadiene)phosphaneiron complexes are easily accessible by this "one pot" procedure and internal light filter problems[30] which can complicate their photochemical preparations from *(1)*, are avoided.

Bis(diene)monocarbonyliron complexes like *(1)* at *ca.* 100 °C in the presence of triphenylphosphane are catalysts for the dimerization of dienes, *e. g.* of butadiene to 4-vinylcyclohexene and 1,5-cyclooctadiene[28, 31], and are especially suitable for the mixed dimerization of dienes with acrylates yielding heptadienoates[30]. The direction and amount of catalytic activity are strongly affected in *(1)* by replacing CO with phosphanes (see Fig. 8). This example shows that the tailoring of organometallic catalysts is possible using metal atom reactions.

In contrast to iron, the co-condensation of chromium atoms with butadiene and subsequent treatment with CO results in a 4% yield of tetracarbonyl(butadiene)chromium *(5)* which represents the first example of a 1,3-dienetetracarbonylchromium complex[11]. *(5)* decomposes above 0 °C.

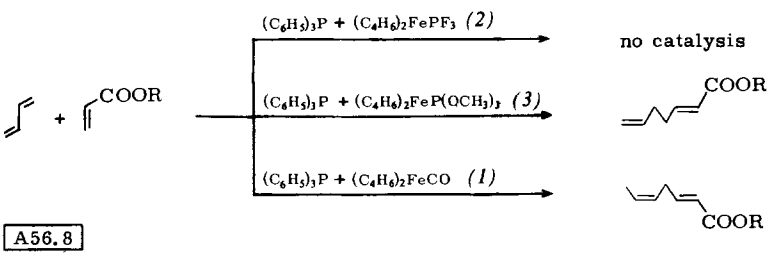


(5)

Compounds like *(5)* are postulated, but not yet isolated intermediates[32] in the photochemically initiated hydrogenation of dienes with $Cr(CO)_6/H_2$[33, 34]. Having established the unstable nature of *(5)* its photochemical synthesis was achieved by irradiation of $Cr(CO)_6$ in the presence of excess butadiene at −40 °C[35]; this represents another example of the complementary nature of metal atom reactions and photosubstitution.

3.3. Cyclooctadiene Chromium Complexes

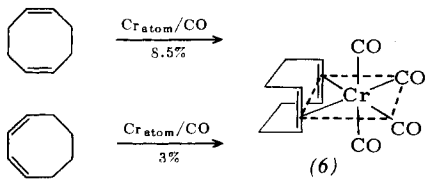
1,5-Cyclooctadiene (1,5-COD) forms a variety of well defined transition metal complexes, the stability of which, *inter alia*, has been ascribed to the chelating character of this ligand[36]. In contrast, complexes with 1,3-COD which can be isolated are quite rare[37, 38]. Cr(0) complexes of 1,3-COD are unknown[39], whereas with 1,5-COD a tetracarbonylchromium complex has been reported, which was formed in 2% yield by the thermal reaction of $Cr(CO)_6$ with 1,5-COD. Attempts to substitute CO in 1,5-COD-$Cr(CO)_4$ have been unsuccessful since 1,5-COD is very easily eliminated[41]; the synthesis of arene- and cyclotrienetricarbonylchromium compounds has been a preparative application of this facile elimination[42].



A56.8

Fig. 8. Effect of axial ligands in bis(butadiene)iron complexes *(1)* to *(3)* on their catalytic activity in the mixed dimerization of acrylate and butadiene. (Besides the main products shown in this figure, further isomeric heptadienoates are formed [30].)

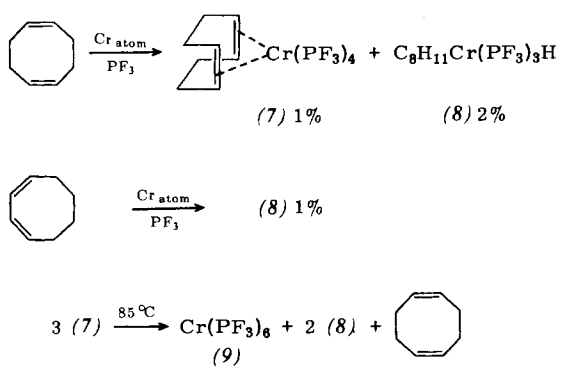
We have therefore investigated the co-condensation of 1,3- and 1,5-COD with chromium atoms with subsequent exposure to CO and PF_3.



(6)

From the reaction of either 1,3- or 1,5-cyclooctadiene with chromium atoms and CO, 1,5-COD-$Cr(CO)_4$ *(6)*[24] is produced. As expected, *(6)* shows 4 IR active CO stretching vibrations (in pentane)[43][*]. A corresponding isomerization with H-shift has also been observed in the thermal reaction of 1,3-COD with $Mo(CO)_6$ and $W(CO)_6$ leading to the 1,5-COD complexes[40]. Apparently this rearrangement cannot be avoided even under our mild conditions.

The co-condensation of 1,5-COD with chromium and PF_3 leads, in addition to the expected 1,5-cyclooctadienetetrakis-(trifluorophosphane)chromium *(7)*, to a red compound *(8)*[24], which is also formed on reaction of 1,3-COD with chromium atoms and PF_3. Heating of *(7)* to 85 °C provided another route to *(8)*, which in this case is formed together with hexakis-(trifluorophosphane)chromium *(9)* and 1,5-COD.



X-ray structural analysis[44] shows *(8)* to be (1—5-η-cyclooctadienyl)hydridotris(trifluorophosphane)chromium (see Fig. 9). The hydridic hydrogen could not be localized. However, in Figure 9 one can recognize the "hole" at the chromium in which it should be situated. Evidence for a hydrido proton is provided by a signal in the ^{1}H-NMR spectrum at $\tau = 22.4$ (at −50 °C in D_8-toluene). With the isolation of *(8)* we have simply captured an intermediate in the transformation of the two cyclooctadienes into each other according to the π-allylhydrido mechanism[45] which was postulated some time ago.

From the ^{1}H- and ^{19}F-NMR spectra[46] solid *(8)* when dissolved rearranges by hydrogen migration into *(8"L')* [most probably *via* the intermediate *(10)*], and appears to be a fluxional molecule at room temperature.

There are parallels in the literature for the hydride addition to the central C atom of a dienyl system[47], as well as for the structural type *(8"L')*[48]. The oxidation of *(8"L')* with Ce^{IV} leads exclusively to 1,3-COD.

[*] ν_{CO}: 2030 w, 1956 m, 1940 vs, 1911 cm^{-1} s.

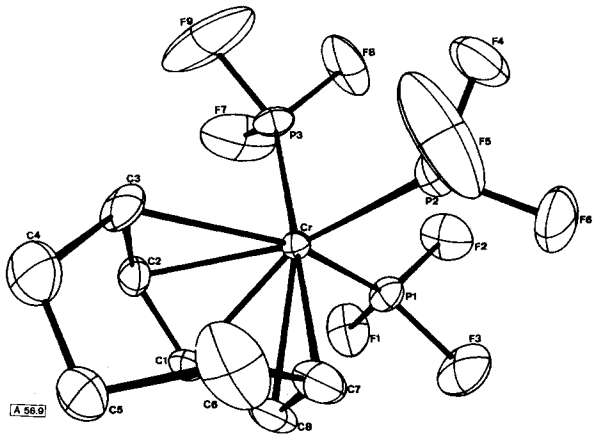
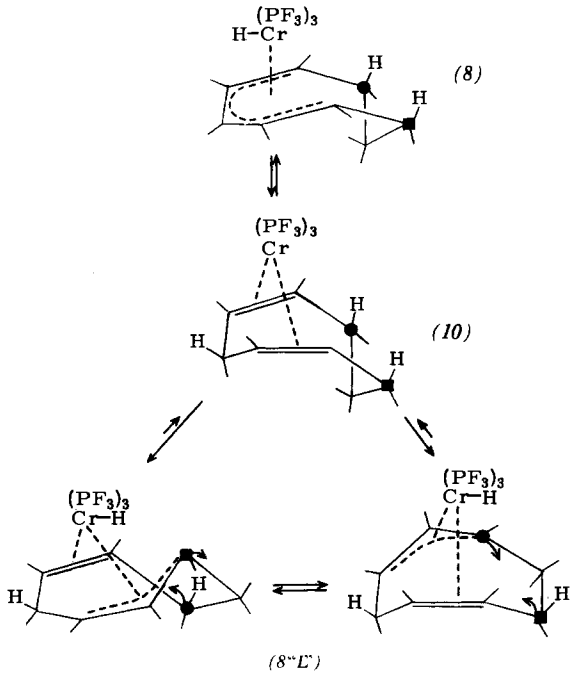


Fig. 9. X-ray structure [44] of (1—5-η-cyclooctadienyl)hydridotris(trifluorophosphane)chromium ($C_8H_{11}Cr(PF_3)_3H$) *(8)*. The hydridic H on chromium was not localized.

In parallel photochemical investigations we have succeeded in synthesizing *(6)* in yields of 20% by the substitution of



(8"L')

CO in $Cr(CO)_6$[35]. Whether *(7)* can be obtained analogously from *(6)* still needs further clarification.

3.4. Reaction of Cycloheptatriene with Chromium and Iron Atoms

In tricarbonyl(cycloheptatriene)chromium the cycloheptatriene moiety can be replaced thermally by other ligand systems, *e.g.* phosphanes[49]; attempts to substitute the CO fail. CO substitution can however be achieved photochemically; one CO can be replaced by $P(C_6H_5)_3$ and $P(OC_6H_5)_3$[50], as well as by $P(OCH_3)_3$[51]; with $P(OCH_3)_3$ even two CO groups can be replaced but with some complication and small yields.

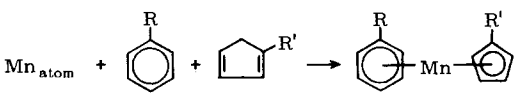
In this case the usefulness of metal atom synthesis as a complementary procedure can be demonstrated again. Co-condensation of chromium atoms with cycloheptatriene and PF_3 yields, after chromatographic work-up, 1% of yellow (1—6-

η-cycloheptatriene)tris(trifluorophosphane)chromium[24].
Work-up without subsequent treatment with PF_3 leads to a mixture of products[52] which contains, besides components of higher molecular weight, a compound according to its mass spectrum of composition $C_{14}H_{17}Cr$, the fragmentation pattern of which corresponds to that of (1—4-η-cycloheptadiene)(η-cycloheptatrienyl)chromium(−1) reported by *E. O. Fischer et al.*[53]. In some fractions a compound $(C_7H_8)_2Cr$ can be observed as reported by *Skell et al.*[54].

The reaction of iron atoms with cycloheptatriene is much smoother and gives good yields of red $(C_7H_9)Fe(C_7H_7)$, in which a cycloheptadienyl system and a valence isomer of the tropylium system are coordinated to iron[52].

3.5. Co-condensation of Manganese Atoms with Arenes and Cyclopentadiene

Timms[1] achieved the synthesis of ferrocene (from Fe and cyclopentadiene) and dibenzenechromium (from Cr and benzene). These findings suggest an investigation for an alternative route to the synthesis of benzene(cyclopentadienyl)manganese(I) *(11)*[55, 56] by the co-condensation of manganese atoms with a mixture of benzene and cyclopentadiene. Indeed pure *(11)* could be produced in this way[24, 57] in yields of 0.5% (with respect to evaporated manganese).



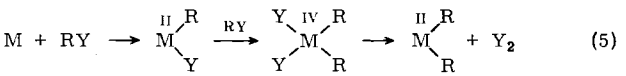
(11), R = R' = H
(12), R = CH_3, R' = H
(13), R = R' = CH_3

The fate of the hydrogen which has to be abstracted from the cyclopentadiene in this reaction is still not clear. The corresponding reactions of manganese atoms with a mixture of toluene and cyclopentadiene give 0.7% of *(12)*. With toluene and methylcyclopentadiene *(13)* actually could only be detected in admixture with components of higher molecular weight. The yields are very unsatisfactory. However, if one considers the yields of *(11)* which are 2—3% for the reaction of C_5H_5Na with $MnCl_2$ and C_6H_5MgBr[55] or 0.4% for the reaction of C_6H_5MgBr with C_5H_6 and $MnCl_2$[56], respectively, then the co-condensation procedure is not so unsatisfactory after all.

D'Aniello and *Barefield*[58] have recently shown that in the reaction of cyclopentadiene with molybdenum and tungsten atoms, the dihydrides $(C_5H_5)_2MH_2$ (M = Mo, W) are formed according to the principle of oxidative addition. Most probably the formation of *(11)* involves a similar intermediate.

3.6. Synthesis of Metal Acetylacetonates

In oxidative addition reactions[59] as briefly mentioned in Section 3.5, according to the general eq. (5) a formal transfer of electrons occurs from the metal to the reacting substrate (in most cases involving bond cleavage), as for instance in the formation of Grignard reagent from magnesium atoms and alkyl halides[60]. Metals which are capable of existing in higher oxidation states can undergo several steps of oxidative addition. Sometimes reductive elimination, *e.g.* of Y_2 in eq. (5), can follow. The detailed mechanism of oxidative addition reactions is a matter of current discussion[61] and is represented schematically in eq. (5).



(5)

We have applied this reaction principle to synthesizing anhydrous metal acetylacetonates by the co-condensation of metal atoms with 2,4-pentanedione (acetylacetone), Y = H[62, 63]. Collective properties of the condensed phase such as overvoltage and passivation do not exist for the isolated metal atoms. The reactions proceed very smoothly and, as shown in Table 3, in acceptable yields[64]. According to preliminary experiments with rare earth metals, erbium, dysprosium, and holmium, can also be converted into the corresponding tris(acetylacetonates) by the co-condensation procedure[52].

Table 3. Synthesis of metal acetylacetonates [M(acac)$_n$] by co-condensation of metal atoms with 2,4-pentanedione (acetylacetone, acacH). Yields are based on evaporated metal.

M	*n*	Yield [%]
Mn	2	30
Cr	3 [a]	32
Fe	2	25
Fe	3 [a]	24
Ni	2	36
Cu	2	10
Zn	2	28
Al	3	14
Sn	2	11
Pb	2	10

[a] Work-up in presence of oxygen.

Amongst the classical procedures of synthesizing metal acetylacetonates, the reaction of metal salts, metal oxides, and hydroxides with 2,4-pentanedione or its metal salts (mostly in water), plays a special role[65, 66]. This method is not without problems for the preparation of the anhydrous compounds and moreover the separation of starting material from the product can also cause difficulties[67]. It was only in 1973 that the sensitive bis(pentanedionato)tin(II) was reported[68]. The direct reaction of the metals themselves with 2,4-pentanedione, which is important for the synthesis of anhydrous metal acetylacetonates in low oxidation states, has long been restricted to the alkali and alkaline earth metals, to aluminum (as an amalgam), and to lead and copper (in the presence of oxygen)[65]. It was only recently that this principle was applied to the transition metals manganese, iron, cobalt, and nickel, which were converted electrochemically into the anhydrous metal acetylacetonates[69].

Complementary to the metal atom synthesis is the preparation of acetylacetonates and their carbonyl derivatives by reaction of 2,4-pentanedione with carbonylmetal derivatives[66] which, for instance, in the case of $Fe(CO)_5$, can be accomplished most efficiently by photolysis[70].

3.7. Reaction of Chromium Atoms with Methanol and Acetic Acid

We have co-condensed chromium atoms with methanol in order to find out whether the reaction of 2,4-pentanedione

with metal atoms can also be applied to other OH-acidic compounds. In a 28% yield we obtained gray/green $Cr(OCH_3)_3$ (oxygen was not excluded during the work-up procedure); its elemental analysis deviated by several percent from the required values[62]. However, the same is observed for the products described in the literature[71].

It was found that isopropanol and *tert*-butanol also react with chromium atoms. However, we were not successful in the purification of the products due to their poor solubility[62].

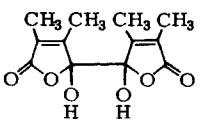
With acetic acid mixtures of chromium(II) and chromium(III) acetate were obtained in approximately 30% yield; the composition of these mixtures was dependent on the work-up conditions.

The atom synthesis of $Cr(OCH_3)_3$ is again paralleled by its photochemical formation from benzene(tricarbonyl)chromium in methanol[71].

3.8. Reductive Coupling of Dimethylmaleic Anhydride with Iron

Our success in the reactions of iron and chromium with dienes to form π-complexes (see Section 3.2) suggested that the corresponding synthesis of olefin complexes should be investigated. It was expected that, in the case of iron, subsequent treatment with CO should lead to the formation of tetracarbonyl(olefin)iron[72] and tricarbonyl[bis(olefin)]iron or ferracyclopentane derivatives as secondary products of the latter[73].

However, the pyrophoric product of the co-condensation of dimethylmaleic anhydride and iron atoms (yield 10—15%) did not react with CO. It was identified as a paramagnetic material of composition Fe(dimethylmaleic anhydride)$_2$[52]. Hydrolysis with hydrochloric acid produced dimethylmaleic anhydride (30%), some as yet unidentified organic material, and in a yield of 50% the novel[74] coupling product *(14)*. Its formation results from a transfer of two electrons from iron to two dimethylmaleic anhydride molecules[75].



(14)

It is worth mentioning that the photoreaction of dimethylmaleic anhydride with $[(C_6H_5)_2PC_2H_5]_3FeH_2N_2$ (which easily loses all ligands on electronic excitation[76]) leads to the same products as in the reaction with "naked" iron[75].

4. Closing Remarks

One can expect that in the future the evaporation of metals with lasers will acquire special importance in the processing of materials since it provides the advantages of evaporation with electron beams without the disadvantage of radiation damage to a sensitive substrate. It should be remembered that the increasing general trend of using lasers in technology will result in a considerable reduction in initial outlay.

In the production of metal atoms for chemical reactions, the laser method provides special advantages. Due to the high energy flux density, heating of very small areas of material, as well as the "containerless" method, are possible. Furthermore the laser evaporation can be pulsed because of the low inertia of the method. The special importance of these advantages in comparison with other methods can only be evaluated in connection with a specific problem.

Chemical syntheses with metal atoms already have a permanent position in the arsenal of the chemists' methods. Now that complete sets of apparatus have become commercially available[77], a rapid increase in the application of this method can be expected. The syntheses of organometallic compounds, of metal complexes and clusters, (especially those with catalytic properties) and of rare inorganic chemicals, should remain in the focal point of the general interest for some time. It is important that the reaction of non-volatile substrates with metal atoms is now possible by using metal evaporation in a rotary reactor, a procedure which is based on the work of *Green*[78] and *Timms*[79]. Experimental studies on the controlled incorporation of metals into macromolecules have therefore become possible. This advance into substrates of low volatility allows higher temperatures for the co-condensation and thus reduces cooling problems which could interfere with an industrial application of chemical syntheses with "naked" atoms. Here one can only say "a man at work in the fields must not go back home to fetch his clothes"[80].

C. R. E. is indebted to The Royal Society, London, for a European Fellowship.—The construction of our metal evaporation apparatus would have been impossible without the enthusiastic co-operation of Messrs Friedhelm Hahn, Wolfgang Köster, and Eckhardt Steinhoff from the Workshop, and of Mr. Wolfgang Küpper from the Electronics Section of the Institute für Strahlenchemie.—Dr. Richard J. Blackborow, Mrs. Marion Budzwait, Dr. Ingrid Fischler, and Dr. Alberto Scrivanti have carried out the quoted current work. We are most grateful to all of them. The kind support of our "venture" by Prof. Dr. O. E. Polansky is gratefully acknowledged.

Received: February 3, 1975 [A 56 IE]
German version: Angew. Chem. 87, 300 (1975)

[1] *P. L. Timms*, Chem. Commun. *1969*, 1033.
[2] *P. L. Timms*, Advan. Inorg. Chem. Radiochem. *14*, 121 (1972).
[3] *E. Koerner von Gustorf* and *O. Jaenicke*, Nachr. Chem. Tech. *21*, 95 (1973).
[4] *B. Siegel*, Quart. Rev. Chem. Soc. *19*, 77 (1965).
[5] *W. Reichelt*, Angew. Chem. *87*, 239 (1975); Angew. Chem. internat. Edit. *14*, 218 (1975).; *M. Auwärter*, Angew. Chem. *87*, 227 (1975); Angew. Chem. internat. Edit. *14*, 207 (1975).
[6] *R. Schaeffer* and *R. K. Pearson*, J. Amer. Chem. Soc. *91*, 2153 (1969), were the first to evaporate carbon (in amounts of 1.5 mg) with a pulsed YAG laser; C_2 produced this way reacted with H_2 to give acetylene. Boron evaporated in the same way (no quantities specified) reacted with HCl to give BCl_3.
[7] *H. Weber* and *G. Herziger*: Laser, Grundlagen und Anwendungen. Physik Verlag GmbH, Weinheim 1972, p. 97.
[8] Landoldt-Börnstein, Vol. 2, Part 8, 6th Edit.; Optical Constants.
[9] Cf. ref. [7], p. 207.
[10] *N. G. Basov, V. A. Boiko, O. N. Krokhin, O. G. Semenov*, and *G. V. Sklizkov*, Sov. Phys. Tech. Phys. *13*, 1581 (1969).
[11] *E. Koerner von Gustorf, O. Jaenicke*, and *O. E. Polansky*, Angew. Chem. *84*, 547 (1972); Angew. Chem. internat. Edit. *11*, 533 (1972).
[12] Cf. ref. [2], p. 135.
[13] *O. Jaenicke*, Dissertation, Universität Wien 1973.
[14] *P. L. Pauson*: Organometallic Chemistry. Edward Arnold, London, 1967.
[15] *C. H. Langford* and *H. B. Gray*: Ligand Substitution Processes. Benjamin, New York 1965.
[16] *E. Koerner von Gustorf* and *F.-W. Grevels*, Fortschr. Chem. Forsch. *13*, 366 (1969).
[17] *M. Wrighton*, Chem. Rev. *74*, 401 (1974).
[18] *R. L. DeKock*, Inorg. Chem. *10*, 1205 (1971).
[19] *M. A. Graham, M. Poliakoff*, and *J. J. Turner*, J. Chem. Soc. *A 1971*, 2939.

[20] *E. P. Kündig* and *G. A. Ozin*, J. Amer. Chem. Soc. *96*, 3820 (1974).
[21] *G. A. Ozin* and *A. Vander Voet*, Accounts Chem. Res. *6*, 313 (1973).
[22] For instance $Mn_2(CO)_{10}$ is commercially available for several US $ per gram.
[23] *R. B. King:* Organometallic Syntheses, Vol. 1, Transition-Metal Compounds. Academic Press, New York 1965.
[24] *C. R. Eady, O. Wolfbeis*, and *E. A. Koerner von Gustorf*, unpublished results.
[25] *E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, Angew. Chem. *87*, 314 (1975); Angew. Chem. internat. Edit. *14*, 292 (1975).
[26] *M. Baudler* and *M. Bock*, Angew. Chem. *86*, 124 (1974); Angew. Chem. internat. Edit. *13*, 147 (1974).
[27] *E. A. Koerner von Gustorf* and *R. Wagner*, unpublished results.
[28] *E. Koerner von Gustorf, J. Buchkremer, Z. Pfajfer*, and *F.-W. Grevels*, Angew. Chem. *83*, 249 (1971); Angew. Chem. internat. Edit. *10*, 260 (1971).
[29] *D. L. Williams-Smith, L. R. Wolf*, and *P. S. Skell*, J. Amer. Chem. Soc. *94*, 4042 (1972).
[30] *J. Buchkremer*, Dissertation, Universität Bochum 1973.
[31] *J. M. Kelly, D. V. Bent, H. Hermann, D. Schulte-Frohlinde*, and *E. Koerner von Gustorf*, J. Organometal. Chem. *69*, 259 (1974).
[32] *G. Platbrood* and *L. Wilputte-Steinert*, J. Organometal. Chem. *85*, 199 (1975).
[33] *J. Nasielski, P. Kirsch*, and *L. Wilputte-Steinert*, J. Organometal. Chem. *27*, C 13 (1971); *G. Platbrood* and *L. Wilputte-Steinert*, J. Organometal. Chem. *70*, 393, 407 (1974).
[34] *M. Wrighton* and *M. A. Schroeder*, J. Amer. Chem. Soc. *95*, 5764 (1973); *M. A. Schroeder* and *M. S. Wrighton*, J. Organometal. Chem. *74*, C 29 (1974).
[35] *E. A. Koerner von Gustorf, M. Budzwait*, and *I. Fischler*, to be published. *trans,trans*-2,4-Hexadiene gave the corresponding $Cr(CO)_4$ complex.
[36] *M. A. Bennett*, Advan. Organometal. Chem. *4*, 353 (1966).
[37] *E. Koerner von Gustorf* and *J. C. Hogan*, Tetrahedron Lett. *1968*, 3191. *J. C. Hogan*, Doctoral Dissertation, Boston College 1969.
[38] *F. A. Cotton, A. J. Deeming, P. L. Josty, S. S. Ullah, A. J. P. Domingos, B. F. G. Johnson*, and *J. Lewis*, J. Amer. Chem. Soc. *93*, 4624 (1971); *A. J. Deeming, S. S. Ullah, A. J. P. Domingos, B. F. G. Johnson*, and *J. Lewis*, J. C. S. Dalton *1974*, 2093.
[40] *E. O. Fischer* and *W. Fröhlich*, Chem. Ber. *92*, 2995 (1959); *G. J. Leigh* and *E. O. Fischer*, J. Organometal. Chem. *4*, 461 (1965).
[39] Gmelins Handbuch der anorganischen Chemie, Vol. 3, Chrom-Organische Verbindungen. Verlag Chemie, Weinheim 1971, p. 141.
[41] *T. Fukumoto, Y. Matsumura*, and *R. Okawara*, Inorg. Nucl. Chem. Letters *9*, 711 (1973).
[42] *H. Werner* and *R. Prinz*, Z. Naturforsch. *22b*, 260 (1967).
[43] Values from ref. [40]: $\tilde{\nu}_{CO} = 2028$ and $1984\,cm^{-1}$.
[44] *D. J. Brauer, C. Krüger, P. J. Robert*, and *Yi-H. Tsay*, to be published.
[45] *T. A. Manuel*, J. Org. Chem. *27*, 3941 (1962).
[46] The ^{1}H-NMR spectrum of *(8 "L")* recorded at room temperature (in D_8-toluene) shows the following groups of signals: $\tau = 4.88$ (2H), 5.46 (2H), 8.88 (3H), 9.55 (3H), and 15.6 (2H). Of the three PF_3 groups, two are chemically equivalent at room temperature. Of those fluxional molecules containing a mirror plane only the proposal shown allows an understanding of the observed ratio of groups of protons. At -50 °C the following groups of signals are observed in the ^{1}H-NMR spectrum: $\tau = 4.60$ (1H), 5.60 (3H), 8.4—9.0 (3H), 9.73 (4H), 22.4 (1H).
[47] *B. F. G. Johnson, J. Lewis, T. W. Matheson, I. E. Ryder*, and *M. V. Twigg*, J. C. S. Chem. Comm. *1974*, 269.
[48] *J. Evans, B. F. G. Johnson*, and *J. Lewis*, J. C. S. Dalton *1972*, 2668; *R. B. King* and *M. N. Ackermann*, Inorg. Chem. *13*, 637 (1974).
[49] *E. W. Abel, M. A. Bennett*, and *G. Wilkinson*, J. Chem. Soc. *1959*, 2323; *R. B. King* and *T. F. Korenowski*, Inorg. Chem. *10*, 1188 (1971).
[50] *W. P. Anderson, W. G. Blenderman*, and *K. A. Drews*, J. Organometal. Chem. *42*, 139 (1972).
[51] *E. Koerner von Gustorf* and *M. Budzwait*, unpublished results.
[52] *R. J. Blackborow, C. R. Eady, A. Scrivanti*, and *E. A. Koerner von Gustorf*, unpublished results.
[53] *E. O. Fischer, A. Reckziegel, J. Müller*, and *P. Göser*, J. Organometal. Chem. *11*, P 13 (1968).
[54] *P. S. Skell, D. L. Williams-Smith*, and *M. J. McGlinchey*, J. Amer. Chem. Soc. *95*, 3337 (1973).
[55] *E. O. Fischer* and *S. Breitschaft*, Chem. Ber. *99*, 2213 (1966).
[56] *R. G. Denning* and *R. A. D. Wentworth*, J. Amer. Chem. Soc. *88*, 4619 (1966).
[57] *P. L. Timms*, according to a personal communication, has made similar observations.
[58] *M. J. D'Aniello* and *E. K. Barefield*, J. Organometal. Chem. *76*, C 50 (1974).
[59] *J. Halpern*, Accounts Chem. Res. *3*, 386 (1970).
[60] *P. S. Skell* and *J. E. Cirard*, J. Amer. Chem. Soc. *94*, 5518 (1972).
[61] *R. G. Pearson* and *W. R. Muir*, J. Amer. Chem. Soc. *92*, 5519 (1970); *A. V. Kramer* and *J. A. Osborn*, J. Amer. Chem. Soc. *96*, 7832 (1974), and literature quoted therein.
[62] *O. Wolfbeis* and *E. A. Koerner von Gustorf*, to be published.
[63] *E. Koerner von Gustorf, O. Jaenicke*, and *O. Wolfbeis*, VI. International Conference on Organometallic Chemistry, Amherst 1973, Abstract 68.
[64] Only *ca.* 40% of the metal evaporated can in general be reacted with the organic substrate since only a part of the walls of our apparatus is cooled, and it is only in this area where co-condensation occurs.
[65] *W. C. Fernelius* and *B. U. Bryant*, Inorganic Syntheses *5*, 105 (1957).
[66] *J. P. Fackler*, Progress Inorg. Chem. *7*, 361 (1966).
[67] *R. G. Charles* and *M. A. Pawlikowski*, J. Phys. Chem. *62*, 440 (1958); *G. Rudolph* and *M. C. Henry*, Inorg. Chem. *3*, 1317 (1964).
[68] *K. D. Bos, H. A. Budding, E. J. Bulten*, and *J. G. Noltes*, Inorg. Nucl. Chem. Letters *9*, 961 (1973).
[69] *W. Eisenbach* and *H. Lehmkuhl*, Liebigs Ann. Chem., in press.
[70] *J. C. Goan, C. H. Huether*, and *H. E. Podall*, Inorg. Chem. *2*, 1078 (1963).
[71] *D. A. Brown, D. Cunningham*, and *W. K. Glass*, Chem. Commun. *1966*, 306.
[72] *E. Koerner von Gustorf, M. C. Henry*, and *D. J. McAdoo*, Liebigs Ann. Chem. *707*, 190 (1967).
[73] *F.-W. Grevels, D. Schulz*, and *E. Koerner von Gustorf*, Angew. Chem. *86*, 558 (1974); Angew. Chem. internat. Edit. *13*, 534 (1974).
[74] *J. H. Brewster, A. M. Fusco, L. E. Carosino*, and *B. G. Corman*, J. Org. Chem. *28*, 498 (1963).
[75] *I. Fischler* and *E. A. Koerner von Gustorf*, to be published; *I. Fischler*, Dissertation, Universität Bochum 1974.
[76] *E. Koerner von Gustorf, I. Fischler, J. Leitich*, and *H. Dreeskamp*, Angew. Chem. *84*, 1143 (1972); Angew. Chem. internat. Edit. *11*, 1088 (1972).
[77] G. V. Planar Ltd., Sunbury-on-Thames, Middlesex, England 1974.
[78] *F. W. S. Benfield, M. L. H. Green, J. S. Ogden*, and *D. Young*, J. C. S. Chem. Comm. *1973*, 866.
[79] *R. Mackenzie* and *P. L. Timms*, J. C. S. Chem. Comm. *1974*, 650.
[80] The Gospels in Modern English, translated by *J. B. Phillips*, The Gospel according to St. Matthew, 24, vs. 18.

Reactions of Metal Atoms with Fluorocarbons[**]

By Kenneth J. Klabunde[*]

1. Introduction[***]

With the advent of *Skell*'s carbon vapor reactor[1], interest in the use of high temperature species as reagents for carrying out syntheses has increased greatly, as recently pointed out by *Timms*' excellent review[2]. The most advantageous use of this technique has been in organotransition metal chemistry. Thus, high temperature transition metal atoms are condensed at low temperature (usually −196°C) simultaneously with vapors of organic substrates. The high temperature atoms are formed by vaporizing metals from resistively heated crucibles, by arcing[3] or by laser heating[4]. These atoms have a high chemical potential, and react at low temperature with the organic substrates to form many unusual compounds. Thus, the method can be termed the "metal atom technique" or "freeze-fry chemistry."

Our main interest has been in using the metal atom technique as a way of making some rather unusual and interesting organometallic species. To do this we have assembled a simple metal atom reactor (see Section 6), in which all of the first row transition metals (excepting scandium) as well as Pd, Pt, Zn, and Ag have been studied.

We have been most interested in the metals V(123), Cr(95), Ni(103), Pd(89), and Pt(135). Shown in parentheses are the heats of formation (kcal/mol) of these metals which indicates the amount of energy needed for vaporization, and thus gives a rough idea of the high reactivity of these species.

Three main areas have interested us: (1) the synthesis of polyhalogenated π-complexes of the transition metals; (2) oxidative insertion of metal atoms into carbon-halogen, carbon-carbon, and carbon-oxygen bonds; and (3) preparation of clean, finely-divided active metals.

2. Polyhalogenated π-Complexes

Normal solution techniques have not been successful in preparations of most polyhalogenated π-complexes of the transition metals. Thus, polyhalogenated bis(arene)-complexes of V and Cr, and π-allyl complexes of Co, Ni, Pd, Pt have not been prepared by classical methods. There are several possible reasons for the failure of such procedures, but probably the most important reasons are the presence in solution of nucleophiles (*e.g.* fluoride ions) and/or solvent that can cause facile rearrangements, decompositions, or competitions for open sites on the metal. The metal atom technique avoids these problems. In the case of bis(arene) complexes, the metal atom technique has been quite useful, as has been previously shown by *Timms*[5], *Skell*[6], *Green*[7], and their co-workers. We have been mainly concerned with F, Cl, and CF_3 substitution on bis(arene)vanadium and bis(arene)chromium complexes as well as a hexafluorobenzene nickel complex[8].

The bis(arene)vanadium complexes shown in Table 1 can be synthesized using the metal atom technique. The yields are not high, and when more than one electron withdrawing substituent on the arene (F or CF_3) are present very low yields are obtained. However, the presence of one CF_3 group/arene is acceptable, and imparts considerably increased air stability to the complexes. Substituents F and Cl do not impart much added air stability to these vanadium complexes.

Table 1. Synthesis of bis(arene)vanadium(0) and bis(arene)chromium(0) complexes employing the metal atom technique.

Compound	Yield [%] [a]	Properties
$(C_6H_5F)_2V$	13	red, air sensitive, sublimes 50—70°C/10^{-3} torr
$(C_6H_5Cl)_2V$	7	orange-red, air sensitive, sublimes 50—60°C/10^{-3} torr
$(p\text{-}F_2C_6H_4)_2V$	1	red, air sensitive, sublimes 25°C/10^{-3} torr, odor of organic sulfide
$(C_6H_5CF_3)_2V$	22	orange, moderately air sensitive, sublimes 25°C/10^{-3} torr (80—90°C decomp.)
$(C_6H_5CF_3)_2Cr$	26	yellow, m.p. 91—91.5°C, decomp. 170°C, slightly air sensitive
$[m\text{-}(CF_3)_2C_6H_4]_2Cr$	17	yellow-green, m.p. 91.5—92.5°C, decomp. 200°C, sublimes rapidly at 100°C/10^{-2} torr, very air stable
$[p\text{-}(CF_3)_2C_6H_4]_2Cr$	38	amber, m.p. 150—152°C, decomp. 266°C, sublimes rapidly at 100°C/10^{-2} torr, very air stable
$(o\text{-}ClC_6H_4CF_3)_2Cr$	33	yellow-green, m.p. 81—82.5°C, decomp. 165°C, sublimes rapidly at 100°C/10^{-2} torr, very air stable

[a] Based on metal vaporized.

The bis(arene)chromium complexes (Table 1) are formed readily using the metal atom technique. The presence of two CF_3 groups/arene is acceptable, and imparts remarkable air stability to the materials. The $[m\text{-}(CF_3)_2C_6H_4]Cr$ and $[p\text{-}(CF_3)_2C_6H_4]Cr$ complexes are indefinitely stable in air at room temperature, and are even stable for short periods of time at over 200°C in air. Good, but less air stability was found for the $(CF_3C_6H_5)Cr$ and $(o\text{-}ClC_6H_4CF_3)Cr$ complexes. Chlorinated solvents such as CCl_4, $CHCl_3$, and CH_2Cl_2, however, accelerate the decomposition.

The unusual air stability of these complexes possessing highly electronegative substituents might have been predicted since the first step in the facile oxidative decomposition of dibenzenechromium(0) is probably the one electron oxidation of Cr yielding a Cr^+ complex. This process would be disfavored by the arenes possessing electronegative substituents.

Examination of the IR spectra of $(C_6H_6)_2Cr(0)$ *vs* $(p\text{-}(CF_3)_2C_6H_4)_2Cr(0)$ yielded some information concerning the metal-ring bonding. *Yamada*, *Nakamura*, and *Tsuchida*[9] showed that the 1500 cm^{-1} band in benzene shifts to 1428 cm^{-1} upon complexation with Cr ($\Delta\nu_{C=C}=72$ cm^{-1}). In $[p\text{-}(CF_3)_2C_6H_4]Cr$ the analogous band at 1529 cm^{-1} shifts to

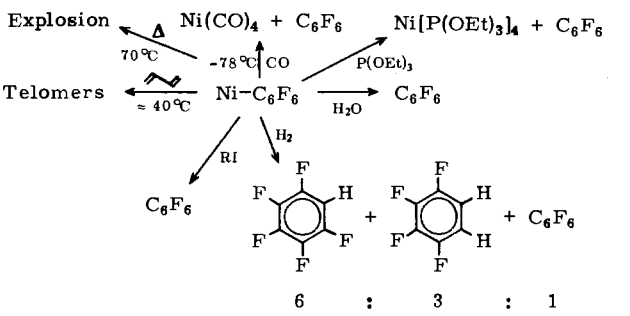
[*] Prof. Dr. K. J. Klabunde
Department of Chemistry
University of North Dakota
Grand Forks, North Dakota 58201 (USA)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

[***] Abbreviations used: Alk = (halo)alkyl; Ar = (halo)aryl; Et = ethyl; R = (halo)alkyl and (halo)aryl; R_f = perfluoroalkyl and perfluoroaryl.

1480 cm^{-1} upon complexation ($\Delta\nu_{C\equiv C} = 49\ cm^{-1}$). Thus, there is less C=C bond weakening upon complexation in the *p*-(CF_3) complex, which would in turn suggest a slightly weaker ring-metal bond in this complex than in dibenzenechromium.

Thus, we find that CF_3 substitution on these Cr(0) complexes has the most advantageous effect on air stability, still allows good thermal stability, and we have not found them to possess any explosive character as has been found for monofluorobenzene-[10] and polyfluorobenzenechromium(0) complexes and the corresponding vanadium(0)complexes[8, 10]. Thus the hexafluorobenzene complexes of vanadium, chromium, and nickel formed by the metal atom technique, were found to be extremely sensitive and explosive[8]. The novel C_6F_6—Ni complex could not be isolated in a pure state[8].



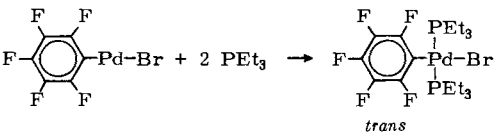
3. Oxidative Insertion of Metal Atoms

Oxidative insertion of metal atoms into carbon-halogen bonds (alternatively termed "oxidative addition" of carbon-halogen bonds to metal atoms) provides a rare opportunity for production and study of non-solvated non-ligand stabilized RMX compounds at low temperature under inert conditions. In the case of transition metals, highly coordinatively unsaturated species can be produced. We have previously reported on a number of reactions of this type:

Zn atoms + $CF_3I \rightarrow CF_3ZnI$	Ref. [11]
Ca atoms + $C_6F_6 \rightarrow C_6F_5CaF$	Ref. [12]
Pd atoms + $C_6F_5Br \rightarrow C_6F_5PdBr$	Ref. [13]
Pd atoms + *n*-$C_3F_7COCl \rightarrow C_3F_7COPdCl$	Ref. [14]

There are good reasons for carrying out these types of studies. Species such as RPdCl (no other ligands) have been proposed as reaction intermediates in palladium promoted olefin arylations, alkylations, carboalkylations, *etc.*[15]. Similarly, RCOPdCl has been discussed as a likely short lived species in palladium catalyzed CO insertion reactions, olefin carbonylations, and reaction mechanisms relating to the Rosenmund reduction[15, 16].

We have concentrated our efforts on the Ni, Pd, Pt triad because of the importance of the corresponding RMX species. Also, we have employed fluorinated alkyl and aryl halides extensively as substrates because it is well known that stronger carbon-metal bonds are formed with these fluorinated systems. Thus, probably higher stability of the non-ligand stabilized R_fMX over the RMX species would result. Considering only the Ni and Pd compounds, the ideal case for highest predicted stability would be C_6F_5PdX. In fact we have produced the very coordinatively unsaturated organometallic species C_6F_5PdBr, and it has exhibited remarkable stability even at room temperature in acetone or the dry state (no ligands). In benzene as solvent it slowly decomposes to C_6F_5—C_6F_5, Pd, and $PdBr_2$ (1 : 1 : 1)[13]. $(C_6F_5PdBr)_n$ is extremely reactive with donating ligands (sulfides, phosphanes, *etc.*) and immedi-



ately takes up two molecules of triethylphosphane to form the bis(phosphane) adduct. This complex is very stable and was shown by NMR data to have *trans* geometry; other phosphanes react similarly[14].

A wide ranging series of Ar_fMX and RMX (M = Ni, Pd) compounds have now been produced in our laboratory. Many of these species are not stable at room temperature, and we have used phosphane trapping techniques in order to determine their thermal stabilities. That is, first the metal atom reaction was carried out at −196 °C, then the matrix warmed from −196 °C to some desired temperature and held there about $^1/_2$ hour, and then triethylphosphane added in order to trap the RMX intermediate as a stable, isolable compound. The results of trapping experiments at a series of different temperatures are collected in Table 2. They will be discussed in sections:

1. (Halo)aryl halides and palladium: Reaction efficiencies for the halides C_6F_5X decrease in the series $C_6F_5I > C_6F_5Br \gtrsim C_6F_5Cl$. All of the resultant compounds C_6F_5PdX were found to be stable at room temperature, soluble in organic solvents, and extremely reactive with phosphane ligands. In the C_6H_5X system, the bromide is more reactive than the chloride. C_6H_5PdBr could not be trapped at 25 or −78 °C, but could at −116 °C. At −78 °C, biphenyl, Pd, and $PdBr_2$ are formed. Thus, the C_6H_5 compounds are thermally far less stable than the C_6F_5 analogs.

2. (Halo)alkyl halides and palladium: CF_3PdBr was generated and trapped by triethylphosphane at either 25 or −70 °C. Both experiments yielded about the same amount of $(Et_3P)_2PdBr(CF_3)$. CF_3PdBr could be washed out of the reactor with acetone while open to the atmosphere, filtered at room temperature, and then triethylphosphane added; about the same amount of adduct was still obtained. Thus, the CF_3PdBr species was stable at room temperature in the air in the dry or dissolved (acetone) state. The yield was low (about 4 %), but only a trace of $PdBr_2$ was formed, and no other products could be detected. Thus, we do not have a very efficient formation of CF_3PdBr at the low temperatures involved; the main competing reaction is Pd—Pd recombination to the bulk metal.

Some R_fPdI compounds are also stable at room temperature; $(CF_3)_2CFPdI$, however, could not even be trapped at −78 °C. Apparently at least two α-fluorine substituents are necessary to impart good thermal stability. In these R_fI reactions (but not R_fBr) large amounts of PdI_2 were always formed, which indicates either free radical abstraction reactions by Pd were important, or the R_fPdI species were formed in vibrationally excited and labile states. R_fBr behaves differently. Trapping experiments were not successful with halides such as CCl_3Br or CF_2Br_2 which shows that the presence of α-halogen other than fluorine (*e.g.* $CF_2BrPdBr$) imparts poor

Table 2. Reactions of alkyl or aryl halides with palladium or nickel atoms followed by trapping of RMX with triethylphosphane:

M atom + R—X → R—M—X $\xrightarrow{2Et_3P}$ $(Et_3P)_2MX(R)$

Decompositions:

ArMX →→ Ar—Ar + M + MX_2

RMX →→ R• + •MX →→ M + MX_2

└→ coupling and disproportionation

Overall stability orders:

$C_6F_5 > CF_3 \approx C_2F_5 \approx n\text{-}C_3F_7 > C_6H_5 > CH_3 \approx n\text{-}C_3H_7 \approx CF_2Br \approx (CF_3)_2CF$

RMX	Thermally stable to about [°C]	Trapping temperature [°C]	Yield [%] [a]
C_6F_5PdCl	> 25	25	7
C_6F_5PdBr	> 25	25 (−196 °C simul. dep.)	8 (30)
C_6F_5PdI	> 25	25	23
C_6H_5PdCl	−116	−116	2
C_6H_5PdBr	−116	−116 (25 and −78 °C failed)	11
CF_3PdBr	> 25	25	3
CF_3PdBr	> 25	− 70	4
CF_3PdI	> 25	25	10
C_2F_5PdI	> 25	25	8
$n\text{-}C_3F_7PdI$	> 25	25	9
$i\text{-}C_3F_7PdI$	< − 78	25 (−78)	0
$CF_2BrPdBr$	< − 78	− 78	trace
CCl_3PdBr	< 0	0	0
CH_3PdBr	< −100	−131	trace
CH_3PdI	< −100		[b]
C_2H_5PdI	< −100		[c]
C_6F_5NiCl	− 80	25	trace
C_6F_5NiCl	− 80	− 45	1
C_6F_5NiCl	− 80	− 90	7
C_6F_5NiCl	− 80	−131 (−196 °C simul. dep.)	10 (32)
C_6F_5NiBr	− 80	−131	10
CF_3NiBr	− 78	− 78	1
CF_3NiI	< − 78	− 78	0
CH_3NiI	< −100		[d]
C_2H_5NiI	< −100		[c]

[a] Yield of trapped product, based on metal vaporized.
[b] Decomposition to methane and ethylene.
[c] Decomposition to ethane, ethylene, and *n*-butane.
[d] Methane cleavage during co-condensation, later decomposition to ethylene.

stability to the RPdX species. Also, non-fluorinated alkylpalladium halides could only be trapped in very small amounts, and decomposition products resulted that can be rationalized in terms of free radicals being formed at very low temperatures:

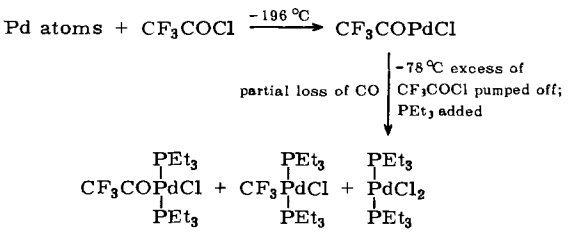
Pd atoms + CH_3CH_2I → (CH_3CH_2PdI) → $CH_3CH_2^{\bullet}$

$CH_3CH_2^{\bullet}$ → $CH_2{=}CH_2$ + CH_3CH_3 + $CH_3CH_2CH_2CH_3$

Overall, the thermal stabilities of the RPdX species vary greatly, and are in the order $C_6F_5 > CF_3 \approx C_2F_5 \approx n\text{-}C_3F_7 > C_6H_5 > CH_3 \approx C_2H_5 \approx CF_2Br \approx i\text{-}C_3F_7$.

3. (Halo)aryl and (halo)alkyl halides and nickel: Nickel atoms yield RNiX compounds that are much less thermally stable than the corresponding Pd species. For example, C_6F_5NiCl was shown to decompose at about −80 °C to perfluorobiphenyl, Ni, and $NiCl_2$. The trapping experiments showed that hardly any insertion products are formed at −45 °C or higher, whereas the yield of decomposition products is high. At −131 °C the opposite is the case. Similar results were found for C_6F_5NiBr. C_6H_5NiX could not be trapped, and only small amounts of CF_3NiBr could be trapped at −78 °C. With non-fluorinated alkyl halides, extremely unstable organometallic species are formed. Free radicals were apparently formed at very low temperatures. In fact, in the case of CH_3I + Ni atoms, methane was given off even during the cocondensation reaction at −196 °C. Overall, stability orders for the nickel system approximate $C_6F_5 > CF_3 > C_6H_5 > CH_3 \approx C_2H_5$.

Acyl halides also react with Pd and Ni atoms (Table 3). The product of insertion of Pd in heptafluorobutyl chloride can be trapped as fairly pure $(Et_3P)_2PdCl(COCF_2CF_2CF_3)$ at −78 °C. Trapping at higher temperatures yields mainly $(Et_3P)_2PdCl_2$. Thus, the primary insertion product was stable at −78 °C. With CF_3COCl and Pd, three products were formed in a trapping experiment at −78 °C.



A similar but more striking result was found in the C_6F_5COCl—Pd reaction where *only* the C_6F_5PdCl was trapped by triethylphosphane (CO completely lost). When non-fluorinated acyl chlorides were reacted with Pd, neither

Table 3. Reaction of acyl halides with palladium or nickel; trapping of product with triethylphosphane:

$$\text{M-Atom} + \text{RCOCl} \rightarrow (\text{RCOMCl}) \xrightarrow{Et_3P} (Et_3P)_2MCl(COR)$$

Decompositions:

$$\text{RCOMX} \xrightarrow{-CO} \text{RMX} \xrightarrow{\text{if unstable}} \text{RX} + \text{R—R} + MX_2 + M$$

$$\xrightarrow[Et_3P]{\text{if stable}} (Et_3P)_2MX(R)$$

Overall stability order:

$$n\text{-}C_3F_7 > CF_3 > C_6F_5 > C_6H_5 > CH_3$$

RCOMCl	Therm. stable to about [°C]	Trapping temp. [°C]	Products	Yield [%] [a]
$CF_3COPdCl$	− 78 (—CO)	−78	$(Et_3P)_2PdCl(CF_3)$	4
			$(Et_3P)_2PdCl(COCF_3)$	7
			$(Et_3P)_2PdCl_2$	5
$n\text{-}C_3F_7COPdCl$	> − 78	−78	$(Et_3P)_2PdCl(CO\text{-}n\text{-}C_3F_7)$	9
$n\text{-}C_3F_7COPdCl$	> − 78	0	$(Et_3P)_2PdCl(CO\text{-}n\text{-}C_3F_7)$	1
			$(Et_3P)_2PdCl_2$	9
$C_6F_5COPdCl$	< − 50 (—CO)	40	$(Et_3P)_2PdCl(C_6F_5)$	23
$C_6H_5COPdCl$	< − 50	40	$C_6H_5—C_6H_5$	10
			C_6H_5Cl	8
			$(Et_3P)_2PdCl_2$	8
$CH_3COPdCl$	< −100	0 (−78)	$(Et_3P)_2PdCl_2$	17
$CF_3CONiCl$	< − 78 (—CO)	−78	$(Et_3P)_2NiCl(CF_3)$	1
			$(Et_3P)_2NiCl_2$	20
$CH_3CONiCl$	< −100 (—CO)	−78	$(Et_3P)_2NiCl_2$	10

[a] Based on vaporized metal.

RCOPdCl or RPdCl could be trapped, and CO was released at very low temperatures.

$$\text{Pd atoms} + C_6H_5COCl \rightarrow (C_6H_5COPdCl) \xrightarrow[-CO\ <-50\,°C]{} C_6H_5\text{–}C_6H_5 + C_6H_5Cl + PdCl_2$$

Nickel reacted with CF_3COCl, and CO was released below −78 °C. At this temperature the excess acyl chloride was pumped out, triethylphosphane added, and CF_3NiCl trapped in low yield.

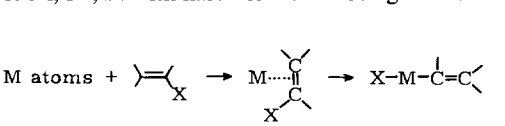
Summarizing the oxidative insertion reactions of Pd and Ni with ArX and RX it can be said: (1) the existence of these coordinatively unsaturated ArMX, AlkMX species has been demonstrated; (2) the effects of Ar or Alk on thermal stability have been determined by means of trapping experiments; (3) we have learned something about the modes of decomposition of ArMX and AlkMX; (4) aryl halides are better than alkyl halides in terms of efficiency of insertion and resultant stability of the intermediates; (5) these reactions have been useful for the preparation of a large number of new bis(phosphane)palladium halide complexes. (Our main interest was in the ArMX and RMX species rather than the phosphane adducts; therefore, not much effort was made toward optimizing the yields of the adducts, although we know the yields go up greatly when the phosphane is deposited simultaneously with ArX and metal atoms[14].) Triethylphosphane has been the most convenient trapping ligand to use due to its high volatility for vacuum transfers. This property also lends volatility to the metal complexes, and nearly all of the phosphane adducts could be studied conveniently by mass spectrometry. In fact the mass spectra are extremely characteristic due to isotopic distribution patterns for Ni and Pd.

Recently some new and very interesting RMX species have been generated. For Pt, the C_6F_5PtBr species has been prepared, has good stability, and reacts with triethylphosphane to yield both *cis* and *trans* phosphane adducts, whereas the Ni- and Pd-analogs yield only the *trans* complexes.

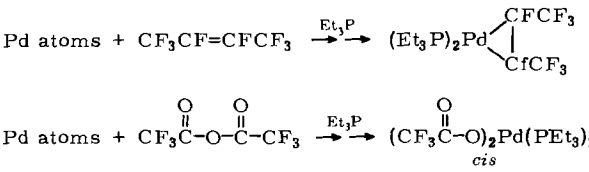
A stable non-fluorinated RMX species, $C_6H_5CH_2PdCl$, has been synthesized from benzyl chloride and Pd atoms. This material is air sensitive, but, surprisingly, does not decompose on warming to room temperature. This result is quite different from other alkylpalladium chlorides (AlkPdCl), and has important implications concerning the question of why some RPdX species are thermally stable and others are thermally very labile. It seems likely to us that bridging aromatic π-systems may be important in coordinating with the open sites on these RPdX species; possibly even more important than the electronegativity of the R group involved.

Reaction of titanium atoms with C_6F_5Br yielded a very unstable material of unknown structure. This unknown material is capable of polymerizing butadiene almost explosively at −78 °C. We have not been successful at trapping or characterizing a species of the type C_6F_5TiBr.

Future efforts in this area should be directed toward learning more about the structural and chemical properties of the more interesting RMX species, and toward learning more about the C—X insertion reaction. Stereochemical aspects of the insertion are being studied with the aid of optically active 1,1,1-trifluoro-2-chloro-2-phenylethane. Also, π and/or σ complexes of Ni, Pd, Pt with halo-olefins are being studied.



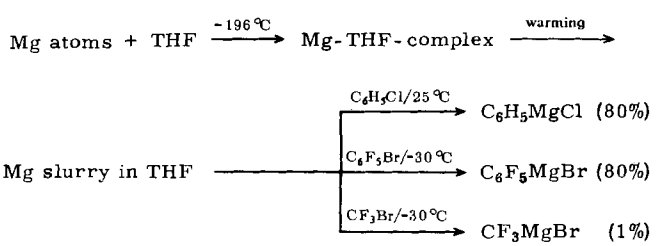
Besides C—X insertions, many other oxidative insertion studies can be envisioned (*i.e.*, Si—X, S—X, N—X, C—C, C—O, O—O, S—S, *etc.*). We have indeed been successful at carrying out C—C and C—O insertions[14]. We have attempted insertion reactions in C—CN bonds with C_6H_5CN and $C_6H_5CH_2CN$, but have not been successful.



4. Production of Clean, Finely-divided Active Metals

Recent literature indicates an intense interest in the production and chemistry of clean, finely-divided metals. Active Mg[17], Zn[18], Ni[19], U[20], and Cr[21] are usually prepared by reduction of metal salts in solution with a reducing agent such as potassium metal.

We have approached the production of active, finely-divided metals using the metal atom technique: metal vapors are co-condensed with solvent, such as tetrahydrofuran (THF) or hexane at −196 °C. On warming, the metal atoms agglomerate, but only to a small degree, and a metal slurry is formed. This slurry can be removed and used as a reagent in normal synthetic procedures. Thus, a Mg-THF slurry has been produced and was very reactive with aryl and alkyl halides that are normally considered unreactive with magnesium. The Mg-THF slurry is useful for the preparation of Grignard reagents at low temperature with no problems of reaction initiation. Both C_6F_5Br and CF_3Br reacted completely at −30 °C. (However, the resultant CF_3MgBr reagent was not very stable at that temperature, and only 1% could be trapped with iodine.)



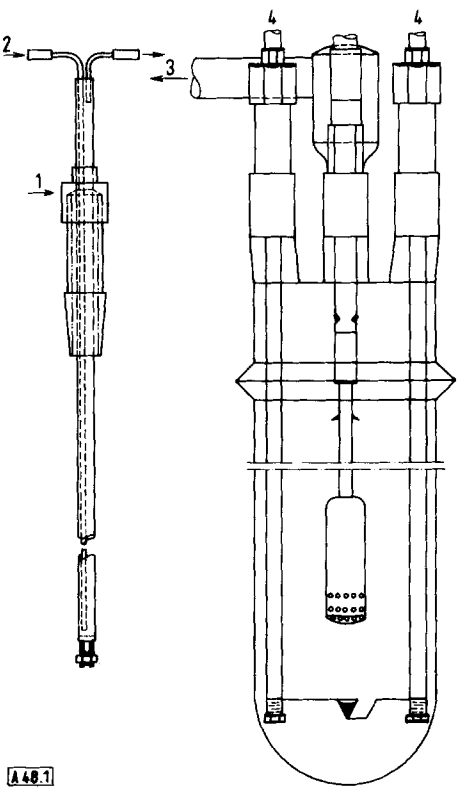
Active nickel, produced by cocondensing Ni vapor with THF followed by warming, serves as a good reagent for coupling alkyl halides such as allyl bromide or benzyl chloride at 40 °C.

5. Practical Considerations

The metal atom technique allows us to produce some unusual compounds and reagents. Our work has shown that highly coordinatively unsaturated organometallic compounds RMX can be produced this way, and these materials may teach us much about catalysis intermediates, especially the homogeneous type. Similarly, active metal slurries produced using this technique may serve as or teach us more about heterogeneous catalysis. Moreover, our interest in polyhalogenated π-complexes of the transition metals stems partly from the fact that some of these compounds can be considered "high energy materials" since there is always the possibility of highly favorable (thermodynamically) decompositions by M—X bond forming processes. Lastly, the metal atom technique in many cases serves as the best (or the only) method for production of new as well as known stable organometallic compounds. Although the yields of these compounds are often quite low (based on metal vaporized), metal wastage can be tolerated since bulk metals are very cheap chemical reagents compared with classical metal complexes as starting materials (*e.g.* $Pd(PR_3)_4$). In most cases even the low yield products are formed in reasonable purity since the main competing reaction is metal atom polymerization to form metal film, which can readily be separated from organometallic compounds.

6. The Reactor

We have succeeded in keeping our metal atom apparatus as simple as possible for reasons of expense as well as to make it attractive to workers in other laboratories. Our present setup can be assembled almost completely from commercially available parts (including crucibles and glass reactor chamber), and can be connected to any normal vacuum line by means of a 24/40 ground glass joint. Usually about 0.3 g of metal



A 48.1

Fig. 1. Reactor (right) and electrode (left) for metal atom reactions. 1, current supply; 2, cooling water; 3, to vacuum line; 4, electrodes.

is vaporized in a typical experiment, although we can readily vaporize 3 g if desirable. Liquid nitrogen is usually used as a coolant for the reactor (about 10 liters is used in a typical experiment) although Dry-Ice cooling has also been employed.

I would like to acknowledge the outstanding work of the graduate students who have been involved in these projects: Dr. James Y. F. Low, Mr. Howard F. Efner, John S. Roberts, Bruce Anderson, and Thomas Murdock. Also, the support of

the National Science Foundation (GP-34493 and GP-42376), and Research Corporation is greatly appreciated.

Received: June 11, 1974 [A 48 IE]
German version: Angew. Chem. 87, 309 (1975)

[1] *P. S. Skell, L. D. Wescott, Jr., J. P. Goldstein,* and *R. R. Engel,* J. Amer. Chem. Soc. *87,* 2829 (1965).
[2] *P. L. Timms,* Advan. Inorg. Chem. Radiochem. *14,* 121 (1972), and references therein.
[3] *P. S. Skell* and *J. E. Girard,* J. Amer. Chem. Soc. *94,* 5518 (1972).
[4] *E. Koerner von Gustorf, O. Jaenicke,* and *O. E. Polansky,* Angew. Chem. *84,* 547 (1972); Angew. Chem. internat. Edit. *11,* 532 (1972).
[5] *R. Middleton, J. R. Hull, S. R. Simpson, C. H. Tomlinson,* and *P. L. Timms,* J. C. S. Dalton *1973,* 120.
[6] *M. P. Silvon, E. M. VanDam,* and *P. S. Skell,* J. Amer. Chem. Soc. *96,* 1945 (1974).
[7] *F. W. S. Benfield, M. L. H. Green, J. S. Ogden,* and *D. Young,* J. C. S. Chem. Comm. *1973,* 866.
[8] *K. J. Klabunde* and *H. F. Efner,* J. Fluorine Chem. *4,* 115 (1974).
[9] *S. Yamada, N. Nakamura,* and *R. Tsuchida,* Bull. Chem. Soc. Jap. *30,* 647 (1957).
[10] Private communications with *P. L. Timms.*
[11] *K. J. Klabunde, M. S. Key,* and *J. Y. F. Low,* J. Amer. Chem. Soc. *94,* 999 (1972).
[12] *K. J. Klabunde, J. Y. F. Low,* and *M. S. Key,* J. Fluorine Chem. *2,* 207 (1972).
[13] *K. J. Klabunde* and *J. Y. F. Low,* J. Organometal. Chem. *51,* 33 (1973).
[14] *K. J. Klabunde, J. Y. F. Low,* and *H. F. Efner,* J. Amer. Chem. Soc. *96,* 1984 (1974).
[15] *R. F. Heck,* J. Amer. Chem. Soc. *90,* 5518, 5526, 5531, 5535, 5546 (1968); *P. M. Henry,* Tetrahedron Lett. *1968,* 2285; *T. Hosokawa, C. Calvo, H. B. Lee,* and *P. M. Maitlis,* J. Amer. Chem. Soc. *95,* 4914, 4924 (1973).
[16] *J. Tsuji, M. Morikawa,* and *J. Kiji,* J. Amer. Chem. Soc. *86,* 4851 (1971); Tetrahedron Lett. *1963,* 1437; *T. Tsuji, K. Ohno,* and *T. Kajimoto, ibid. 1965,* 4565.
[17] *R. D. Rieke* and *S. E. Bales,* J. Amer. Chem. Soc. *96,* 1775 (1974).
[18] *R. D. Rieke, S. J. Uhm,* and *P. M. Hudnall,* J. C. S. Chem. Comm. *1973,* 269.
[19] *C. A. Brown* and *V. K. Ahuja,* J. Org. Chem. *38,* 2226 (1973).
[20] *D. F. Starks* and *A. Streitwieser, Jr.,* J. Amer. Chem. Soc. *95,* 3423 (1973).
[21] *R. D. Rieke,* personal communications.

Transition Metal Atoms in the Synthesis of Binuclear Complexes

By E. P. Kündig, M. Moskovits, and G. A. Ozin[*]

1. Introduction

The vapors above the liquid transition metals scandium through to zinc have been extensively studied using a combination of high temperature Knudsen cell and mass spectrometric techniques[1]. Without exception, small concentrations of the transition metal diatomic molecules M_2 could be detected in the presence of the respective monatomic species M which formed more than 99% of the vapour[1-4]. It is because of this state of affairs that the chemistry of transition metal diatomic molecules has not previously been exploited although considerable information regarding their physical properties has been reported[5].

In searching the literature one finds scattered reports on the diffusion and aggregation properties of monatomic metal species frozen in rare gas solids at cryogenic temperatures. Electronic spectroscopy[5-13] and more recently Mössbauer spectroscopy[3,7] have proven to be of considerable value in this respect as it is sometimes possible to observe the spectra of the monatomic, diatomic and higher aggregate metal species in the presence of each other[5-13]. In this paper we wish to consider the factors which determine the aggregation of metal atoms in matrices to form dimers and binuclear complexes.

Mainly as a result of the elegant work of *Kant et al.*[1] it has proven possible to study the temperature dependence of the M/M_2 ratio using mass spectrometric techniques. These data have been analyzed and yield bond dissociation energies for M_2. They show an interesting "double hump" dependence on atomic weight (Fig. 1).

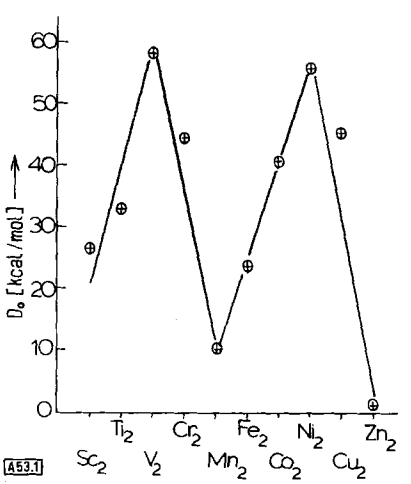


Fig. 1. Dissociation energies of the transition metal diatomic molecules Sc_2 through to Zn_2.

Semiempirical molecular orbital calculations have been reported for the M_2 molecules[14a] and Mulliken overlap population analyses at r_e indicate that σ-bonding predominates in the metal-metal bond, mainly from the 4s orbital. This has recently been confirmed by an *ab initio* SCF-MO calculation on Cu_2[14b]. The valence state electronic configurations for the metal atoms in M_2 are agreed to be $4s3d^{n+1}$. It is interesting to note that when the bond dissociation energy

[*] Dr. E. P. Kündig, Prof. Dr. M. Moskovits, and Prof. Dr. A. Ozin
Lash Miller Chemistry Laboratory and Erindale College, University of Toronto
Toronto, Ontario (Canada)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

D_0 is corrected for the promotion energy term from the electronic ground state $4s^23d^n$ using $D_{vs}=D_0+2E_{vs}$, the valence state dissociation energies D_{vs} are all found to lie in the range 56 ± 10 kcal/mol[1a]. The extremely low D_0 value for Mn_2 is attributed to the high E_{vs} for manganese, and for Zn_2, due to the presence of filled $4s^2$ and $3d^{10}$ valence shells. Aside from Mn_2 and Zn_2, the transition metal diatomic molecules have substantial bond dissociation energies and would be expected to have an independent and interesting matrix chemistry. In Fig. 2 we have presented a tabulation in 'periodic table form' of the known diatomic molecules of the elements.

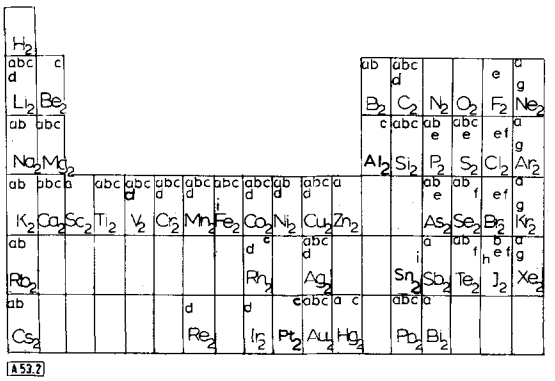


Fig. 2. Periodic table of the known homonuclear diatomic molecules. Detection by a) mass spectroscopy, b) UV-VIS spectroscopy in the gas phase, c) UV-VIS spectroscopy in the matrix, d) matrix chemistry, e) Raman spectroscopy in the gas phase or in the matrix, f) laser-induced resonance fluorescence in the gas phase, g) microwave spectroscopy in the gas phase, h) resonance-Raman effect, i) matrix Mössbauer.

It is generally accepted by matrix spectroscopists that diffusion of atoms or molecules occurs continually in all systems at all temperatures[15]. At very low temperatures (4.2—10°K) the mobilities of matrix isolated species are very small and diffusion is insignificant. However, warming the matrix in order to induce diffusion can be a very powerful tool in the hands of a skillful experimentalist in order, for example, to induce the sharpening of spectral lines, to monitor diffusion controlled chemical reactions, to study *in situ* matrix photolyses, and, of central interest here, to control the aggregation processes of metal atoms.

Even though diffusion in the crystalline solid state is a well-known phenomenon, details of the process are difficult to define or predict quantitatively in matrices owing to their non-uniform nature. Diffusion processes occurring during matrix annealing are complex and numerous. However, only low energy mechanisms such as vacancy migration and diffusion along grain boundaries need be considered[15]. On the other hand, the diffusion processes that can occur in the liquid-like interface formed on quenching gas beams onto a cold target are by no means well understood.

Several authors have reported on the electronic spectra of atoms trapped in matrices which generally show multiplets the centers of which are usually shifted to higher energies than the energy of the gaseous atom (blue shift). A number of explanations have been offered to explain the origin of the multiplet structures of the spectral lines, such as removal of orbital degeneracy by low site symmetries in the host lattice, Jahn-Teller effects, interactions between pairs of trapped atoms on non-nearest neighbour sites in the host lattice, *etc.* The generally-accepted rationale of the matrix shifts is in terms of a van der Waals interaction between the trapped atom and its matrix host[8-11].

Other spectral features, usually an order of magnitude less intense than the atomic lines, which escaped reasonable assignments to atomic lines, have usually been attributed to dimeric or higher metal aggregates.

Recently, some detailed investigations[10, 12, 37] of the experimental parameters which contribute to the formation of these "aggregates" have begun to appear in the literature and are of vital importance to the following discussions.

2. Isolation of Metal Atoms

In order to establish spectroscopically the relative proportion of metal monomer to dimer in a matrix it is necessary to know the extinction coefficients of the metal atom M and the corresponding M_2 molecule. This can be achieved from a careful study of the electronic spectra of the metal atom deposited in a solid inert matrix as a function of metal : matrix concentration. From the data that have previously been reported[7-13] the general consensus is that isolation improves as the metal and matrix atomic weights increase and as the metal concentration and temperature of deposition decrease. Since the M_2 molecules account for less than 1% of the metal vapor during deposition, at very low metal concentrations only metal atoms should be isolated. From the areas of the atomic absorption lines, the atom extinction coefficient ε_M can be deduced. Once ε_M is established, the quantity of isolated M atoms can be calculated in higher concentration runs. The remainder of the metal deposited can be assumed to be present as M_2 from which the M_2 molecule extinction coefficient ε_{M_2} can be deduced.

Andrews and *Pimentel*[12] have reported, for instance, such data for lithium in inert gas matrices from which they calculated a lower limit of about 300:1 for the $\varepsilon_{Li}/\varepsilon_{Li_2}$. More recently, similar experiments have been performed in our laboratories on a number of transition metals[18]. In all cases studied so far, the oscillator strengths of the M_2 molecules are considerably smaller than those of the corresponding atoms. Thus weak, broad M_2 absorptions often observed in the presence of extremely intense atomic absorptions could well reflect the presence of *substantial* concentrations of M_2 molecules and not of well isolated M atoms as has often been proposed[7-13]. This idea received convincing support from recent studies in our laboratories of the effect of metal concentration on the nature of the products of transition metal atom-carbon monoxide matrix reactions. These experiments show quite unambiguously that under certain matrix co-condensation conditions, many transition metals can be induced to react partly or wholly as diatomic molecules.

3. Diffusion of Metal Atoms in Matrices

A number of metals have been isolated as atoms in inert matrices in order to gain an insight into the effect of the matrix upon the spectra of trapped species and in order to study the formation of dimers, higher polymers and the diffusion mechanism of metal atoms in low temperature matrices. Extremely light atoms such as Li[12] and Be[16] have been

observed to diffuse readily in rare gas solids below 40°K, whereas heavier atoms such as Mg[9], Ca[17], Pb[10], Cu[11], Ag[7, 8, 11], Au[11] etc. have less tendency to diffuse and aggregate *after* the deposition has been completed. Matrix annealing with heavier atoms has little effect other than causing the sharpening and/or shifting of spectral lines usually attributable to the increasing regularity and/or phase changes in the host matrix. The low diffusion coefficients of most metal atoms in rare gas solids can be attributed, either or both, to their large masses and/or to van der Waals interaction of M with the matrix. At matrix temperatures the van der Waals energy between large atoms can be several times larger than kT. This essentially increases the size of the diffusing species, it now being a van der Waals molecule which diffuses.

4. Origin of M_2 Molecules and M_2L_n Complexes

The origin of M_2 molecules is of central concern in investigations of the diffusion properties of metal atoms in inert gas matrices. A detailed knowledge of the aggregation process is also vital to our understanding of the formation of binuclear complexes in metal atom-ligand matrix co-condensation reactions. Experiments have been designed which can give a detailed insight into both the origin of M_2 molecules and their respective M_2L_n complexes. For example, when manganese vapor effusing from a tantalum Knudsen cell was condensed with pure $^{12}C^{16}O$ onto a CsI plate cooled to 6—10°K (using Mn deposition rates arranged so that the probability of a Mn atom having another Mn atom as nearest neighbor in the f.c.c. lattice of CO was approximately 1 in 10^3), the matrix infrared spectrum[19] was identical with that obtained from $Mn_2(CO)_{10}$ deposited in an argon matrix (Fig. 3).

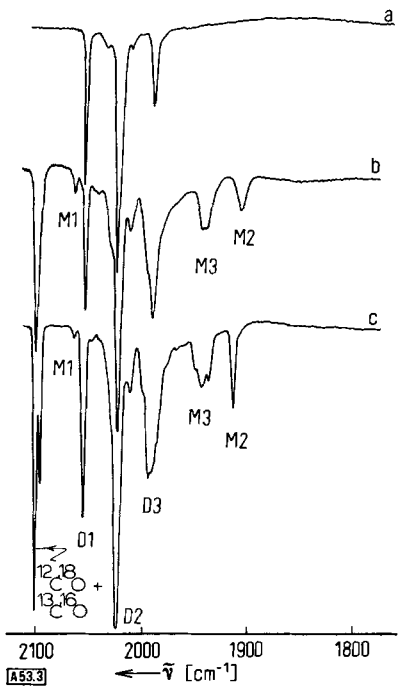


Fig. 3. IR spectra of a) $Mn_2(CO)_{10}$ isolated in Ar (approximately $1:10^3$), b) and c) the products of the matrix co-condensation reaction of Mn atoms with CO/Ar ≃ 1/5 and pure CO respectively showing $Mn_2(CO)_{10}$ (D) and $Mn(CO)_5$ (M) (the splitting of M_3, the E mode of $Mn(CO)_5$, was most pronounced in pure CO and is assigned to a matrix site effect).

These results were thought to be somewhat disquieting in that the mass-spectroscopic data[1c] for manganese vapor effusing from a Knudsen cell establishes a vapor composition of about 99% *atomic* manganese. In addition *Schnepp*[13] and *Mann*[6] have studied the electronic spectrum of manganese vapor deposited into pure Ar at 4.2°K and obtained data consistent with the presence of matrix isolated Mn atoms with very little evidence for molecular Mn_n species. Furthermore, at the high Mn:CO dilutions employed, one would expect the almost exclusive formation of mononuclear carbonyl species $Mn(CO)_n$. However, the data show the "exclusive" formation of the binuclear decacarbonyldimanganese, $Mn_2(CO)_{10}$.

The three possible sources of $Mn_2(CO)_{10}$ were considered to be (i) diffusion and dimerization of a $Mn(CO)_5$ species in the matrix, (ii) high concentrations of Mn_2 effusing from the Knudsen cell, and (iii) surface diffusion and dimerization of Mn atoms or reaction of a Mn atom with a $M(CO)_n$ fragment during deposition. We will consider each of these possibilities in turn.

In the light of *Rest* and *Crichton*'s[20] recent matrix photolysis experiments for $Mn_2(CO)_{10}$ in Ar, the diffusion of $Mn(CO)_5$ in Ar seems an unlikely source of $Mn_2(CO)_{10}$. Their results indicate that mononuclear carbonyl species are *not* formed on mercury arc photolysis of polynuclear carbonyl complexes in argon matrices, but instead $Mn_2(CO)_n$ species are favored. Although the $Mn_2(CO)_n$ products could not be characterized, the data strongly suggested that either the Mn—Mn bond is retained or that the bond is broken during photolysis but the $Mn(CO)_n$ fragments are too bulky to diffuse in argon and remain as nearest neighbors within the argon cage. On terminating the photolysis the dimer species will reform.

In a number of different experiments in which the orifice size of the Knudsen cell was varied between 0.1—1.0 mm, the results with pure $^{12}C^{16}O$ showed only the formation of $Mn_2(CO)_{10}$[19]. Thus the possibility that Mn_2 dimers were being formed in supersonic molecular beams[21] of manganese, effusing from the Knudsen cell with very small orifice diameters (0.1 mm), was considered to be most unlikely, as the results were identical with those with large diameter orifices (1.0 mm). Furthermore, at the low pressures employed (10^{-6}—10^{-7} torr), dimerization in flight is most unlikely as a source of Mn_2.

Double oven Knudsen cell techniques were used to superheat the manganese vapors effusing from the Knudsen cell[19]. In these experiments, designed to dissociate any dimanganese to monatomic manganese, the results were found to be *identical* with those of the single Knudsen cell experiments, showing only the formation of $Mn_2(CO)_{10}$, indicating the unlikelihood of Mn_2 being a major constituent of the effusing vapor.

However, when the Mn:CO ratio was reduced to $1:10^4$ or less, it was found that in addition to the main $Mn_2(CO)_{10}$ carbonyl absorptions (see Fig. 3) three new carbonyl absorptions grew in at 1938 ms, 1911 w and *ca.* 2060 vw cm^{-1}. These new lines always appeared with approximately the same relative intensities after deposition, implying that they are all associated with one species. Extensive experimental and theoretical studies have shown this species to be the square pyramidal $Mn(CO)_5$ radical[19]. $Mn(CO)_5$ was reluctant to diffuse at temperatures as high as 40—45°K (where argon is slowly

boiling off), again implying that matrix diffusion and dimerization of $Mn(CO)_5$ is an unlikely source of $Mn_2(CO)_{10}$.

These results are analogous in many respects to the data for the Co/CO and Cu/CO reactions[22, 23] which yield $Co(CO)_4$ and $Cu(CO)_3$ respectively under conditions of slow metal deposition, yet exclusively $Co_2(CO)_8$ and $Cu_2(CO)_6$ with high metal deposition rates. Furthermore, neither $Co(CO)_4$ nor $Cu(CO)_3$ was observed to dimerize readily during matrix warm-up experiments. It would therefore appear that the relative concentration of binuclear to mononuclear species (whether M_2 molecules or M_2L_n complexes) depends on the metal concentration in the matrix, the mononuclear species being favored at very low metal concentrations.

The dimerization process can therefore be specified to take place during matrix condensation and probably involves surface diffusion of highly mobile atoms in the quasi-liquid phase before they are frozen into the solid matrix.

5. The Effect of the Atomic Weight of M on the Dimerization Process

The data collected for the first row transition metals indicate quite clearly that dimerization of the atoms occurs readily during matrix condensation at metal-matrix ratios greater than 1:1000 and can be attributed to a surface diffusion process occurring during deposition. One would have anticipated from these data that on proceeding to the heavier transition metals, dimerization would be less facile (under comparable conditions) on at least two accounts. First, the rate of diffusion of a metal atom under matrix conditions has a mass dependence of between $M^{-1/2}$ to M^{-1}, depending on whether the diffusion layer is more closely approximated by a gas-like or a liquid-like region, which would reduce the tendency of the heavier transition metal atoms to dimerize, compared to the first row metals. Second, as the heavier metals are more polarizable, van der Waals type interaction

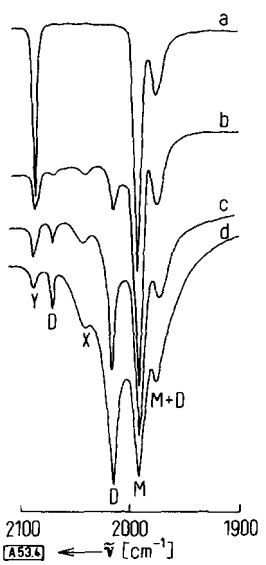


Fig. 4. IR spectra of the products of the matrix cocondensation reaction of Re atoms with CO at 10—15°K. a) Re:CO≃1:10⁵, b) Re:CO≃1:10⁴, c) Re:CO≃1:10³ and d) Re:CO≃1:10², showing the reactions of both Re atoms to yield $Re(CO)_5$ and $Re_2(CO)_{10}$ (M=$Re(CO)_5$; D=$Re_2(CO)_{10}$; X=unidentified, higher aggregate species; Y=$^{13}C^{16}O$, $^{12}C^{18}O$ in natural abundance).

with the matrix material will increase, thereby tending to stabilize atoms rather than M_2 molecules.

That dimerization is far less pronounced with the heavier transition metals is borne out by recent experiments with Re[24], Rh[25] and Ir[25]. For example, using Re/CO flow conditions comparable to those used in the Mn/CO reaction which yielded exclusively $Mn_2(CO)_{10}$, it is found that the only observable reaction product is the mononuclear $Re(CO)_5$ radical[24] (Fig. 4). Reasonable quantities of the binuclear species $Re_2(CO)_{10}$ could be induced to form only by increasing the Re concentration by a factor of at least 100 (see Fig. 4c). Similarly, with Rh/CO and Ir/CO flow conditions comparable to those used in the Co/CO reaction, which yielded exclusively $Co_2(CO)_8$[23], the matrix infrared spectra showed the presence of only $Rh(CO)_4$ and $Ir(CO)_4$[26]. It was found necessary to increase the Rh and Ir metal concentration by a factor of 100 to produce reasonable concentrations of the binuclear complexes $Rh_2(CO)_8$[25] and $Ir_2(CO)_8$[25] analogous to the bridge-bonded form of $Co_2(CO)_8$.

These data support the proposal that the heavier metals form M_2 molecules and M_2L_n complexes in their matrix reactions far less readily than their first row transition metal congeners.

6. The Effect of the Matrix Material on the Dimerization Process

Aside from the prerequisite of high guest to host dilutions for efficient isolation of a chemical species, one must deposit the sample at a temperature lower than $\frac{1}{2}\ T_{m.p.}$ of the matrix host material[27]. At these temperatures the matrix is sufficiently rigid to prevent long-range diffusion and subsequent unwanted reactions of the matrix guest. The degree of isolation of the guest is often very sensitive to the rate at which the matrix is laid down. Thus one can envisage a situation in which the latent heat of condensation of the matrix host on deposition is sufficiently high to cause warming of the matrix and hence diffusion of guest species. This phenomenon, originally discussed by *Bent* and *Fately*[28] is referred to as the "internal blanket effect" and sets an upper limit on the rate at which a matrix can be deposited to ensure efficient isolation.

The parameters that control the degree of isolation of unstable (or stable) molecules, free radicals and molecular ions are well documented. Less well understood, however, are the properties of the matrix which influence the isolation of metal atoms and diatoms. From the limited amount of experimental data presently available for Li/Li_2[12] and Pb/Pb_2[10] and Cr/Cr_2[46] it would appear that for the inert gases the efficiency of isolation of atoms generally increases in the order Xe > Kr > Ar > Ne. This order cannot be explained in terms of a thermal conductivity effect as Ar, which is the most thermally conductive, would be predicted to be most effective at trapping atoms. This is not found to be the case. However, the order is consistent with a rationale in terms of either atomic polarizability and/or rigidity effects. Thus xenon being the most polarizable would interact more strongly in a van der Waals sense with the metal atom (during the deposition) than would argon, thus tending to favor the isolation of metal atoms. Xenon can therefore be thought to be competing with the metal in the dimerization process. Moreover, the most rigid matrix

material, at deposition temperature T°K, would tend to quench metal atoms more efficiently, again consistent with the order of isolating efficiency, Xe > Kr > Ar > Ne. Few other matrix supports have been investigated from this point of view although preliminary studies with SF_6[10] show that it is ideal for isolating Pb_2 molecules, implying that the polarizability of the fluorine atoms in SF_6 is very small. SF_6 has also been used as a matrix for studies of the electronic spectra of Cu, Ag and Au atoms[11], where the degree of isolation of atoms appears to be greatest for Au, which is not unexpected in the light of our earlier discussions of metal atom diffusion as a function of its atomic weight and polarizability.

7. Chemical Evidence for Reactions Leading to Binuclear Transition Metal Complexes

Most of the information concerning matrix reactions leading to binuclear transition metal complexes has been derived from metal atom-carbon monoxide co-condensation reactions. Evidence for the formation of binuclear products comes from the following sources: i) observations of known binuclear carbonyl complexes; ii) synthesis of new binuclear complexes; iii) observation of bridging CO stretching modes; iv) observation of a mononuclear carbonyl complex in the presence of its binuclear counterpart; v) ligand and metal concentration studies; vi) ligand and mixed metal isotope substitution studies; vii) co-deposition of two different metals.

Let us formalize the chemical evidence for the matrix formation of binuclear complexes by discussing each of the above experiments in turn, with reference to selected examples from work performed in our own laboratories.

7.1. Observation of Known Binuclear Complexes

When Mn or Co atoms were deposited with pure $^{12}C^{16}O$ at M/CO ratios of about 1/1000, the matrix infrared spectra

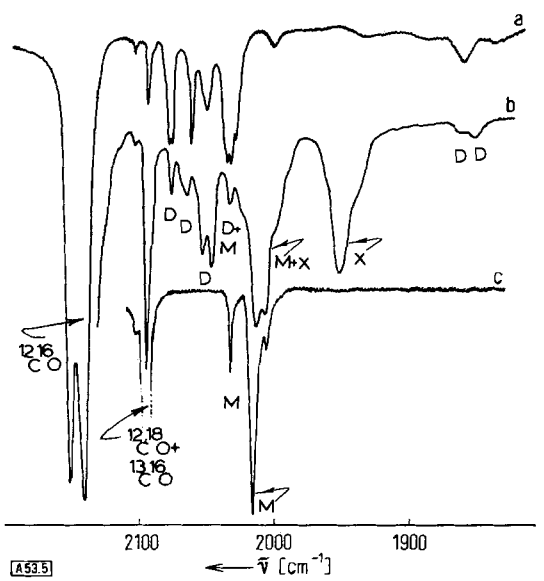


Fig. 5. IR spectra of a) $Co_2(CO)_8$ in Ar (approximately $1:10^3$), b) and c), the products of the matrix co-condensation reaction of Co atoms with CO at $Co:CO \simeq 1:10^3$ and $Co:CO \simeq 1:10^4$ showing the presence of $Co(CO)_4$ (M) and $Co_2(CO)_8$ (D) respectively (the lines marked X belong to cobalt cluster compounds $Co_x(CO)_n$ [22, 26]).

showed the presence of mainly $Mn_2(CO)_{10}$[19] and $Co_2(CO)_8$[22]. The identification of these reaction products was established by comparing the spectra with those obtained by depositing $Mn_2(CO)_{10}$ and $Co_2(CO)_8$ in Ar matrices using gas flow Knudsen cell techniques (Fig. 3 and 5). The similarity of the two sets of data proves, therefore, that manganese and cobalt, under the conditions of a matrix co-condensation experiment, can be induced to yield exclusively binuclear compounds.

7.2. Synthesis of New Binuclear Complexes

The matrix reactions of transition metal atoms can in principle provide chemical pathways to the synthesis of new binuclear complexes which cannot be prepared by conventional methods of chemical synthesis. The carbonyl complexes of the Co, Rh, Ir group of metals can be used to illustrate the potential usefulness of the method.

Until very recently, octacarbonyldicobalt, in its bridged and non-bridged forms, was the only well-defined "parent" binuclear carbonyl complex of the Co, Rh, Ir group of metals[29], although the tetranuclear $M_4(CO)_{12}$ and hexanuclear $M_6(CO)_{16}$ cluster complexes have been well characterized for all three metals. In brief, the synthesis of $Rh_2(CO)_8$ and $Ir_2(CO)_8$ was first claimed in 1940—43 by *Hieber* and *Lagally*[30] by the action of CO on the freshly prepared metal at high CO pressures and temperatures (*ca.* 450 atm, 200 °C). Since then many groups of workers[31] have tried various different approaches, without success, to substantiate the authenticity of $Rh_2(CO)_8$ and $Ir_2(CO)_8$. However, in 1970 *Whyman*[32] reported infrared spectroscopic data for the solution equilibrium of $Rh_4(CO)_{12}$ under conditions of high CO pressure (*ca.* 430 atm) and low temperatures (*ca.* −19 °C). Aside from the CO absorptions associated with $Rh_4(CO)_{12}$, new absorptions were observed which by comparison with the bridge bonded form of $Co_2(CO)_8$ were assigned to the bridge bonded form of $Rh_2(CO)_8$ (Table 1), presumably arising from the disproportionation equilibrium:

$$Rh_4(CO)_{12} + 4CO \rightleftharpoons 2Rh_2(CO)_8$$

The only criticism of this study is that one cannot eliminate the possibility that the spectral changes might have simply arisen from the freezing out of one or more unstable isomers of $Rh_4(CO)_{12}$ (see for example the fluxional behavior of $Rh_4(CO)_{12}$ in solution[33]).

Table 1. IR spectra of $M_2(CO)_8$ (M = Co, Rh or Ir).

$Co_2(CO)_8$ bridged	$Co_2(CO)_8$ non-bridged	$Rh_2(CO)_8$ bridged	$Ir_2(CO)_8$ bridged	$Rh_2(CO)_8$ [32] bridged
2071 vs		2060 s	2095 ms	2086 s
	2069 vs			
2044 } vs		2043 ssh [a]		
2042 }		2038 s }	2068 sbr	2061 s
	2031 ms			
	2022 vs			
1866 sh		1852 wsh	1848 wsh	1860 w
1857 s		1830 mw	1822 m	1845 m

[a] Appears as a doublet or a singlet (2040 cm^{-1}) depending on the deposition conditions.

Whyman[31b] has more recently tried a number of similar approaches to substantiate the existence of $Ir_2(CO)_8$, but as yet without success, and prior to metal vapor experiments to be described, the parent binuclear complex $Ir_2(CO)_8$ remained elusive.

Previously, the radicals $Rh(CO)_4$ and $Ir(CO)_4$ had been synthesized from the matrix reactions of Rh and Ir atoms with pure CO[26]. The complexes were characterized using $^{12}C^{16}O/^{13}C^{16}O$ mixed isotope experiments.

Using high Rh atom concentrations which favor the matrix formation of binuclear complexes, the infrared spectra of the products in pure CO show, in addition to the absorptions

Table 2. IR spectra of $Rh(CO)_4$, $Rh_2(CO)_8$, $Rh_4(CO)_{12}$ and $Rh_6(CO)_{16}$ [a].

$Rh(CO)_4$	$Rh_2(CO)_8$	$Rh_4(CO)_{12}$ [b]	$Rh_6(CO)_{16}$ [c]
			2070 sbr
		2064 s	
	2060 s		
	2040 ssh [d]		2040 wsh
		2035 ms	
2020 m			2020 wsh
2010 s		1870 s	
	1852 wsh		
	1830 mw		
			1798 m

[a] Recorded under dynamic vacuum (10^{-6} torr).
[b] The reported infrared spectrum of $Rh_4(CO)_{12}$ shows CO absorptions at 2076, 2071 vs, 2045 s, 1886 s cm^{-1} (in solution; Ref. [32]).
[c] The reported infrared spectrum of $Rh_6(CO)_{16}$ shows CO absorptions at 2070 s, 2043 w, 2021 mw and 1798 s cm^{-1} (in solution; Ref. [31a]) and 2077, 2074 s, 2041 m, 2016 m and 1770 s (solid; Ref. [34]).
[d] Appears as a doublet (2043, 2038 cm^{-1}) depending on the deposition conditions.

assigned to $Rh(CO)_4$, four new CO absorptions which were proven to belong to a single species. Inspection of Tables 1 and 2 shows that the new absorptions are very similar, in terms of frequency and intensity, to the infrared absorptions of the bridged form of $Co_2(CO)_8$ as well as *Whyman*'s bridged form of $Rh_2(CO)_8$. The close correspondence of these sets of data is quite striking, and serves to authenticate the existence of $Rh_2(CO)_8$ in its bridge-bonded form.

Table 3. IR spectra of $Ir(CO)_4$, $Ir_2(CO)_8$ and $Ir_4(CO)_{12}$ [a].

$Ir(CO)_4$	$Ir_2(CO)_8$	$Ir_4(CO)_{12}$ [b]
	2095 ms	
		2068 s
	2060 s	
		2035 ms
2022 ms		
2010 s		
		1869 m
	1845 wsh	
	1822 m	

[a] Recorded under dynamic vacuum conditions.
[b] Assigned to bridged form of $Ir_4(CO)_{12}$ by analogy with $Rh_4(CO)_{12}$. The non-bridged form of $Ir_4(CO)_{12}$ shows CO absorptions at 2072 s and 2032 s cm^{-1} (Ref. [31b]). At room temperature, the strongest lines of $Ir_6(CO)_{16}$ are just beginning to grow in (by comparison with the spectra of Reference [31a]).

Entirely analogous results were obtained with the iridium-carbon monoxide system. These are summarized in Tables 1 and 3. The close correspondence between the sets of data for Co, Rh and Ir shown in Table 1 is quite striking and serves to authenticate the existence of $Ir_2(CO)_8$ in a low temperature bridge-bonded form.

When $Rh_2(CO)_8$ and $Ir_2(CO)_8$ were allowed to warm up on the optical plate under conditions of dynamic vacuum, the infrared spectra showed that a transformation occurred at about $-48\,^{\circ}C$ for $Rh_2(CO)_8$ and about $-58\,^{\circ}C$ for $Ir_2(CO)_8$ to yield the bridge-bonded forms of $Rh_4(CO)_{12}$ and $Ir_4(CO)_{12}$, presumably by loss of CO through the disproportionation reaction.

$$2M_2(CO)_8 \rightarrow M_4(CO)_{12} + 4CO \quad \text{(where M = Rh or Ir)}$$

A further disproportionation of $Rh_4(CO)_{12}$ to $Rh_6(CO)_{16}$ was observed at room temperature (Table 2). The onset of the analogous disproportionation of $Ir_4(CO)_{12}$ to $Ir_6(CO)_{12}$ (Table 3) can just be observed. By comparing the temperatures at which $Rh_2(CO)_8$ and $Ir_2(CO)_8$ disproportionate to the respective bridge forms of $Rh_4(CO)_{12}$ and $Ir_4(CO)_{12}$, one is led to believe that under comparable conditions $Ir_2(CO)_8$ is slightly less stable than $Rh_2(CO)_8$ although it is not possible to estimate the magnitude of this difference from the present data. The instability of $Ir_2(CO)_8$ and $Rh_2(CO)_8$ with respect to disproportionation to $Ir_4(CO)_{12}$ and $Rh_4(CO)_{12}$ above $-48\,^{\circ}C$ is certainly consistent with the fact that the non-bridged forms of the complexes have not been observed and with the difficulties previously experienced by various groups of workers in attempting to synthesize and characterize $Rh_2(CO)_8$ and $Ir_2(CO)_8$.

7.3. Observation of Bridging CO Stretching Modes

The bonding in a bridging carbonyl ligand can be pictured as ketonic which in a valence bond sense would imply a formal oxidation state of +1 for each bridgehead metal. Alternatively the bonding can be discussed in a more flexible generalized way in which a 3-center molecular orbital scheme is considered, involving the 5σ orbital of the CO ligand and the symmetry allowed σ type orbital on each metal atom. A similar 3-center scheme can be envisaged for the π-bonding description of the molecule in order to correlate the CO stretching frequencies (or CO bond stretching force constants) with the extent of π- and σ-bonding. When part of the same complex, bridging carbonyl groups characteristically absorb at lower infrared frequencies than terminal carbonyl groups. Thus the observation of CO bridge stretching modes is indicative of binuclear complex formation and hence matrix reactions of M_2 molecules.

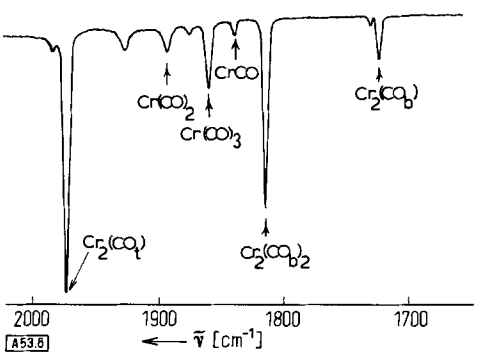
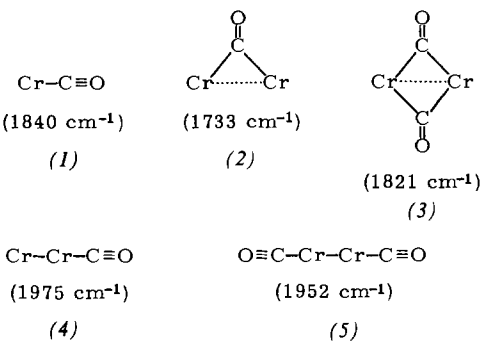


Fig. 6. Infrared spectra of the products of the matrix co-condensation reaction of Cr vapor with CO/Ar = 1/100 (Cr : Ar ≃ 1 : 10^3).

An example of this comes from the Cr/CO/Ar matrix reaction[35] which at high CO concentrations (CO:Ar = 1:20) shows the presence of mainly binary mononuclear $Cr(CO)_n$ complexes (where $n = 6$, 5 and 4). However, on reducing the CO concentration below 1:20 the formation of binuclear complexes become favored and molecules such as $Cr_2(CO_t)$, $Cr_2(CO_b)$ and $Cr_2(CO_b)_2$ (where t = terminal CO and b = bridge CO ligands) are observed (Fig. 6) in the presence of the mononuclear complexes $Cr(CO)_2$ and $Cr(CO)_3$. The stoichiometry with respect to the carbon monoxide ligand, in all cases, was established from $^{12}C^{16}O/^{13}C^{16}O$/Ar mixed isotope experiments (see Section 7.6). The binuclear and mononuclear complexes could be distinguished by retaining the gas flow constant and varying the rate of Cr metal deposition. Details of this technique are discussed in a later section. Experiments of this type served to define the molecules *(1)* to *(5)*.



The monotonic rise to higher frequencies on passing from $Cr_2(CO_b)$ to $Cr_2(CO_b)_2$ is consistent with a decrease in the charge delocalization of the Cr_2 electrons into the π^* orbitals of the CO bridge ligand(s) concomitant with the monotonic increase in the formal oxidation state of the Cr from Cr^I to Cr^{II}. The rise to higher frequencies on passing from Cr(CO) to $Cr_2(CO_t)$ can be rationalized using an inductive argument, in which the charge density associated with the electron used in the Cr—Cr bond of $Cr_2(CO_t)$ spends in CrCO relatively more of its time within the Cr electron core, so shielding the outer d-electrons more from the nucleus and allowing better Cr—CO back bonding which results in a higher CO stretching frequency for $Cr_2(CO_t)$ compared to CrCO.

7.4. Observation of a Mononuclear Carbonyl Complex in the Presence of its Binuclear Counterpart

7.4.1. Comparison of Mononuclear and Binuclear Complexes with Known Species

The Co/CO matrix reaction[22] exemplifies the above situation. Under $Co:CO \simeq 1:10^3$ concentration conditions, $Co_2(CO)_8$ can be identified (Fig. 5). In addition a doublet at 2029 and 2011 cm^{-1} is observed[22]. *Rest* and *Crichton*[36] have independently investigated the matrix photolysis reaction of $Co(CO)_3(NO)$ in argon matrices doped with CO:

$$Co(CO)_3NO \xrightarrow[Ar/CO]{} Co(CO)_4$$

The product of this reaction also shows a doublet at 2029 and 2011 cm^{-1} with an identical intensity ratio to the similar lines observed in the Co/CO reaction. Mixed $^{12}C^{16}O/^{13}C^{16}O$ isotope experiments proved that the product giving rise to the 2029/2011 cm^{-1} doublet in both the matrix photolysis[36] and the Co/CO reactions[22] is one and the same species, namely the C_{3v} $Co(CO)_4$ radical. Further confirmation that both mononuclear and binuclear cobalt carbonyls can result from the matrix reaction of Co atoms with pure CO stems from experiments at *high* Co atom concentrations ($Co:CO \simeq 1:100$) and very *low* Co atom concentrations ($Co:CO \simeq 1:10^5$), the infrared spectra of which show mainly $Co_2(CO)_8$ and mainly $Co(CO)_4$ respectively[22, 26].

7.4.2. Assignment of the Mononuclear Species by Inference

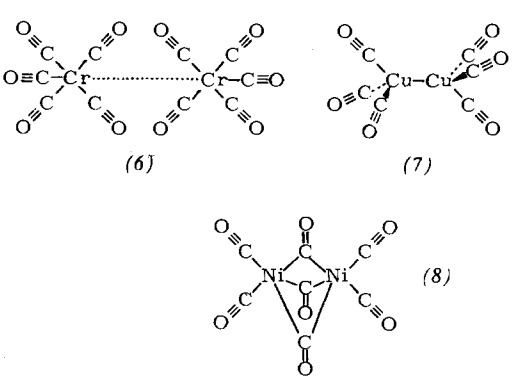
When the mononuclear species has not previously been detected, one has to resort to comparative methods of identification, using isostructural and isoelectronic species (or mixed isotope experiments whenever possible).

For example, when Mn atoms are co-condensed with pure CO at very low concentrations $Mn:CO \simeq 1:10^4$, aside from the absorptions assigned to $Mn_2(CO)_{10}$, *three* new carbonyl absorptions are observed (see Section 4)[19]. This species is assigned to a C_{4v} pentacarbonylmanganese radical, based on the numbers, frequencies and relative intensities of the observed infrared active carbonyl stretching modes. The assignment is further strengthened by comparison of the infrared data with those for other known C_{4v} square pyramidal complexes, for example, $Cr(CO)_5$[38] and $Cr(CO)_5^-$[39] or indeed any $Mn(CO)_5X$ species (X = H, Cl, Br, I or CH_3) containing the C_{4v} $Mn(CO)_5$ residue[40].

7.4.3. Assignment of Bands to M_2L_n Type Molecules

Although it is possible, in principle, to detect the metal-metal stretching vibration belonging to molecules of the type M_2L_n using matrix Raman spectroscopy, distinguishing that band from metal ligand vibrations would be difficult. It is therefore more expeditious to try to discover ways of identifying which bands in the ligand-stretching portion of the spectrum belong to binuclear metal species.

One technique that has been used successfully by us is to investigate the relative absorbances of bands as a function of metal/matrix gas ratio (see Section 7.5).



Using these methods, several binuclear complexes have been prepared and identified, among them being the van der Waals dimer $[Cr(CO)_5]_2$ *(6)*[41], the metal-metal bonded dimer $Cu_2(CO)_6$ *(7)*[23] and a dimeric nickel carbonyl species $Ni_2(CO)_7$ *(8)*[42].

7.5. The Dependence of the Concentration of Binuclear Species on Metal/Matrix Gas Ratio

As indicated earlier, binuclear species can arise in the matrix in two ways. The first is statistical, that is, metal dimers arising from the finite and calculable probability that in one of the nearest neighbor sites about a metal atom there resides another metal atom, while the second is due to reactions in the surface region of the matrix during the first few moments following deposition and before the kinetic energy of the reagents has been accommodated, hence, while the molecules are still fairly mobile.

We will now show that both of these mechanisms give rise, at least in the case of metal atoms deposited into a "reactive matrix" and under such circumstances that mononuclear species still predominate, to binuclear species whose concentration is proportional to the square of the metal/matrix gas ratio, while the concentration of mononuclear species is directly proportional to that ratio. In fact our experience to date indicates that at least in the case of first row transition metals, the surface reaction mechanism far exceeds in importance the statistical generation of dimers.

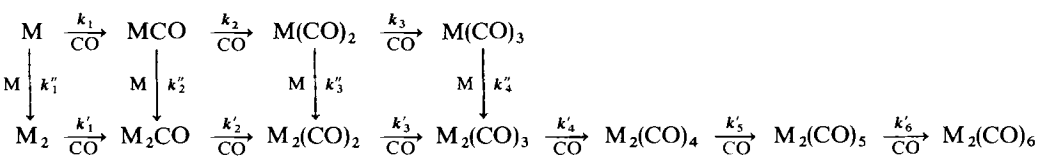
Consider the matrix reaction between a metal atom M and CO which gives rise to mononuclear carbonyls $M(CO)_n$ where $n=1$, 2, or 3 and binuclear species $M_2(CO)_m$ where, for example, $m=1$ to 6 as in the case of the Cu/CO system. Species containing higher aggregates of metal are in general also possible. We will assume, however, that the matrix ratio, [M], never becomes high enough to result in the formation of appreciable quantities of these. Let us now consider the surface reaction and the statistical factor separately.

7.5.1. Surface Reaction

We assume that only CO and M are mobile species. Accordingly only those reactions which involve at least one mobile species will be admitted. This implies that reactions of the form

$$M(CO)_n + M(CO)_{n'} \rightarrow M_2(CO)_{n+n'}$$

are admissible. The total reaction scheme for the formation of $M(CO)_3$ and $M_2(CO)_6$ is therefore as follows.



The backward steps in these reactions are assumed to be negligible slow and are thus not considered.

Mononuclear Species: The rate equations for formation of mononuclear species can be written directly:

$$\frac{d[MCO]}{dt} = k_1[M][CO] - k_2[MCO][CO] - k_2''[MCO][M] \quad (1)$$

$$\frac{d[M(CO)_2]}{dt} = k_2[MCO][CO] - k_3[M(CO)_2][CO] - k_3''[M(CO)_2][M] \quad (2)$$

$$\frac{d[M(CO)_3]}{dt} = k_3[M(CO)_2] - k_4''[M(CO)_3][M] \quad (3)$$

Since the reaction is carried out in pure CO all species of the form $M(CO)_n$ will become $M(CO)_3$ upon quenching, hence the final concentration of $M(CO)_3$ is given by

$$[M(CO)_3] = \int_0^{\tau_q} \left\{ \frac{d[MCO]}{dt} + \frac{d[M(CO)_2]}{dt} + \frac{d[M(CO)_3]}{dt} \right\} dt + [M]_{\tau_q} \quad (4)$$

where τ_q is the average quenching time, *i. e.*, the average lifetime of a species before it is immobilized within the matrix.

Substituting from equations (1), (2) and (3) into (4) one obtains

$$[M(CO)_3] = [M]_{\tau_q} + \int_0^{\tau_q} [M]\{k_1[CO] - (k_2''[MCO] + k_3''[M(CO)_2] + k_4''[M(CO)_3])\} dt \quad (5)$$

where $k_2'' \simeq k_3'' \simeq k_4''$ if the reactions are assumed to be diffusion limited. Integral (5) can therefore be written

$$[M(CO)_3] = [M]_{\tau_q} + \int_0^{\tau_q} [M]\{k_1[CO] - k_2''([M(CO)] + [M(CO)_2] + [M(CO)_3])\} dt$$

Under the experimental conditions considered the CO concentration far exceeds the sum of concentrations of all mononuclear species. Moreover, k_2'' is not expected to be markedly different from k_1. Accordingly integral (5) reduces to

$$[M(CO)_3] \simeq \int_0^{\tau_q} k_1[M][CO]dt + [M]_{\tau_q} \quad (6)$$

The rate of change of concentration of metal can also be written as

$$\frac{-d[M]}{dt} = k_1[M][CO] + k_1''[M]^2$$

which reduces, for the same reasons stated above, to

$$\frac{-d[M]}{dt} \simeq k_1[M][CO]$$

which has the following solution

$$M = [M]_0 e^{-k_1[CO]t} \quad (7)$$

in which [CO] being in great excess is taken to be a constant and where $[M]_0$ is the initial metal concentration, hence proportional to the metal/CO ratio.

Substituting equation (7) into equation (6) and integrating, one obtains

$$[M(CO)_3] \simeq [M]_0$$

Binuclear Species: The kinetic equations governing the production of binuclear species may also be written down as follows:

$$\frac{d[M_2]}{dt} = \tfrac{1}{2}k_1''[M]^2 - k_1'[M_2][CO] \quad (8)$$

together with six other equations of the form

$$\frac{d[M_2(CO)_n]}{dt} = k_n'[M_2(CO)_{n-1}][CO] + k_{n+1}''[M][M(CO)_n] - k_{n+1}'[M_2(CO)_n][CO] \quad (9)$$

for $n \leq 3$ and deleting the term in k'' for $n > 3$.

Using similar arguments as those stated for production of mononuclears the concentration of $M_2(CO)_6$ is given by

$$[M_2(CO)_6] = \tfrac{1}{2}k_1'' \int_0^{\tau_q} [M]^2 dt + k_2'' \int_0^{\tau_q} [M] \left(\sum_{n=1}^{3} M(CO)_n \right) dt \quad (10)$$

We have assumed throughout that the concentration of binuclear species is always smaller than that of mononuclears, consequently the quantity

$$\sum_{n=1}^{3} M(CO)_n \simeq [M]_0 - [M] \quad (11)$$

Substituting (11) into (10) and (7) into the resulting expression and integrating, we obtain

$$[M_2(CO)_6] = K_2[M]_0^2$$

where

$$K_2 = \frac{k_1''}{4k_1[CO]}(1 - e^{-2k_1[CO]\tau_q}) + \frac{k_2''}{2k_1[CO]}[1 + e^{-2k_1[CO]\tau_q} - 2e^{-k_1[CO]\tau_q}]$$

which is $\simeq \tfrac{1}{2}k_1''\tau_q$ to first order in τ_q.

The result of this analysis indicates, therefore, that the ratio of the concentration of binuclear species to that of mononuclear should increase proportionally to the matrix ratio $[M]_0$. A similar analysis for metal trimers indicates that the analogous ratio involving trinuclears increases as the square of the metal-to-CO ratio.

7.5.2. Statistical Concentrations of Dimers

Assuming that aggregates larger than dimers are in negligible abundance and that there are 12 nearest neighbor sites associated with every substitutional site in the CO matrix one can write down the metal dimer and metal monomer concentrations directly.

$$[M_2(CO)_6] = 12([M]_0^2)(1 - [M]_0)^{11}$$

and $[M(CO)_3] = [M]_0(1 - [M]_0)^{12}$

$$[M_2(CO)_6]/[M(CO)_3] = 12[M]_0/(1 - [M]_0)$$

which reduces to approximately $12[M]_0$ for $[M]_0$ not too large.

We see therefore that both the statistical and surface reaction pathways lead to binuclear/mononuclear concentration ratios which are proportional to the matrix ratio while the appropriate ratios related to species containing larger metal aggregates vary as some higher power of the matrix ratio. It is therefore apparent that one can distinguish binuclear species from both higher aggregates and mononuclears by observing the effect of varying the matrix ratio on the relative absorbances of the appropriate spectral bands.

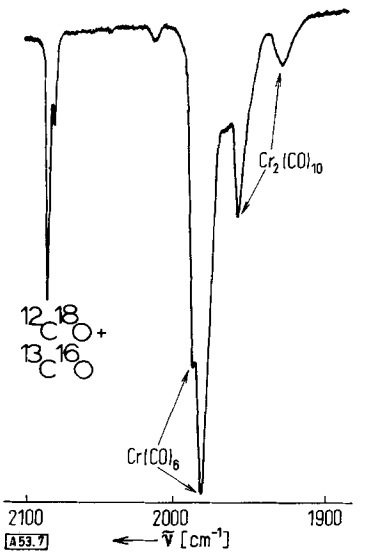


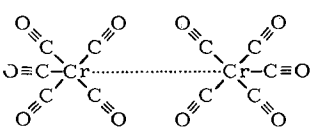
Fig. 7. Infrared spectrum of the products of the matrix co-condensation reaction of Cr vapor with CO at 10—15°K with Cr:CO ≃ 1:10³.

Let us illustrate this by considering the results for the Cr/CO reaction in more detail.

When Cr atoms are co-condensed with pure $^{12}C^{16}O$ at 10—15°K, the major product of the reaction is seen to be $Cr(CO)_6$ (Fig. 7). However, *two* other intense carbonyl absorptions at 1962 and 1933 cm^{-1} always accompanied the hexacarbonylchromium. These two new lines appeared with the *same* relative intensities in a number of different runs, and are ascribed to a species X. The intense carbonyl absorptions have very similar frequencies and relative intensities (approximately 3:1) to those of *Turner*'s pentacarbonylchromium[38] produced by photolyzing $Cr(CO)_6$ in Ar ma rices. Furthermore, annealing of the CO matrix at 40—45°K had essentially *no* effect on the spectrum, a result which parallels the annealing behavior of *Turner*'s pentacarbonylchromium in Ar/CO matrices[38].

If X is indeed a coordinatively unsaturated square pyramidal pentacarbonylchromium, its reluctance to react with CO is most unusual, especially in a "pure" CO matrix, which leads one to believe that the vacant coordination site in the C_{4v} $Cr(CO)_5$ fragment is blocked.

One explanation is that the lines belong to a weakly interacting dimer *(9)*.


(9)

That the weakly interacting dimer $Cr_2(CO)_{10}$ *(9)* is indeed a likely formulation for complex X in keeping with the results of a careful study of the dependence of the absorbance ratio $A_X/A_{Cr(CO)_6}$ on the Cr/CO ratio: The absorbance ratio is observed to increase proportionally with increasing Cr concentration.

The Cu/CO co-condensation reaction in pure CO and in dilute CO/Ar matrices provides another example of the use of this method to determine metal stoichiometry[23].

On the basis of known first row mononuclear and binuclear binary carbonyl complexes $V_2(CO)_{12}$, $Cr(CO)_6$, $Mn_2(CO)_{10}$, $Fe(CO)_5$, $Co_2(CO)_8$, $Ni(CO)_4$, all of which conform to the 18 electron formalism, one would have predicted the existence of $Cu_2(CO)_6$ as the next member of the series. However, binary carbonylcopper complexes long sought after by conventional methods of chemical synthesis[43] have so far remained elusive, their instability being a reflection of the presence of a very stable filled 3d valence shell, a situation not conducive to $d\pi$-π^* back bonding.

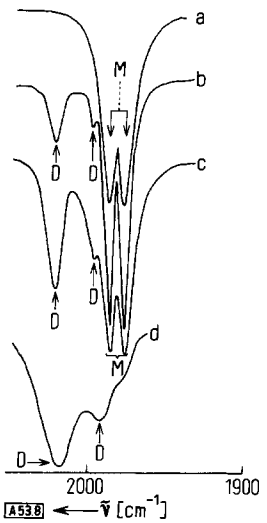


Fig. 8. IR spectra of the products of the matrix cocondensation reaction of copper vapor with pure CO. a) Cu:CO≃1:10^5, b) Cu:CO≃1:10^4, c) Cu:CO≃1:10^3 and d) Cu:CO≃1:10^2. The spectra show the gradual progression from $Cu(CO)_3$ (M) to $Cu_2(CO)_6$ (D) formed from the matrix reactions of CO with Cu atoms.

The infrared spectrum of the product of the reaction of Cu atoms with pure CO at Cu:CO concentrations in the range 1:10^5 (Fig. 8a) shows a doublet at 1990, 1977 cm^{-1}[23]. The $^{12}C^{16}O/^{13}C^{16}O$ mixed isotope experiments define the product as a tricarbonyl complex (M). At the low Cu concentrations used, the product is best assigned to $Cu(CO)_3$. (This formulation is confirmed by mixed metal studies.)

By retaining the CO flow constant and studying the spectrum as a function of the rate of Cu atom deposition, two new CO lines (D) at higher frequencies than those of $Cu(CO)_3$ are seen to grow in as the Cu concentration increases (Figure 8b—8d). A proportional increase in the absorbance ratio D/M is observed with increasing Cu concentrations. At Cu:CO concentrations of 1:100, $Cu(CO)_3$ is not observed, the only detectable product being the new carbonyl species. In addition, the new carbonylcopper species (D) grows in when CO/Ar matrices containing only $Cu(CO)_3$ are allowed to warm up to 40—45 °K (at which temperature the Ar matrix is slowly boiling off).

The infrared spectra, the Cu concentration dependence, and the formation of the new copper carbonyl species on allowing $Cu(CO)_3$ to diffuse, suggest a dimerization process with the formation of a binuclear $Cu_2(CO)_6$ complex having a structure containing a copper-copper bond[23a].

The results in dilute CO/Ar (1/100) matrices also present an intriguing problem, showing in addition to small concentrations of $Cu(CO)_3$, *two* new species absorbing at 2010 and 1890 cm^{-1}. Mixed $^{12}C^{16}O/^{13}C^{16}O$ isotope experiments prove these to be a mono and dicarbonyl respectively (Fig. 9). By studying the absorbance of these compounds as a function of Cu concentration, retaining the CO/Ar concentration constant (but with the ligand in excess for reasons delineated earlier), one discovers that the absorbance ratio $A_{Cu(CO)_3}$: $A_{Cu_X(CO)_2}$: $A_{Cu_Y(CO)}$ remains constant over a 300-fold change in Cu concentration, proving the new complexes to be mononuclear with respect to copper, namely, $Cu(CO)_2$ and Cu(CO).

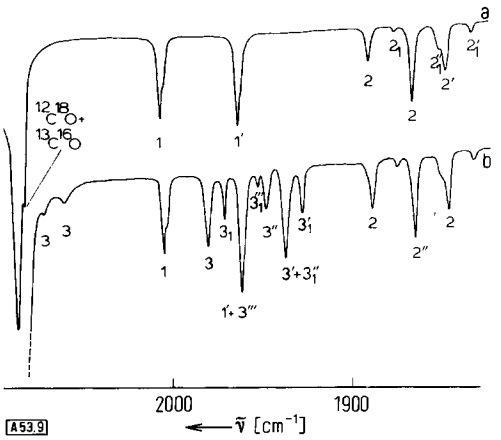


Fig. 9. IR spectra of the products of the matrix cocondensation reaction of copper atoms with a) $^{12}C^{16}O:^{13}C^{16}O:Ar \simeq 1:1:100$ after deposition at 6—10 °K showing the presence of $Cu(^{12}C^{16}O)$, (1); $Cu(^{13}C^{16}O)$, (1'); $Cu(^{12}C^{16}O)_2$, (2); $Cu(^{13}C^{16}O)_2$, (2'); $Cu(^{12}C^{16}O)(^{13}C^{16}O)$, (2'') (where 2_1, $2'_1$ and $2''_1$ represent a matrix splitting of the respective isotopic dicarbonyl complexes $Cu(^{12}C^{16}O)_n(^{13}C^{16}O)_{2-n}$); b) after warm-up to 30 °K, showing the growth of the CO stretching modes of the isotopic tricarbonyls $Cu(^{12}C^{16}O)_n(^{13}C^{16}O)_{3-n}$ (where $n=0$—3) ($3/3_1$ notation refers to a matrix splitting of the tricarbonyl complex).

7.6. Mixed Isotopic Substitution

It is well established that mixed isotopic substitution experiments provide a useful method for determining the stoichiometry and structure of a matrix isolated species. Two distinct situations can be considered. On the one hand one can co-condense an isotopically *pure* metal atom with a *mixture* of isotopic ligands such as $^nX_2/^mX_2$; alternatively one can co-condense a *mixture* of metal atom isotopes $^pM/^qM$ with a *pure* ligand. Barring an isotope effect in the kinetics of formation, the product distribution can be expected to be statistical and an analysis of the number, frequencies and infrared and Raman intensities of the isotopic components can, in principle, determine the product stoichiometry with respect to both ligand and metal, the molecular structure of the product, the vibrational assignments and force fields. Studies of this type are fundamental to almost any matrix isolation experiment.

An outline will now be given of how this method has been applied in determining the binuclear complexes formed in matrix co-condensation reactions. When manganese atoms are co-condensed with $^{12}C^{16}O:Ar = 1:250$, using Mn deposition rates which favor the formation of Mn_2 (Fig. 10a), two prominent low frequency CO absorptions are observed at 1835.4 and 1688.2/1680.0 cm^{-1}[19] (the latter was shown to

be a matrix site splitting), together with a high frequency weak absorption at 1964.4 cm^{-1}. Using an isotopic mixture $^{12}C^{16}O : {}^{13}C^{16}O : Ar \simeq 1 : 1 : 500$, the matrix infrared spectrum shown in Fig. 10b was obtained in which a characteristic isotope pattern of a symmetrical dicarbonyl and a low and high frequency monocarbonyl are easily discernible (Table 4). Matrix warm-up experiments at about 25—30 °K showed the dicarbonyl to grow at the expense of the low frequency monocarbonyl.

Table 4. Infrared spectra of $Mn_2(CO_t)$, $Mn_2(CO_b)$ and $Mn_2(CO_b)_2$. (t refers to terminal and b to bridging ligands.)

Observed	Calculated [a]	Assignment
1964.4	—	$Mn_2(^{12}C^{16}O_t)$
1920.6	—	$Mn_2(^{13}C^{16}O_t)$
1945.6	1945.6	$Mn_2(^{12}C^{16}O_b)(^{13}C^{16}O_b)$
1835.4	1835.3	$Mn_2(^{12}C^{16}O_b)_2$
1809.6	1809.2	$Mn_2(^{12}C^{16}O_b)(^{13}C^{16}O_b)$
1790.6	1791.1	$Mn_2(^{13}C^{16}O_b)_2$
1688.2/1680.0 [b]	—	$Mn_2(^{12}C^{16}O_b)$
1646.4/1638.2 [b]	—	$Mn_2(^{13}C^{16}O_b)$

[a] Calculated Cotton-Kraihanzel force constants [in mdyn/Å]:

$Mn_2(CO_b)$: $f_r = 11.45$
$Mn_2(CO_b)_2$: $f_r = 14.61$; $f_{rr} = 1.00$
$Mn_2(CO_t)$: $f_r = 15.58$

[b] Matrix splitting.

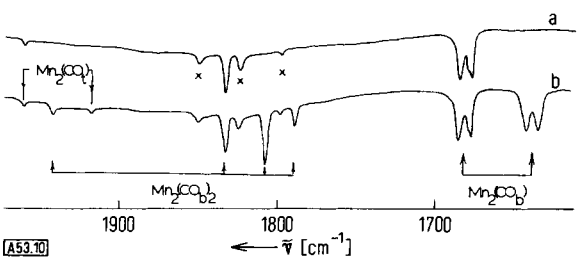
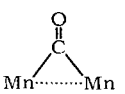
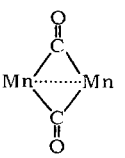


Fig. 10. IR spectra of the products of the matrix co-condensation reaction of Mn atoms with a) $^{12}C^{16}O : Ar \simeq 1 : 250$; b) $^{12}C^{16}O : {}^{13}C^{16}O : Ar \simeq 1 : 1 : 500$ at 6—10 °K at $Mn : CO \simeq 1 : 1000$ (x refers to Mn trace impurities).

On the basis of the frequencies of the observed carbonyl stretching modes when compared to $Mn_2(CO)_{10}$ or $Mn(CO)_5$, together with the prior knowledge that Mn_2 should constitute a major proportion of the reacting metal species in the matrix under the experimental conditions used, the low frequency CO stretching modes are best assigned to a binuclear bridged monocarbonyl species *(10)* and a binuclear bis-carbonyl bridged species *(11)*. Whether or not a Mn—Mn bond should be included in a description of their bonding will be elucidated using ESR experiments. The monocarbonyl absorbing at high CO stretching frequencies is assigned to the binuclear species *(12)* by analogy with $Cr_2(CO_t)$ described earlier.

(10)  1688.2/1680.0 cm^{-1}

(11)  1835.4 cm^{-1}

(12) Mn–Mn–C≡O 1964.4 cm^{-1}

7.7. Co-deposition of Two Different Metals

If the product of a matrix co-condensation reaction is suspected to contain more than a single metal atom then, in principle, simultaneous deposition of *two* different metals (chosen usually from the same group in order to maintain similar chemical properties and to avoid major structural changes in the trapped product) with the reacting gas can verify the molecular composition and aid the vibrational assignments.

This technique is particularly useful for monoisotopic metals or when isotopes of the metal are *not* readily accessible. Few examples using mixed metals can be referred to in the literature other than *Andrews'* studies of alkali metal peroxides[44] Na_2O_2, K_2O_2, Rb_2O_2 and Cs_2O_2 formed by secondary reactions of the alkali metal atom M with the respective superoxide MO_2 in the matrix.

Brewer used metal co-deposition studies (for example, Pb/Ag, Cu/Ag, Cu/Au, Ag/Au) in order to investigate the origin of the multiplet splitting in the electronic spectra of Pb, Cu, Ag and Au atoms in inert matrices[10, 11]. He discovered that even at one atom percent of metal, the atomic spectra remained essentially unperturbed, indicating that the fine structure was not due to nearest neighbor M—M interactions but, rather, site symmetry lattice perturbations. However, detailed investigations of the electronic spectra of the diatomic species present in these mixed metal experiments were not feasible, presumably because of the low absorption intensities associated with the diatomic molecules. In the infrared the situation is quite different, as dimeric carbonyl reaction products usually have high extinction coefficients and are easily observed and in principle the mixed metal experiment is an ideal way by which one can ascertain the stoichiometry of the products with respect to the metal. For example, when Cu and Ag atoms were simultaneously co-condensed with pure CO[23a] the spectrum obtained was essentially a superposition of the spectra of the respective Cu/CO and Ag/CO reaction products, consistent with our earlier conclusions of a mononuclear formulation, namely, $Cu(CO)_3$ and $Ag(CO)_3$[23, 45].

8. Conclusion

The information presented in this paper demonstrates that the diffusion properties of metal atoms may be probed and their aggregation processes, at least to dimeric molecules, controlled by utilizing matrix isolation techniques. The chemistry of the transition metal diatomic molecules, their spectroscopy and the characterization of the reaction products should prove very fruitful indeed in providing a large number of new molecules and in helping to understand the chemical nature of diatomic molecules. Moreover, the possibility exists for tailor-making new polynuclear molecules with features of interest to those interested in compounds containing metal-

metal bonds, the reactivity and selectivity of transition metal based catalysts or the relationship of the binuclear complex M_2L_n to L chemisorbed on bulk metal M. Finally, a great deal of knowledge concerning the energetics of metal formation might be obtained by carefully studying metal atom aggregation processes using matrix isolation infrared, laser Raman, UV-visible and ESR spectroscopy.

We would like to thank Mr. H. Huber, Mr. J. Hulse, Miss L. Hanlan and Mr. D. McIntosh for invaluable technical assistance and for many stimulating discussions. We also gratefully acknowledge the financial assistance of the Research Corporation and the National Research Council of Canada.

Received: May 15, 1974 [A 53 IE]
German version: Angew. Chem. *87*, 314 (1975)

[1] a) *A. Kant* and *B. Strauss*, J. Chem. Phys. *41*, 3806 (1964); *45*, 3161 (1966); b) *A. Kant, ibid. 41*, 1872 (1964); c) *A. Kant, S. S. Lin*, and *B. Strauss, ibid. 49*, 1983 (1968); d) *S. S. Lin* and *A. Kant*, J. Phys. Chem. *73*, 2450 (1969).
[2] *P. Schissel*, J. Chem. Phys. *26*, 1276 (1957).
[3] *M. Ackerman, F. E. Stafford*, and *J. Drowart*, J. Chem. Phys. *33*, 1784 (1960).
[4] *D. N. Travis* and *R. F. Barrow*, Proc. Chem. Soc. (London) *1962*, 64.
[5] *B. Siegel*, Quart. Rev. Chem. Soc. *19*, 77 (1965).
[6] *D. M. Mann* and *H. P. Broida*, J. Chem. Phys. *55*, 84 (1971).
[7] *F. Schoch* and *E. Kay*, J. Chem. Phys. *59*, 718 (1973).
[8] *L. Brewer, B. A. King, J. L. Wang, B. Meyer*, and *G. F. Moore*, J. Chem. Phys. *49*, 5209 (1968).
[9] *L. Brewer* and *J. L. F. Wang*, J. Mol. Spectrosc. *40*, 95 (1971).
[10] *L. Brewer* and *C.-A. Chang*, J. Chem. Phys. *56*, 1728 (1972).
[11] *L. Brewer* and *B. King*, J. Chem. Phys. *53*, 3981 (1970).
[12] *L. Andrews* and *G. C. Pimentel*, J. Chem. Phys. *47*, 2905 (1967).
[13] *O. Schnepp*, J. Phys. Chem. Solids *17*, 188 (1961).
[14] a) *W. F. Cooper, G. A. Clarke*, and *C. R. Hare*, J. Phys. Chem. *76*, 2268 (1972), and references therein; b) *P. Joyes* and *M. Leleyter*, J. Phys., *B 6*, 150 (1973).
[15] *B. Meyer:* Low Temperature Spectroscopy. Elsevier, New York 1971; *N. B. Hannay*, Solid State Chemistry. Prentice-Hall, Englewood Cliffs, New Jersey, 1967.
[16] *W. Weltner*, private communication.
[17] *J. F. L. Wang*, Ph. D. Thesis, University of California, Berkeley 1969.
[18] *T. A. Ford, W. Klotzbücher, E. P. Kündig, D. McIntosh, M. Moskovits*, and *G. A. Ozin*, unpublished results.
[19] *H. Huber, E. P. Kündig, G. A. Ozin*, and *A. J. Poë*, J. Amer. Chem. Soc. *97*, 308 (1975).
[20] *A. J. Rest* and *O. Crichton*, private communication.
[21] *S. E. Novick, P. B. Davies, T. R. Dyke*, and *W. Klemperer*, J. Amer. Chem. Soc. *95*, 8547 (1973).
[22] *L. Hanlan, H. Huber, E. P. Kündig, B. R. McGarvey*, and *G. A. Ozin*, J. Amer. Chem. Soc., in press.
[23] a) *H. Huber, E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, J. Amer. Chem. Soc., in press (April 1975); b) *J. S. Ogden*, Chem. Commun. *1971*, 978.
[24] *H. Huber, E. P. Kündig*, and *G. A. Ozin*, J. Amer. Chem. Soc. *96*, 5585 (1974).
[25] *L. Hanlan* and *G. A. Ozin*, J. Amer. Chem. Soc. 96, 6324 (1974).
[26] *H. Huber, L. Hanlan, E. P. Kündig*, and *G. A. Ozin*, in preparation.
[27] *E. Whittle, D. A. Dows*, and *G. C. Pimentel*, J. Chem. Phys. *22*, 1943 (1954); *G. E. Ewing, W. E. Thompson*, and *G. C. Pimentel, ibid. 32*, 927 (1970); *M. Linewsky, ibid. 34*, 587 (1961).
[28] *W. G. Fateley, H. A. Bent*, and *B. Crawford*, J. Chem. Phys. *31*, 204 (1959).
[29] *G. Bor* and *L. Markó*, Spectrochim. Acta *15*, 747 (1959); *K. Noack, ibid. 19*, 1925 (1963); *O. S. Mills* and *G. Robinson*, Proc. Chem. Soc. (London) *1959*, 157.
[30] *W. Hieber* and *H. Lagally*, Z. Anorg. Chem. *251*, 96 (1943); Z. Anorg. Allg. Chem. *245*, 321 (1940).
[31] a) *L. Malatesta, G. Caglio*, and *M. Angoletta*, Chem. Commun. *1970*, 532; b) *R. Whyman*, J. Organometal. Chem. *24*, C35 (1970); c) *P. Chini* and *S. Martinengo*, Inorg. Chim. Acta *3*, 21 (1969), and references therein.
[32] *R. Whyman*, Chem. Commun. *1970*, 1194; J. C. S. Dalton *1972*, 1375.
[33] *F. A. Cotton, L. Kruczynski, B. L. Shapiro*, and *L. F. Johnson*, J. Amer. Chem. Soc. *94*, 6191 (1972); *J. G. Bullitt, F. A. Cotton*, and *T. J. Marks, ibid. 92*, 2155 (1970).
[34] *W. P. Griffith* and *A. J. Wickham*, J. Chem. Soc. *A 1969*, 834.
[35] *E. P. Kündig* and *G. A. Ozin*, in preparation; and *J. J. Turner*, personal communication.
[36] *O. Crichton, M. Poliakoff, A. J. Rest*, and *J. J. Turner*, J. C. S. Dalton *1973*, 1321.
[37] *A. Bos* and *A. T. Howe*, J. Chem. Soc. Faraday II, *70*, 451 (1974).
[38] *M. A. Graham, M. Poliakoff*, and *J. J. Turner*, J. Chem. Soc. *A 1971*, 2939.
[39] *P. A. Breeze* and *J. J. Turner*, J. Organometal. Chem. *44*, C7 (1972).
[40] *H. D. Kaesz, R. Bau, D. Hendrickson*, and *J. M. Smith*, J. Amer. Chem. Soc. *89*, 2844 (1967), and references therein.
[41] *E. P. Kündig* and *G. A. Ozin*, J. Amer. Chem. Soc. *96*, 3820 (1974).
[42] *J. Hulse* and *M. Moskovits*, in preparation.
[43] *M. I. Bruce*, J. Organometal. Chem. *44*, 209 (1972), and references therein.
[44] *L. Andrews*, J. Chem. Phys. *54*, 4935 (1971); J. Phys. Chem. *73*, 3922 (1969); *R. R. Smardzewski* and *L. Andrews*, J. Chem. Phys. *57*, 1327 (1972).
[45] *E. P. Kündig, D. McIntosh*, and *G. A. Ozin*, unpublished.
[46] *E. P. Kündig, M. Moskovits*, and *G. A. Ozin*, Nature Phys. Science, April 8, 1975.

Photochemistry in Matrices and Its Relevance to Atom Synthesis[**]

By James J. Turner[*]

1. Introduction

In the matrix isolation technique, developed largely by *Pimentel*[1] the object is to isolate a reactive species in a large excess of an inert rigid matrix, usually at very low temperatures. The species can then be spectroscopically examined at leisure.

Several techniques have been used, mostly vibrational, electronic, and ESR spectroscopy, but also including Mössbauer, and magnetic circular dichroism. There is always the assumption that the appropriate spectroscopic energy levels of a trapped species are only slightly perturbed by the matrix environment. Comparison of gas-phase and matrix-isolated vibrational spectra of *stable* molecules suggests that the assumption is reasonably valid and hence that structures of *unstable* species deduced from matrix vibrational data are unlikely to be grossly misleading.

Reactive species may be trapped in matrices by a variety of techniques, summarized below:

1) *In situ photolysis of a stable parent, e.g.*

$$OF_2/Ar \xrightarrow{h\nu} OF + F$$

The parent gas mixture, OF_2 diluted in argon, is deposited on a cold window (4K) and then irradiated with UV light[2].

2) *Deposition from the gas phase, e.g.*

$$Xe + Cl_2 \xrightarrow[\text{discharge}]{\text{electric}} XeCl_2 \text{ in Xe}$$

The gas leaving the discharge is condensed on a window at 20K and the $XeCl_2$ identified by both infrared[3] and Raman[4] spectra.

$$BH_3CO/Ar \xrightarrow{\Delta} BH_3$$

The carbon monoxide-borane in argon passes through a hot tube and a very carefully designed nozzle. The detection of BH_3 by thermal decomposition is something of a triumph[5] in view of the number of attempts to isolate the species.

$$SiO_2/Ar \xrightarrow{\Delta} SiO, Si_2O_2, Si_3O_3$$

The silicon-oxygen species effusing from a Knudsen cell are co-condensed with a large excess of inert gas[6].

Atom synthesis, e.g.

$$Li + NO/Ar \longrightarrow LiON$$

$$Ni + (N_2)/Ar \longrightarrow Ni(N_2)_x \quad (x = 1\text{-}4)$$

$$Li + OF_2/Ar \longrightarrow \text{'LiF'} + OF$$

[*] Prof. Dr. J. J. Turner
Department of Inorganic Chemistry, The University
Newcastle upon Tyne NE1 7RU (England)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12—15, 1974).

The first mentioned reaction was the first matrix synthesis using metal atoms[7]. As is evident from this symposium program, there have been major strides since then. The second example also involves direct addition[8], whereas the third is an "abstraction" reaction[9] and it is noteworthy that the infrared spectrum of the OF radical confirms the original photochemical generation by *Arkell et al.*[2].

However, this paper is concerned with *photochemical* generation of unstable species in a matrix and particularly the relevance to atom synthesis.

2. Photochemical Generation of Unstable Species

The major problem with matrix photochemistry is the "cage effect". The matrix atoms surrounding an isolated species are in general impermeable to all species except the smallest atoms such as C, N, O, and F. Photochemistry will therefore only lead to isolation if one or both of the following conditions is met:

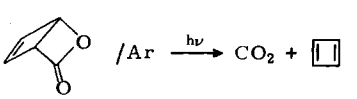
1) the species produced are stable with respect to recombination, in which case it will not matter if the photochemically generated fragments are adjacent;

2) one of the photochemically generated products can escape from the cage.

The following brief sections illustrate the principle ways in which matrix photochemistry can be promoted.

2.1. Photochemical Fission

Two examples will serve to illustrate this technique:



$$OF_2/Ar \xrightarrow{h\nu} OF + F \xrightarrow{\Delta} OF_2 + [O_2F_2]$$

The first of them shows the generation of the long-sought cyclobutadiene[10]; although neither CO_2 nor cyclobutadiene escape from the cage, the two species are stable with respect to the reverse reaction.

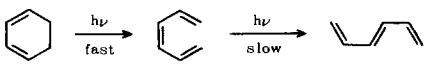
In the second example, already mentioned briefly in Section 1, gas phase[11] studies indicate that F and OF will combine with almost zero activation energy; hence they are not stable when adjacent in the matrix. Although gaseous OF_2 can be photodissociated up to 580 nm, *Arkell et al.*[2] showed that no OF was observed in the matrix unless $\lambda < 365$ nm. Thus the F atom needs a thermal "kick" to eject it from the surrounding argon cage. Softening of the argon matrix by warming allows F and OF to diffuse and they recombine; there is also some production of O_2F_2 due to OF/OF combination.

Two examples where the cage prevents isolation involve diazomethane (CH_2N_2) and chromyl chloride (CrO_2Cl_2). Contrary to expectations based on gas phase studies, photolysis of these in matrices shows no production of CH_2 and CrO_2Cl, respectively. The CH_2 and N_2 recombine, as can

be shown by photolysis in a $^{15}N_2$ matrix[12]; presumably also CrO_2Cl and Cl recombine[13]. The cage effect can however be turned to advantage. For example, vacuum UV photolysis of $CHCl_3$ in argon leads to the isolation of CCl_3[14]; presumably the photochemically produced H atoms readily diffuse away, whereas any Cl atoms produced cannot escape.

2.2. Photoisomerization

There is little reported evidence for this in matrices, but it is clear that conclusions must be treated with considerable caution. For example, in solid argon, the reaction



differs from the photochemical behavior in solution[15].

2.3. Bimolecular Reactions

These can be conveniently divided into two categories—"reactive matrix" and "tunneling". In the first category the matrix technique is inverted in the sense that a matrix is chosen because of its reactivity rather than inertness. It is often not convenient or possible to use a pure reactive matrix but a ratio of reactive to inactive matrix of about 5:100 to 10:100 is usually enough to ensure that photochemically generated fragments are in direct contact with the reactive matrix. Two examples will illustrate this technique[16, 17]:

$$HI + CO \xrightarrow{h\nu} HCO + I$$

$$Ni(CO)_4 + N_2 \xrightarrow{h\nu} Ni(CO)_3N_2 + CO$$

The term "tunneling" simply means that at least one of the photochemically generated species has to travel through the matrix to react with the substrate. For example:

$$F_2 + O_2/Ar \xrightarrow{h\nu} \underset{\text{(very dilute)}}{2\,F + O_2} \longrightarrow O_2F + F$$

where the F atom travels through the argon till it encounters an O_2 molecule[18].

2.4. Electron Transfer

Kasai et al.[19] was the first to use this technique, in the generation of the radical anion $B_2H_6^-$:

$$B_2H_6 + Na/Ar \xrightarrow{h\nu} B_2H_6^- + Na^+$$

The loss of Na and production of $B_2H_6^-$ was followed by ESR spectroscopy. It should be noted that this is a concerted process since the light used is of much lower energy than that required for the ionization of sodium. Ions can also be generated by vacuum UV photolysis[20, 21] or electron bombardment of the condensing parent molecule[22].

$$C_2H_2/Ar \xrightarrow[UV]{\text{Vacuum-}} C_2^-$$

$$Ni(CO)_4/Ar \xrightarrow[UV]{\text{Vacuum-}} Ni(CO)_3^-$$

$$Cr(CO)_6/Ar \xrightarrow[e^{\ominus}]{\substack{+Na,\ h\nu(vis) \\ \text{Vacuum-UV}}} Cr(CO)_5^-$$

3. Relevance of Photochemistry to Atom Synthesis

Two examples will serve to illustrate some of the difficulties. Some years ago *Andrews* and *Pimentel*[23] obtained IR evidence for CH_3 by co-condensing Li atoms with CH_3I/Ar. However, the spectrum of CH_3 obtained on vacuum UV photolysis of CH_4/Ar was different[24]. It was subsequently shown that *Pimentel et al.* had in fact stabilized $CH_3 \cdots LiX$ rather than CH_3 itself[25].

Rest and *Turner*[26] described the generation of $Ni(CO)_3$ by photolysis of $Ni(CO)_4$ in various matrices and assigned the two CO stretching vibrations to a pyramidal (C_{3v}) fragment. *DeKock*[27] synthesized all the species $Ni(CO)_x$ ($x = 1$—4) by co-condensation of nickel atoms with CO; however, the IR spectrum of the $Ni(CO)_3$ showed only one band. It has subsequently been shown[28] that the weaker of the two bands in *Rest* and *Turner*'s spectrum was due to dimeric species whose formation is attributed to use of $Ni(CO)_4$ at too high a concentration in the inert matrix gas.

Thus considerable care is needed in the detailed interpretation of results obtained by either technique. However, generally each has its own advantages and disadvantages as considered below.

Isolation

A major problem of atom synthesis is that it is very difficult to ensure that the species formed contain only one metal atom—diffusion on the cold surface can lead to the formation of fairly high polymers[29]. Provided high dilution is used, photochemical generation eliminates this problem. However, it has been shown[30] that even at dilutions as high as 1:20000 there is some evidence for the photolytic production of dimers.

UV/Visible Spectroscopy

Matrices produced by atom condensation are often highly scattering and even if not so, frequently contain excess metal atoms. In either case it is extremely difficult to obtain UV/visible spectra of trapped species. In contrast, such spectra are generally easily obtained for photochemically generated fragments. It is also worth mentioning that the photochemical generation of species is of considerable relevance to the study of intermediates in solution chemistry.

Stable Starting Compound

Clearly the generation of a reactive species by photochemical methods requires a starting compound that is moderately stable and easily handled. The atom technique suffers no such restriction.

Cage Effect

This has been considered above but it is worth emphasizing that it will be unusual for large fragments to sit adjacent

to each other without reacting back to starting material. For example it is well known[31] that $Fe_2(CO)_9$ acts as a source of $Fe(CO)_4$, but photolysis of $Fe_2(CO)_9$ in low temperature matrices[32] leads only to the formation of $Fe_2(CO)_8$ (bridged and unbridged). In atom synthesis, the cage effect is of little relevance, since the initial formation of reactive species occurs at the cooling but instantaneously fluid surface. Subsequent controlled annealing will of course permit diffusion of smaller species at a lower temperature than that for larger species.

Structure

Hints have already been given that the matrix can have some effect on the behavior of trapped species. A fundamental question therefore is whether species generated photochemically in a matrix will have a geometrical structure radically different from that expected in say the vapor phase. After all, photolysis of a large molecule may lead to fragmentation in such a way that the fragments are held in a vice-like grip by the matrix and cannot relax to their preferred equilibrium geometry. There is however no evidence that species generated photochemically in a matrix have a structure different from that generated by atom synthesis. In the following Sections we shall consider, in detail, some specific examples.

4. OF, $Ni(CO)_3$, and $Co(CO)_4$

We have already considered OF and $Ni(CO)_3$, where the photochemical and atom techniques, with suitable allowance for mistakes (!), give the same answer. *Crichton et al.*[33] have generated $Co(CO)_4$ by photolysis of $Co(CO)_3NO$ in a CO matrix and analyzed the ^{13}CO isotopic spectra, concluding that the complex, has C_{3v} symmetry. *Ozin et al.*[34] have generated the species by co-condensation of Co atoms and CO and have assigned the Raman spectra to a D_{2d} structure. Figure 1 compares the IR and Raman spectra from which it is clear that the basic frequencies are the same.

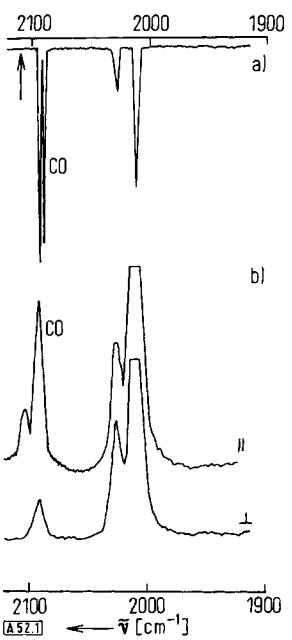


Fig. 1. a) IR spectrum of $Co(CO)_4$ obtained by photolysis of $Co(CO)_3NO$ in a CO matrix [33]; the arrow ↑ indicates position of the very weak A_1 band calculated for C_{3v} symmetry. b) Polarized Raman spectrum of $Co(CO)_4$ from co-condensation of Co atoms and CO [34].

Hence the molecule is clearly distorted from T_d; whether it is C_{3v} or D_{2d} is something of a minor point.

5. Photochemical Fragmentation of Hexacarbonyls of Cr, Mo, W

In 1962 *Sheline et al.*[35] photolyzed the hexacarbonyl compounds $M(CO)_6$, M = Cr, Mo, W in hydrocarbon glasses at 77 K and obtained preliminary infrared evidence for the formation of the pentacarbonyls with C_{4v} symmetry. We have since then performed an extensive study of these carbonyls and several others in inert gas matrices at low temperature.

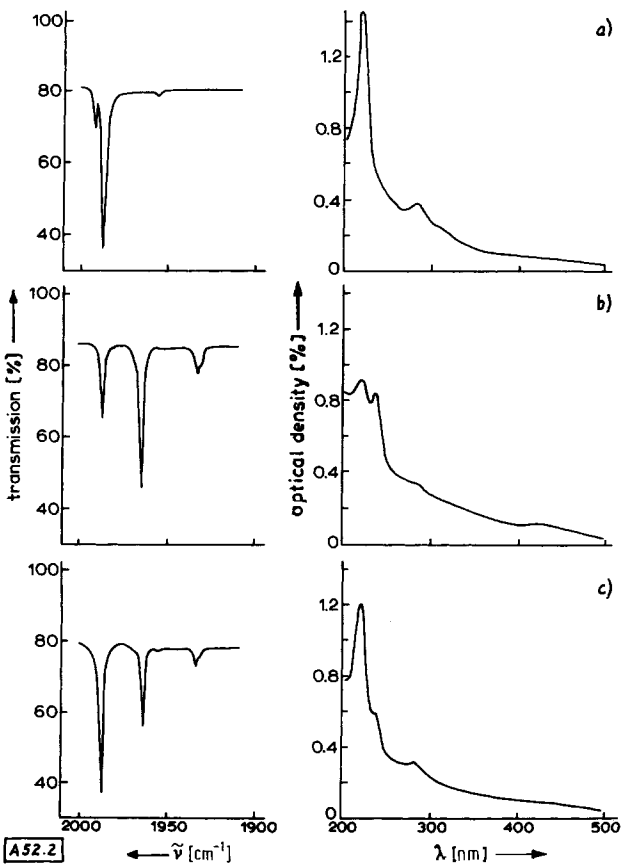


Fig. 2. IR (left) and UV/visible spectra (right) of $W(CO)_6$ in argon: a) after pulsing on to a KBr window at 20 K; b) after 30 s photolysis through a quartz window with an unfiltered medium pressure mercury arc; c) after 1.5 min irradiation through a soda glass filter ($\lambda > 330$ nm) [36].

Figure 2 shows one of our early experiments[36]. It is clear from this that UV photolysis generates a lower carbonyl fragment, which interestingly can be converted back to $W(CO)_6$ by irradiation in the visible. In fact, using a monochromator[37] with the Hg arc it can be shown that irradiation in either of the UV bands of $W(CO)_6$ produces $W(CO)_5$ and irradiation in either the UV or visible band of $W(CO)_5$ converts it back to $W(CO)_6$:

$$W(CO)_6/Ar \underset{h\nu'}{\overset{h\nu}{\rightleftharpoons}} W(CO)_5 + CO$$

The mechanism of this photoreaction has been discussed elsewhere[37].

That the primary photochemical product is $M(CO)_5$ with a C_{4v} structure is demonstrated in Figure 3, from which it will be seen that whereas a C_{4v} structure fits both the frequen-

cies and intensities of the isotopic data, a D_{3h} structure cannot be made to fit[38].

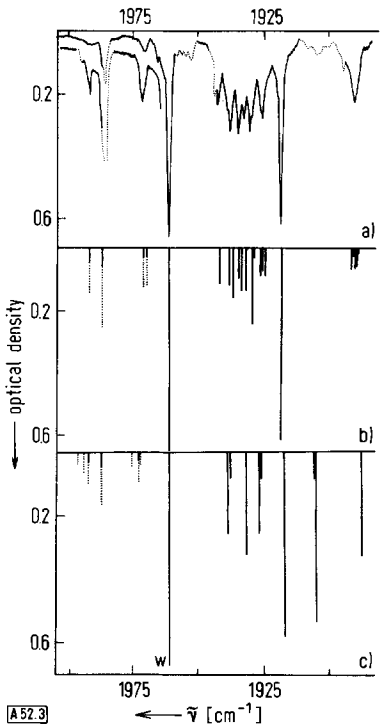


Fig. 3. a) IR spectrum of ^{13}CO-enriched $Cr(CO)_5$ in CH_4 at 20 K; b) calculated spectrum of $Cr(CO)_5$ with C_{4v} symmetry; c) calculated spectrum for D_{3h} symmetry (see ref. [38]).

It has been suggested that the photolysis simply produces an isocarbonyl:

$$M(CO)_6/Ar \xrightarrow{h\nu} (OC)_5MOC$$

This is certainly not the case for the following reasons:

1) No band assignable to an isocarbonyl structure is seen, whereas photolysis leads to production of molecular CO, with frequency virtually identical to that of matrix-isolated CO in argon.

2) Photolysis in a matrix doped with ^{13}CO leads to exchange and generation of $M(^{12}CO)_x(^{13}CO)_{6-x}$ and $M(^{12}CO)_y(^{13}CO)_{5-y}$.

3) The visible absorption of $Cr(CO)_5$ is extremely sensitive to the matrix[39]; corresponding bands appear at 480 nm in xenon and 624 nm in neon. On the other hand the visible band of $Cr(CO)_5NH_3$ is virtually unchanged from matrix to matrix[39]. Thus the inescapable conclusion is that the matrix species blocks the coordination site[*]. It is worth commenting that the sensitivity of $Cr(CO)_5$ to matrix is of considerable relevance to solution photochemistry, suggesting that in a hydrocarbon solvent $Cr(CO)_5$ forms a weak complex with the solvent[30].

Prolonged UV photolysis of $M(CO)_6$ in a matrix effects extensive fragmentation[40] (Fig. 4).

Labels on the bands indicate those that grow and decay together. It is a reasonable assumption that the lower carbonyls will be generated successively.

[*] $Cr(CO)_5$ can also be generated in a CO matrix, in which case an isocarbonyl may be formed but there is still no sign of an isocarbonyl infrared band [39].

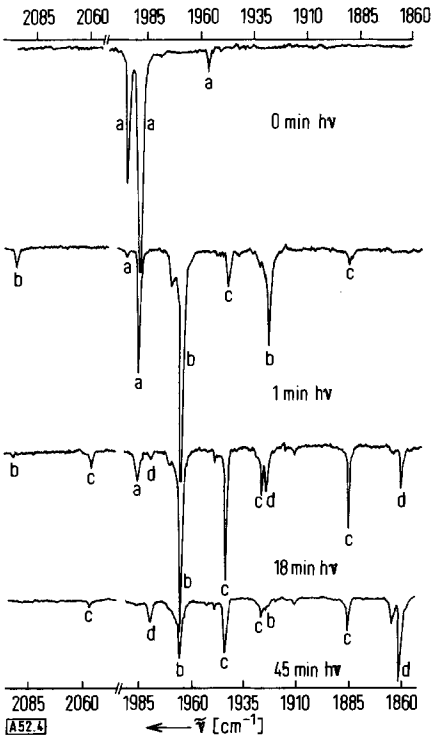


Fig. 4. IR spectra carbonylmolybdenum fragments produced by prolonged photolysis of $Mo(CO)_6$ in a methane matrix; a = $Mo(CO)_6$, b = $Mo(CO)_5$, c = $Mo(CO)_4$, d = $Mo(CO)_3$ (see ref. [40]).

$$Mo(CO)_6 \xrightarrow{h\nu} Mo(CO)_5 \xrightarrow{h\nu} Mo(CO)_4 \quad \text{etc.}$$

The bands are assigned on this basis. Assuming a CO-factored force field, detailed isotopic studies show that the structure of these species are as shown in Figure 5.

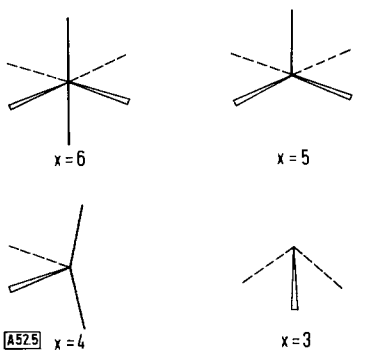


Fig. 5. Schematic structures of $Mo(CO)_x$ fragments deduced from detailed ^{13}CO isotopic studies.

It might be argued that these structures are forced on the fragments by the particular matrix environment (see above). However, polarization[41] studies demonstrate that the fragments can rotate when irradiated. In particular, the $Cr(CO)_5$ C_{4v} fragment changes orientation, probably *via* a D_{3h} intermediate. It is unlikely, therefore, that the matrix acts as a "clamp". Moreover, recent calculations by *Burdett*[42] on carbonyl fragments match remarkably well with those observed experimentally. Perhaps the most convincing argument however is that, although much broader, spectra obtained on M/CO/Ar co-condensation[40] reactions match those of the photolysis products. It is interesting to note that synthesis adds successive CO units to M whereas photolysis removes successive CO units from $M(CO)_6$.

6. Photochemical Synthesis

The fact that photolysis at one frequency removes CO and at another frequency puts it back suggests that it should be possible to substitute CO by another ligand in either a one-step or a two-step process. In practice this is relatively easy to do with small ligands. For example[17]:

$$Ni(CO)_4 + N_2 \xrightarrow{h\nu} Ni(CO)_3N_2 + CO$$

The observed IR frequencies correspond closely to those obtained on co-condensation of $Ni/CO/N_2$[43].

$$Cr(CO)_6 + N_2 \longrightarrow Cr(CO)_5N_2,\ Cr(CO)_4N_2 \quad [40,44]$$

$$\left.\begin{aligned} Fe(CO)_5 + N_2 &\xrightarrow{h\nu} Fe(CO)_4N_2 \\ + Xe &\xrightarrow{h\nu} Fe(CO)_4Xe \\ + CH_4 &\xrightarrow{h\nu} Fe(CO)_4CH_4 \end{aligned}\right\} [45]$$

In the latter two examples there is firm spectroscopic evidence that both "naked" and "complexed" $Fe(CO)_4$ are obtained. The photochemical pattern can be summarized thus[45]:

$$Fe(CO)_5 \underset{\lambda > 320\ nm}{\overset{UV}{\rightleftharpoons}} Fe(CO)_4 + CO \underset{\lambda > 320\ nm}{\overset{UV}{\rightleftharpoons}} Fe(CO)_3 + 2\ CO$$

$$Fe(CO)_4 \underset{\lambda > 375\ nm}{\overset{+Xe,\ \lambda > 320\ nm}{\rightleftharpoons}} Fe(CO)_4Xe$$

In conclusion, therefore, we suggest that photochemical techniques in matrices are of considerable relevance to matrix atom synthesis and that both methods still have a big future.

I should like to acknowledge many hours of discussion with my colleagues and their permission to quote unpublished work in this report.

Received: August 6, 1974 [A 52 IE]
German version: Angew. Chem. *87*, 326 (1975)

[1] See *G. C. Pimentel* in *A. M. Bass* and *H. P. Broida:* Formation and Trapping of Free Radicals. Academic Press, New York 1960. Angew. Chem. *87*, 220 (1975); Angew. Chem. internat. Edit. *14*, 199 (1975).
[2] *A. Arkell, R. R. Reinhard,* and *L. P. Larson,* J. Amer. Chem. Soc. *87*, 1016 (1965).
[3] *L. Y. Nelson* and *G. C. Pimentel,* Inorg. Chem. *6*, 1758 (1967).
[4] *D. Boal* and *G. A. Ozin,* Spectrosc. Lett. *4*, 43 (1971).
[5] *A. Kaldor* and *R. F. Porter,* J. Amer. Chem. Soc. *93*, 2140 (1971).
[6] *J. S. Anderson* and *J. S. Ogden,* J. Chem. Phys. *51*, 4189 (1969).
[7] *W. L. S. Andrews* and *G. C. Pimentel,* J. Chem. Phys. *44*, 2361 (1966).
[8] *J. K. Burdett, M. A. Graham,* and *J. J. Turner,* J. C. S. Dalton *1972*, 1620; *H. Huber, E. P. Kündig, M. Moskovits,* and *G. A. Ozin,* J. Amer. Chem. Soc. *95*, 332 (1973).
[9] *L. Andrews* and *J. I. Raymond,* J. Chem. Phys. *55*, 3078 (1971).
[10] *C. Y. Lin* and *A. Krantz,* J. C. S. Chem. Comm. *1972*, 1111.
[11] See *E. A. V. Ebsworth, J. A. Connor,* and *J. J. Turner* in: Comprehensive Inorganic Chemistry. Vol. 2, Pergamon Press (1973).
[12] *C. B. Moore* and *G. C. Pimentel,* J. Chem. Phys. *41*, 3504 (1964).
[13] *G. Burton,* unpublished observations.
[14] *M. E. Jacox* and *D. E. Milligan,* J. Chem. Phys. *54*, 3935 (1971).
[15] *P. Datta, T. D. Goldfarb,* and *R. S. Boikess,* J. Amer. Chem. Soc. *93*, 5189 (1971).
[16] *D. E. Milligan* and *M. E. Jacox,* J. Chem. Phys. *41*, 3032 (1964).
[17] *A. J. Rest,* J. Organometal. Chem. *40*, C76 (1972).
[18] *A. Arkell,* J. Amer. Chem. Soc. *87*, 4057 (1965); *R. D. Spratley, J. J. Turner,* and *G. C. Pimentel,* J. Chem. Phys. *44*, 2063 (1966).
[19] *P. H. Kasai* and *D. McLeod,* J. Chem. Phys. *51*, 1250 (1969).
[20] *D. E. Milligan* and *M. E. Jacox,* J. Chem. Phys. *51*, 1952 (1969).
[21] *J. K. Burdett,* J. C. S. Chem. Comm. *1973*, 763.
[22] *P. A. Breeze* and *J. J. Turner,* J. Organometal. Chem. *44*, C7 (1972); *P. A. Breeze,* Ph. D. Thesis, Cambridge University 1975.
[23] *L. Andrews* and *G. C. Pimentel,* J. Chem. Phys. *44*, 2527 (1966).
[24] *D. E. Milligan* and *M. E. Jacox,* J. Chem. Phys. *47*, 5146 (1967).
[25] *J. K. Burdett,* J. Mol. Spectrosc. *36*, 365 (1970).
[26] *A. J. Rest* and *J. J. Turner,* Chem. Commun. *1969*, 1026.
[27] *R. L. deKock,* Inorg. Chem. *10*, 1205 (1971).
[28] *A. J. Rest,* unpublished observations.
[29] *E. P. Kündig, M. Moskovits,* and *G. A. Ozin,* Angew. Chem. *87*, 314 (1975); Angew. Chem. internat. Edit. *14*, 292 (1975).
[30] *M. A. Graham, R. N. Perutz, M. Poliakoff,* and *J. J. Turner,* J. Organometal. Chem. *34*, C34 (1972).
[31] See *I. Wender* and *P. Pino:* Organic Syntheses *via* Metal Carbonyls, Vol. 1, Wiley-Interscience, New York 1968.
[32] *M. Poliakoff* and *J. J. Turner,* J. Chem. Soc. *A 1971*, 2403.
[33] *O. Crichton, M. Poliakoff, A. J. Rest,* and *J. J. Turner,* J. C. S. Dalton *1973*, 1321.
[34] *G. A. Ozin* and *A. Vander Voet,* Accounts Chem. Res. *6*, 313 (1973).
[35] *I. W. Stolz, G. R. Dobson,* and *R. K. Sheline,* J. Amer. Chem. Soc. *84*, 3589 (1962); *85*, 1013 (1964).
[36] *M. A. Graham, A. J. Rest,* and *J. J. Turner,* J. Organometal. Chem. *24*, C54 (1970).
[37] *M. A. Graham, M. Poliakoff,* and *J. J. Turner,* J. Chem. Soc. *A 1971*, 2939.
[38] *R. N. Perutz* and *J. J. Turner,* Inorg. Chem. *14*, 262 (1975).
[39] *R. N. Perutz* and *J. J. Turner,* J. Amer. Chem. Soc. *97*, in press (1975).
[40] *M. A. Graham,* Ph. D. Thesis, Cambridge University 1971; *R. N. Perutz* and *J. J. Turner,* J. Amer. Chem. Soc. *97*, in press (1975).
[41] *J. K. Burdett, R. N. Perutz,* and *M. Poliakoff,* J.C.S. Chem. Comm. *1975*, 157.
[42] *J. K. Burdett,* J. C. S. Faraday II *1974*, 1599; Inorg. Chem. *14*, 375 (1975).
[43] *G. A. Ozin* in *H. E. Hallam:* Vibrational Spectroscopy of Trapped Species. Wiley, London 1973.
[44] *R. F. Turner,* unpublished observations.
[45] *M. Poliakoff* and *J. J. Turner,* J. C. S. Dalton *1974*, 2276.

Spectral Evidence for Lanthanoid and Actinoid Carbonyl Compounds[**]

By Raymond K. Sheline and James L. Slater[*]

The co-condensation of actinoid or lanthanoid atoms and a mixture of argon containing small amounts carbon monoxide on a surface cooled with liquid helium leads, after annealing of the argon matrix, to a series of new binary actinoid and lanthanoid carbonyl compounds. Evidence for these new carbonyls is obtained using infrared spectroscopy. Preliminary interpretation of the IR spectra suggests that at least six complexes, $M(CO)_{1-6}$, have been observed for each metal. A distinct difference in the infrared spectra is observed for the ytterbium derivative, probably associated with the fact that ytterbium lacks one electron from having entirely filled 4f orbitals. A brief description of the possible bond hybridization and its effect on the M—C—O bonding, which may explain the difference between ytterbium and the other lanthanoids, is presented.

1. Introduction

Recently, a large number of new binary "metal carbonyls" have been synthesized using two rather different experimental techniques, both of which employ matrix isolation of relatively unstable species.

In the first of these procedures, a stable binary metal carbonyl compound is incorporated in a matrix. Subsequent photolysis results in the expulsion of one or more molecules of CO and the production of a number of less substituted metal carbonyls whose presence is detected using infrared spectroscopy. Initially, our research group[1] prepared a series of pentacarbonyl derivatives $M(CO)_5$ (where M = Cr, Mo, and W) by the photolysis of the appropriate hexacarbonyl compounds in rigid hydrocarbon matrices at temperatures of *ca.* 77 °K. An extensive series of experiments carried out by *Turner et al.*[2] led to the observation of a large number of lower metal carbonyls and their derivatives. In particular, they have observed $M(CO)_{2-5}$ (where M = Cr, Mo, and W). Other starting compounds photolyzed by this group included $Ni(CO)_4$[3], $HMn(CO)_5$[4], and $Fe_2(CO)_9$[5].

In the second technique involving matrix isolation, metal atoms and argon containing small amounts of CO are condensed on a liquid helium cooled surface followed by controlled annealing of the resulting argon matrix. Once again, the compounds formed can be identified spectroscopically. In the first of these studies *DeKock*[6] prepared $Ni(CO)_{1-4}$ and tentatively identified $Ta(CO)_{1-6}$. Using the same apparatus as *DeKock*, *Slater* of our laboratory[7] succeeded in preparing $U(CO)_{1-6}$. Since that time, large numbers of metal carbonyls have been prepared using the co-condensation technique. These include $Cu(CO)_x$[8], $Ag(CO)_x$[8], $Pd(CO)_4$[9], $Pt(CO)_4$[10], $Al_x(CO)_2$[11], $Ge(CO)_x$[12] and $Sn(CO)_x$[12]. Indeed, it seems to be a safe assumption that the co-condensation technique can be used to prepare binary carbonyl compounds of most (and probably all) metals.

This paper represents a status report on the binary carbonyls of the actinoids and lanthanoids[7, 13, 14].

The preparation of uranium carbonyl has historical interest. Volatile uranium compounds were required by the Manhattan Project for the separation of the isotopes ^{235}U and ^{238}U by gas-phase diffusion. It was thought that uranium carbonyl might be particularly suitable since metal carbonyls are generally volatile and would be far less corrosive than the volatile uranium hexafluoride. Most, if not all, of the tested methods for preparing metal carbonyls were tried. These standard methods involve the reaction of uranium metal, hydride, or halide with carbon monoxide and a reducing agent. The reaction conditions were varied but most were carried out at high temperatures in pressurized bombs. No uranium carbonyl was synthesized[15].

2. New Experimental Findings

The route which finally led to the fulfillment of our aim—namely the preparation of binary uranium carbonyls—will be described in some detail, for it is exemplary for the synthesis of other actinoids as well as lanthanoids. The main contribution to the success was an apparatus designed and built by *Weltner*[16] (Fig. 1).

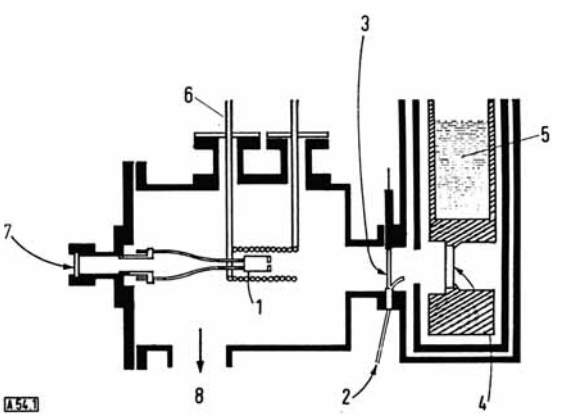


Fig. 1. Apparatus for the preparation of actinoid and lanthanoid carbonyls by matrix isolation [16]. 1: Sample cell for metal evaporation; 2: gas inlet; 3: movable shutter; 4: cooled window; 5: liquid helium; 6: induction heater; 7: window for temperature measurement; 8: high vacuum.

The powdered uranium metal, with a purity of 99.8%, was packed in a sample cell and placed in the induction heater under high vacuum. The sample cells were made of

[*] Prof. Dr. R. K. Sheline
Chemistry Department
Florida State University
Tallahassee, Florida 32306 (USA)
Dr. J. L. Slater
Chemistry Department
University of Virginia
Charlottesville, Virginia (USA)

[**] Based on a lecture delivered at the Symposium "Metall-Atome in der chemischen Synthese" of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. Darmstadt, Germany (12—15 May 1974). This work supported in part by the U.S. Atomic Energy Commission (Contract No. AT-(40-1)-2434).

either tantalum or tungsten and were baked at high temperature prior to deposition of the matrix. A temperature of about 1950 °K was used for the vaporization of the uranium so that the vapor pressure of the metal was about 10^{-5} torr. This insured that only monoatomic species were present in the vapor. All trapping was done at liquid helium temperature. The metal atoms and the argon-CO mixture were allowed to condense onto the cold CsI window for 30 to 50 min. After the matrix has been deposited on the CsI window, the entire system (Dewar window and copper block) was rotated 90° allowing infrared spectra to be taken without interfering with the furnace. It is possible to control the temperature on the window by varying the flow of liquid helium to the copper block.

At 4 °K the argon forms a rigid matrix. At 16 °K the matrix loses its rigidity and the CO molecules begin to diffuse through the solid argon matrix. The diffusion was controlled by careful "annealing" of the matrix. As soon as the temperature had reached the desired level, the matrix was immediately quenched to 4 °K by opening the valve that controls the helium flow to the copper block. Infrared spectra were taken at 4 °K after annealing and the matrix was allowed to warm to higher temperatures on each successive anneal.

The basis of the matrix isolation technique is that high dilution ratios exist between the lattice and the trapped atoms or molecules, so that there are no interactions between the reactive species within the rigid lattice. It is assumed that activation energies are low enough so that the rate of formation of the metal carbonyls will be controlled by diffusion processes within the matrix.

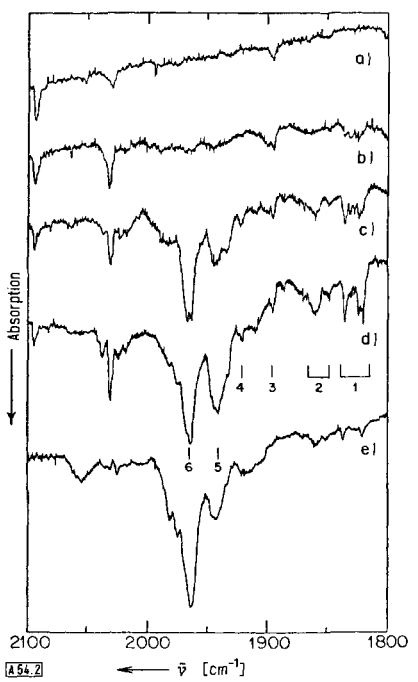


Fig. 2. IR spectra of an Ar-CO matrix (300:1) containing uranium atoms: a) no annealing; b) 17 °K; c) 19 °K; d) 20 °K; e) 30 °K. The arabic numerals refer to the tentative assignment of intermediate carbonyls—*n* in $U(CO)_n$.

Figure 2 shows the infrared spectra in the 1800—2100 cm^{-1} range taken at various stages in the annealing process with a matrix prepared with a 300:1 dilution ratio of carbon monoxide in argon and uranium atoms. The strong ^{12}CO band is present at 2138 cm^{-1} in all spectra but is not shown in the figure. Spectrum a shows the matrix prior to an annealing. The carbon-oxygen stretching frequencies at 2092 cm^{-1} (for natural abundance ^{13}CO) and three very weak bands at 2029, 1893, and 1800 cm^{-1} are found in the spectrum. In spectra b and c, a large number of IR bands are growing into the spectrum as a result of annealing. Spectra d and e, following annealing to higher temperature, show the dominance of higher frequency bands at 1961, 1938 and the broad band around 1920 cm^{-1}.

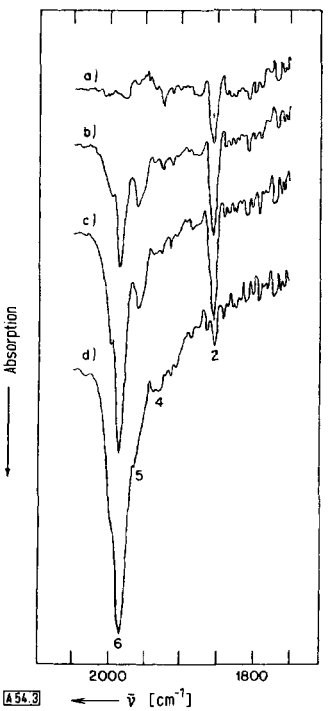


Fig. 3. IR spectra of $Pr(CO)_n$ in an argon matrix with 2 mol-% CO: a) before annealing; b)—d) after various stages of annealing. Cf. Table 1.

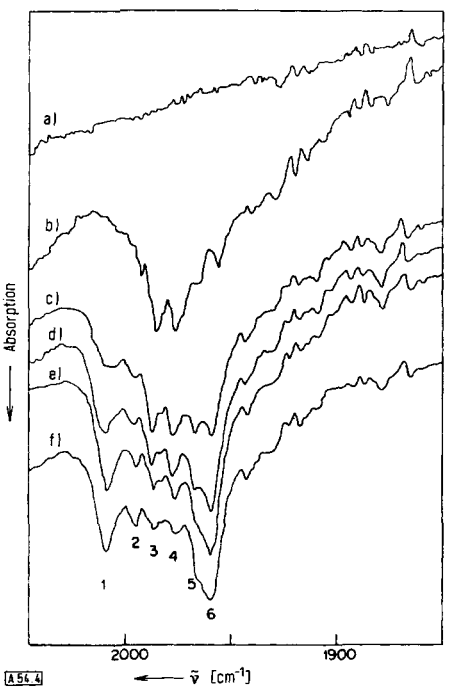


Fig. 4. IR spectra of $Yb(CO)_n$ in an argon matrix with 1 mol-% CO: a) no annealing; b) 32 °K; c) 36 °K; d) 39 °K (2 min); e) 39 °K (35 min); f) 39 °K (80 min). Cf. Table 2.

Similar sets of infrared spectra are available at a variety of controlled annealing stages for argon-carbon monoxide matrices containing a lanthanoid (Pr, Nd, Gd, Ho or Yb) instead of uranium atoms (cf. Figures 3 and 4).

It is immediately obvious that the spectra including the systematic changes resulting from annealing are very similar for uranium, praseodynium, neodymium, gadolinium and holmium carbonyls (Table 1). On the other hand, the spectra of the ytterbium carbonyls differ markedly; the frequencies of their infrared active bands are presented in Table 2. These differences are not unexpected. U, Pr, Nd, Gd and Ho are typical actinoids and lanthanoids in that they have a +3 normal oxidation state. Yb, on the other hand, tends to be more like Sr or Ba in physical properties and has a +2 normal oxidation state[17]. This sudden change in properties results because Yb, which would normally be expected to lack one electron from having filled 4f orbitals, promotes the 5d electron to achieve this more stable filled 4f configuration.

Table 1. C—O Stretching frequencies of actinoid and lanthanoid carbonyls [cm^{-1}].

U	Pr	Nd	Gd	Ho	Tentative Assignment
1961	1989	1990	1986	1982	$M(CO)_6$
1938	1965	1965	1967	1961	$M(CO)_5$
1919	1940	1940	1945	1929	$M(CO)_4$
1893	1885	1891	1901	1902	$M(CO)_3$
1855 1846	1858	1861	1864	1859	$M(CO)_2$
1832 1817	1835	1840	1841	1830	M(CO)

Table 2. CO Stretching frequencies of ytterbium carbonyls [cm^{-1}]; no band assignment.

Yb	1958	1966	1976	1986	1995	2008

The difficulties in assigning IR frequencies to specific carbonyl compounds are compounded by the fact that we do not even know which carbonyl species, and in particular which coordinations, are to be expected. The tentative assignment shown in Table 1 is supported by the following findings: firstly, the lowest frequency bands were observed with little or no annealing, in each of the metal-carbonyl systems considered; secondly, these bands grew and disappeared with progressively higher frequencies occurring in a startlingly similar way as annealing to higher and higher temperatures continued; and thirdly, the observed relationship between carbonyl stretching frequency and the tentatively assigned coordination number. This is shown in Fig. 5 where in the upper part of the diagram the carbonyls produced by matrix photolysis of known hexacarbonyl metal complexes are compared with the actinoid and lanthanoid carbonyls of this study; in the lower part the relationship between coordination number and the CO stretching frequency for the tentatively assigned carbonyl derivative is presented. This relationship is quite linear for the lanthanoid carbonyls, and, analogously, for the uranium carbonyls, with a slightly greater slope. The correlation between $Ta(CO)_{1-6}$ and the lanthanoid and actinoid carbonyls is particularly striking.

There are, however, a number of experimental and theoretical problems with these assignments. In the first place, only mononuclear compounds were considered. In view of the

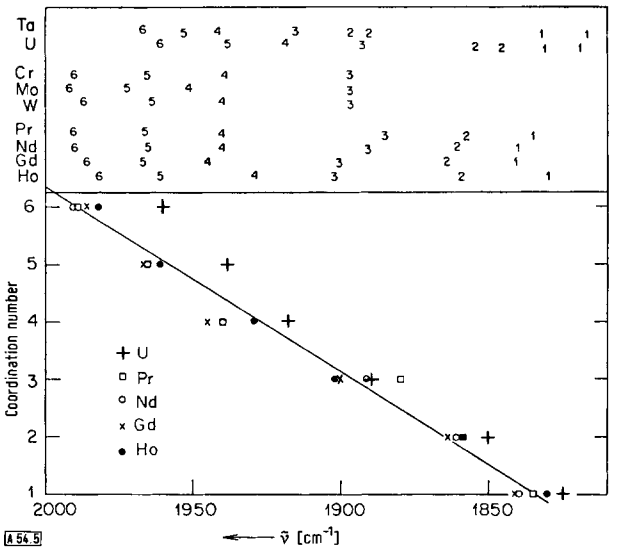


Fig. 5. Relationship between tentative coordination number and CO stretching frequency for metal carbonyl compounds (cf. text).

considerable dilution of the metal and the fact that the lowest frequencies, which were more nearly in the frequency range of bridge-forming CO ligands, formed first, this assumption appears to be borne out by experiment. However, there are a number of weaker bands which appear in the IR spectra of (cf. Figs. 2—4) whose origin is difficult to establish. Most of the coordination numbers tentatively assigned have more than one IR active species. This is shown in Table 3 where the IR activity is presented for a variety of different molecular symmetries of metal carbonyls with coordination numbers from 1 to 8. In order to decide this issue, the molecular configuration as well as the coordination number must be determined. In view of the complexity and quality of the spectra, this is not possible with the present data.

Table 3. Some possible symmetries and the corresponding IR-active C—O stretching modes for $M(CO)_{1-8}$.

Molecule	Symmetry (Geometry)	CO Stretching Mode
M(CO)	$C_{\infty v}$ (linear)	$1\Sigma^+$
$M(CO)_2$	$D_{\infty h}$ (linear)	$1\Sigma_\mu^+$
$M(CO)_2$	C_{2v} (angular)	$1A_1+1B_1$
$M(CO)_3$	D_{3h} (trigonal planar)	$1E'$
$M(CO)_3$	C_{3v} (trigonal pyramidal)	$1A_1+1E$
$M(CO)_4$	T_d (tetrahedral)	$1T_2$
$M(CO)_4$	D_{4h} (tetragonal planar)	$1E_\mu$
$M(CO)_4$	C_{4v} (tetragonal pyramidal)	$1A_1+1E$
$M(CO)_5$	D_{3h} (trigonal bipyramidal)	$1A_2''+1E'$
$M(CO)_5$	C_{4v} (tetragonal pyramidal)	$2A_1+1E$
$M(CO)_6$	O_h (octahedral)	$1T_{1\mu}$
$M(CO)_6$	D_{3h} (trigonal prismatic)	$1A_2''+1E$
$M(CO)_7$	D_{5h} (pentagonal bipyramidal)	$1E_1'+1A_2''$
$M(CO)_7$	C_{2v} (TaF_7^{2-}—structure [a])	$3A_1+1B_1+2B_2$
$M(CO)_8$	C_{2v} (trigonal dodecahedral)	$4A_1+2B_1+2B_2$

[a] Trigonal prism with extra group in one rectangular face.

Another explanation for the "excess" IR bands may be the existence of crystal splitting in the argon matrix (cf. Ref. [6]).

No attempt is made to describe the coordination number or the structure of the ytterbium carbonyls, although it appears that the structures and/or the coordination numbers are quite different from those of the carbonyls of typical lanthanoids or actinoids. It is, however, obvious that a number of mononuclear carbonyl compounds are formed. Indeed, the complexity of the

spectra appears to suggest even more compounds and higher coordination numbers than for the normal f-orbital element carbonyls.

3. Structural Considerations on the Basis of Orbital Hybridization

The considerations of basic identity and possible coordination numbers in the last section are developed from purely experimental reasoning. We are led irrevocably to the existence in each of the spectra of a number of new binary carbonyls with possible coordination numbers from 1 to at least 6. In this section we will attempt to use theoretical arguments for band hybridization of the orbitals of the lanthanoid and actinoid central atom to make some predictions about possible structures.

It should first be noted that the spectra of the normal lanthanoid and actinoid carbonyls (all of these except the ytterbium carbonyls) are remarkably similar. Since the number of f electrons in these species differs, while the spectra indicate the species are the same, we are led to assume that the f electrons, and therefore the f orbitals, do not participate significantly in the bonding. This conclusion is reinforced by the fact that just in those cases where there is a rearrangement of the electrons from the 5d orbital to entirely fill the 4f orbitals in ytterbium, the spectra indicate quite different species. We will operate then with the assumption that the 5d, 6s and 6p, and for uranium the 6d, 7s and 7p, metal orbitals are primarily involved in bonding and in that order in energy. Using these orbitals and assuming that each carbon monoxide molecule brings two electrons to a coordinate covalent bond, it is possible, according to *Kimball*, to predict the structures

Table 4. Bond hybridization and structure in actinoid and lanthanoid carbonyls (ref. [20]).

CN	Hybridization	Structure	"Typical" [a]	Yb [a]	π-Back-bonding [b]	
					Strong	Weak
1	s	linear			p^2d^2	—
1	p	linear			p^2d^2	—
1	d	linear	×	×	p^2d^2	—
2	sp	linear			p^2d^2	—
2	dp	linear			p^2d^2	—
2	p^2	angular			d(pd)[b]	d(sd)
2	ds	angular			d(pd)	d(pd)
2	d^2	angular	×	×	d(pd)	d(spd)
3	sp^2	trigonal planar			pd^2	d^2
3	dp^2	trigonal planar			pd^2	d^2
3	d^2s	trigonal planar			pd^2	p^2
3	d^3	trigonal planar	×	×	pd^2	p^2
3	dsp	unsymmetrical planar			pd^2	(pd)d
3	p^3	trigonal pyramidal			—	$(sd)d^4$
3	d^2p	trigonal pyramidal			—	$(sd)p^2d^2$
4	sp^3	tetrahedral			d^2	d^3
4	d^3s	tetrahedral	×		d^2	p^3
4	dsp^2	tetragonal planar			d^3p	—
4	d^2p^2	tetragonal planar			d^3p	—
4	d^2sp	irregular tetrahedral			—	d
4	dp^3	irregular tetrahedral			—	s
4	d^3p	irregular tetrahedral			—	s
4	d^4	tetragonal pyramidal		×	d	(sp)p
5	dsp^3	trigonal bipyramidal			d^2	d^2
5	d^3sp	trigonal bipyramidal	×		d^2	p^2
5	d^2sp^2	tetragonal pyramidal			d	pd^2
5	d^4s	tetragonal pyramidal		×	d	p^3
5	d^2p^3	tetragonal pyramidal			d	sd^2
5	d^4p	tetragonal pyramidal			d	sp^2
5	d^3p^2	pentagonal planar			pd^2	—
5	d^5	pentagonal pyramidal			—	$(sp)p^2$
6	d^2sp^3	octahedral			d^3	—
6	d^4sp	trigonal prismatic		×	—	p^2d
6	d^5p	trigonal prismatic			—	p^2s
6	d^3p^3	trigonal antiprismatic			—	sd
6	d^3sp^2	mixed (usually octahedral)	×		—	—
6	d^5s	mixed			—	—
6	d^4p^2	mixed			—	—
7	d^3sp^3	pentagonal bipyramidal	×		—	d^2
7	d^5sp	pentagonal bipyramidal			—	p^2
7	d^4sp^2	TaF_7^{2-} structure		×	—	dp
7	d^4p^3				—	ds
7	d^5p^2				—	ps
8	d^4sp^3	trigonal dodecahedral		×	d	—
8	d^5p^3	antiprismatic			—	s
8	d^5sp^2	face centered prismatic			p	—

[a] Hybridization of the orbitals assuming the f electrons do not participate. The "typical" actinoids and lanthanoids include U, Pr, Nd, Gd, and Ho.
[b] Parentheses indicate that there is a choice of more than one orbital, only one of which may be chosen.

that would arise[18]. The possible structures and coordination numbers from 1 to 8 are presented in Table 4. Assuming that the electron configuration utilized in hybridization for the "typical" lanthanoids and actinoids is $5d^36s^06p^0$ and $6d^37s^07p^0$, respectively, one arrives at the hybridizations and structures shown in column 4 of Table 4 for the appropriate coordination numbers. In a similar way, assuming for ytterbium the electron configuration $5d^26s^06p^0$ for hybridization, one arrives at the hybridizations and structures shown in column 5 of Table 4 for the appropriate coordination numbers.

It is immediately obvious that these simple hybridization considerations imply that the typical lanthanoid and actinoid carbonyls should have coordination numbers from 1 to 7, rather than 1 to 6 as was suggested by the experimental data. In the case of ytterbium, coordinations from 1 to 8 are expected.

We are now left with the difficult task of trying to reconcile experimental and theoretical results. Actually, the difference may be less than we might initially suppose. Indeed, on the high wave number side of each of the strong bands in the region of $\approx 2000\,cm^{-1}$, an additional infrared band is observed which could easily represent the sevenfold coordinated metal carbonyl. Furthermore, a number of additional bands are observed which have not been interpreted. Thus, one possibility is that the theoretical suggestions may ultimately be borne out by a more complete experimental interpretation. On the other hand, the considerably lower symmetry of the sevenfold coordinated system may mean that it is not formed—in spite of the expected additional energy available—when the rare gas structure of electrons is obtained.

Two clarifications do come from the theoretical studies. They point very clearly to a mechanism for explaining the widely different spectra of the typical lanthanoid and actinoid carbonyls on the one hand and those of ytterbium on the other. Not only are the maximum coordination numbers different, but also the structures expected for coordination numbers >3. Furthermore, the π back-bonding between metal atoms and CO tend to be weaker with increasing coordination number (cf. column 6 and 7 of Table 4). This effect is enhanced when the decreased π back-bonding is divided among increasing numbers of bonds. The decreased π back-bonding between metal and CO implies increasing C—O bond order and C—O stretching frequency with increasing coordination number, as first pointed out by *DeKock*. Exactly the same behavior was observed in our experiments (see Table 1).

In view of the presence of at least one odd electron in each of the hybridized carbonyl species of the typical lanthanoids and actinoids, the simple symmetrical structures predicted in Table 4 are not allowed by the Jahn-Teller effect. However, the simplicity of the infrared spectra observed in the case of $V(CO)_6$, and the failure to observe P, Q, and R branches in the gas spectrum[19], implies that there is a dynamic Jahn-Teller effect which involves no static distortion of the octahedral (O_h) symmetry in this molecule. In a similar way, it seems probable that the simple symmetries of Table 4 are to be expected for the typical lanthanoid and actinoid carbonyls because of a dynamic Jahn-Teller effect. With the promotion of the d electron in ytterbium, the structures of the carbonyl species of this diamagnetic metal predicted in Table 4 should not be influenced since no Jahn-Teller effect is expected for this molecule.

4. Conclusion

A large number of new actinoid and lanthanoid carbonyls have been observed involving many coordination numbers. It is, however, clear that a great deal of additional experimental and theoretical work is required to understand the complex details of spectra and structure of these new compounds.

One of the most useful experiments would utilize ESR to determine whether the theoretical hybridizations suggested here are consistent with experiment. In particular, it would be of considerable interest to see if the carbonyls of ytterbium are diamagnetic in contrast to the expected paramagnetism of the other lanthanoid or actinoid carbonyls.

It would also be of considerable practical interest to study the stability of these carbonyls at higher temperatures. In view of the extremely small amounts of carbonyls generated in these experiments, it would probably be advisable to use the method of *Timms*[20] to attempt the preparation of macro quantities. Despite the fact that it has not been possible to prepare uranium carbonyls at room temperature, it is by no means certain that uranium carbonyls are unstable at room temperature as shown by *Timms* for other compounds. This possibility might have significance in the separation of uranium isotopes.

We wish to thank Professor William Weltner of the University of Florida for his cooperation and the use of his equipment in the studies of the uranium carbonyls, and Professor V. Calder and Mr. T. C. DeVore of Iowa State University for their cooperation with one of us (JLS) in the study of the lanthanoid carbonyls.

Received: May 15, 1974 [A 54 IE]
German version: Angew. Chem. *87*, 332 (1975)

[1] *I. W. Stoltz, G. R. Dobson,* and *R. K. Sheline*, J. Amer. Chem. Soc. *84*, 3589 (1962); *85*, 1013 (1963).
[2] *M. A. Graham, M. Poliakoff,* and *J. J. Turner*, J. Chem. Soc. *A 1971*, 2939.
[3] *A. J. Rest* and *J. J. Turner*, Chem. Commun. *1969*, 1026.
[4] *A. J. Rest* and *J. J. Turner*, Chem. Commun. *1969*, 375.
[5] *M. Poliakoff* and *J. J. Turner*, J. Chem. Soc. *A 1971*, 2403.
[6] *R. L. DeKock*, Inorg. Chem. *10*, 1205 (1971).
[7] *J. L. Slater, R. K. Sheline, K. C. Lin,* and *W. Weltner, Jr.*, J. Chem. Phys. *55*, 5129 (1971).
[8] *J. S. Ogden*, Chem. Commun. *1971*, 978.
[9] *J. H. Darling* and *J. S. Ogden*, Inorg. Chem. *11*, 666 (1972).
[10] *E. P. Kündig, M. Moskovits,* and *G. A. Ozin*, J. Mol. Struct. *14*, 137 (1972).
[11] *A. J. Hinchcliffe, J. S. Ogden,* and *D. D. Oswald*, J. C. S. Chem. Comm. *1972*, 338.
[12] *A. Bos*, J. C. S. Chem. Comm. *1972*, 26.
[13] *J. L. Slater, T. C. DeVore,* and *V. Calder*, Inorg. Chem. *12*, 1918 (1973).
[14] *J. L. Slater, T. C. DeVore,* and *V. Calder*, Inorg. Chem., in press.
[15] *J. J. Katz* and *E. Rabinawitch:* The Chemistry of Uranium. McGraw-Hill, New York 1951, p. 356—364.
[16] *W. Weltner, Jr.* in *L. Eyring:* Advances in High Temperature Chemistry, Vol. 2. Academic Press, New York 1969, p. 85.
[17] *K. A. Gschneidner*, J. Less-Common Metals *25*, 405 (1971).
[18] *G. E. Kimball*, J. Chem. Phys. *8*, 188 (1940).
[19] *H. Haas* and *R. K. Sheline*, J. Amer. Chem. Soc. *88*, 3219 (1966).
[20] *P. L. Timms*, Chem. Commun. *1969*, 1033; Angew. Chem. *87*, 295 (1975); Angew. Chem. internat. Edit. *14*, 273 (1975).

The Flipping of CO Ligand Groups in Metal Carbonyl Compounds and its Frequency in $Fe(CO)_5$[**]

By Raymond K. Sheline and Harald Mahnke[*]

It has been proven qualitatively by a number of authors using variable temperature NMR experiments that most metal carbonyl complexes are nonrigid. A quantitative determination of the ligand exchange frequency ν_e is often achieved by a line shape analysis or by measurement of the transverse relaxation time T_2 using the Carr-Purcell method. In the case of a "very fast" exchange, however, both methods prove unsuccessful. It is shown in this study that a simultaneous fit of IR or Raman spectra on the one hand and NMR spectra on the other can make possible the determination of ν_e for the "very fast" exchange and can also facilitate the determination of ν_e in "slow" and "medium" exchange cases considerably. The ligand exchange frequency thus found for $Fe(CO)_5$, $1.1 \times 10^{10} s^{-1}$, is unexpectedly high; comparison with variable temperature measurements on solid $Fe(CO)_5$, yields similar energy barriers. A mechanism of exchange closely related to the "Berry mechanism" is proposed. Finally the consequences of this surprisingly large ligand exchange rate are discussed with respect to IR band assignments for molecular "fragments" $M(CO)_x$ (where x = coordination number, and M is a transition metal, typically lanthanoid or actinoid).

1. Introduction

Many physical changes occur in molecules extremely rapidly. These include bond switching such as that which occurs in hydrogen bonding, molecular association, internal rotation or pseudorotation and conformational motions of stereoisomers. If these processes occur between distinguishable sites on a time scale which affects the shape of the NMR resonance lines, it is possible to obtain an estimate of the time required for the physical change.

The shape, Y, of the observed lines in the NMR spectrum can usually be described by[1]

$$Y(\omega-\omega_0) = f(\nu_e, \delta\sigma^0, P_a, P_b) \quad (1)$$

where ω and ω_0 are the variable frequency and the frequency at the absorption maximum, ν_e is the frequency of ligand exchange, $\delta\sigma^0$ is the chemical shift difference between the exchanging sites a and b and P_a, P_b are the populations of these sites. If the populations P_a, P_b are treated as constant the shape of the spectrum depends on ν_e and $\delta\sigma^0$. Three cases can be distinguished.

1. ν_e is at least five times smaller than the line separation, $\Delta\nu$, corresponding to $\delta\sigma^0$ in Eq. (1) in the absence of exchange.
2. ν_e and $\Delta\nu$ have the same order of magnitude.
3. ν_e is at least five times larger than $\Delta\nu$.

In the first case a sharp spectrum corresponding to a rigid structure is observed. The second case results in a very broad unresolved spectrum. Sometimes these broad signals disappear in the background noise. A sharp time-averaged spectrum is observed in the third case. Its appearance is much simpler than in the first case and information like spin-spin coupling constants is lost due to the time averaging.

[*] Prof. Dr. R. K. Sheline and Dr. H. Mahnke
Department of Chemistry, Florida State University
Tallahassee, Florida 32306 (USA)

[**] Based on a lecture delivered at the symposium "Metal Atoms in Chemical Synthesis" held under the auspices of the Merck'sche Gesellschaft für Kunst und Wissenschaft e. V. at Darmstadt (May 12–15, 1974). This work was supported in part by the U.S. Atomic Energy Commission under Contract No. AT-(40-1)-2434.

For the temperature dependence of the exchange frequency ν_e, we can write an Arrhenius-type equation

$$\nu_e = \nu_e^0 \exp(-E_a/kT) \quad (2)$$

where E_a is the activation energy. If E_a is large enough the rate of exchange can be slowed down sufficiently by cooling the compounds so that all three of the above discussed cases can be observed. Such effects have often been observed in the nonrigid metal carbonyls.

To evaluate ν_e quantitatively, it is necessary to do careful line shape analysis involving the functional dependences described in Eq. (1). This analysis is usually more complicated than discussed here because P_a and P_b are also temperature dependent. This difficulty can be overcome using a separate variable temperature IR or Raman study which yields the mole fractions and the populations, P_a and P_b[2]. Unfortunately, most of the examples studied so far by NMR techniques fail to utilize these complementary parallel techniques[3–5]

However, line shape analysis as a tool for the determination of ν_e breaks down if the energy barrier hindering the exchange becomes too small and/or if ν_e becomes too large. The most well known example is $Fe(CO)_5$. As one of the first nonrigid structures to be postulated and established, it stands as the prototype of a number of such molecules with trigonal bipyramidal structure[6, 7]. In these compounds cooling within the experimentally accessible temperature range (+80 °C to −150 °C) does not affect the NMR spectrum, thus entirely ruling out line shape analysis.

In the following we are concerned with ν_e for $Fe(CO)_5$ and therefore with a case not susceptible to line shape analysis. In this fast exchange case the line shape analysis is replaced by a measurement of the transverse relaxation time T_2. In Eq. (1), T_2 and the absorption $Y(\omega-\omega_0)$ are both functions of the same variables. The measurement of T_2 by pulse techniques, however, allows the study of much faster exchange processes than is possible with the analysis of line shape[8]. In view of the close relationship between T_2 measurements and line shape analysis, the same ideas (discussed above) apply. Both are influenced by populations and thus by mole fractions.

If populations are determined independently by variable temperature IR studies, $\delta\sigma^0$ can usually also be determined independently. Thus ν_e, the only unknown which influences T_2 or the NMR line shape, can easily be determined.

X-ray and electron diffraction studies on $Fe(CO)_5$ reveal its structure to be a trigonal bipyramid belonging to the D_{3h} point group with axial and equatorial bond lengths of 1.79 Å and 1.842 Å, respectively[9]. Although the two different M—C bond distances indicate a different electronic environment for the axial C-atoms compared to the equatorially bonded carbon atoms, high resolution ^{13}C NMR studies reveal that all five carbons appear to be equivalent[6, 7]. Such an equivalence would be expected if nonequivalent ligand groups exchange their molecular sites (presumably by an intramolecular process) at a rate which is fast compared to the frequency difference between the chemical shifts of the exchanging nuclei. This situation corresponds to the third case discussed above. The observed chemical shift $\langle\sigma(K)\rangle$ of the K^{th} nucleus in $Fe(CO)_5$ is therefore time-averaged and must be accounted for by an equation of the type,

$$\langle\delta(K)\rangle = \sum_i a_i\sigma_i^0 \qquad (3)$$

where the σ_i^0 are the chemical shifts of the exchanging sites, which are not directly observable in the fast exchange case, and the a_i are statistical populations. For $Fe(CO)_5$ the subscript i can best be denoted as ax and eq and σ_{ax}^0, σ_{eq}^0 are the ^{13}C chemical shifts of the axial and equatorial positions, respectively. Since a trigonal bipyramid has two axial and three equatorial positions, a_{ax} and a_{eq} have the values of 0.4 and 0.6, respectively.

2. A Method for the Determination of $\delta\sigma^0$ and the Populations P_a and P_b

T_2-measurements are well described for the fast exchange case by the equation

$$\frac{1}{T_2} - \frac{1}{T_2^0} \geq P_a P_b (\delta\sigma^0)^2 \tau_e \qquad (4)$$

Here, $1/T_2$ is the total transverse relaxation rate, $1/T_2^0$ is the transverse relaxation rate in the absence of exchange and $\delta\sigma^0 = |\sigma_{ax}^0 - \sigma_{eq}^0|$ and τ_e are the chemical shift difference between the exchanging sites and the mean lifetime of the D_{3h} configuration, respectively. The measurement was performed at 61 MHz and −20°C and gave for $Fe(CO)_5$[10]

$$10^{-3}\,s^{-1} \geq 6/25\,(\delta\sigma^0)^2\tau_e \qquad (5)$$

The product of the populations P_aP_b is in this case determined by the symmetry of the molecule as 6/25. In order to determine the rate of exchange, ν_e, the ^{13}C chemical shift difference $\delta\sigma^0$ between axial and equatorial sites must be determined by an independent measurement.

Using equation (3), it is possible to calculate $\delta\sigma^0 = |\sigma_{ax}^0 - \sigma_{eq}^0|$, if an independent equation in the two unknowns σ_{ax}^0 and σ_{eq}^0 can be obtained. This can only be accomplished by changing the weighting factors, a_{ax} and a_{eq}. Although the weighting factors of $Fe(CO)_5$ cannot be influenced, those of a "pseudo-isotope" do change.

For this purpose the series of compounds $Fe(CO)_x(PF_3)_{5-x}$ has been studied. CO force constants are not significantly influenced by increasing degree of PF_3 substitution for CO in the molecule. This has been interpreted to result from the very similar amount of π-bonding ability of both ligands[11]. The same ought to also apply for the ^{13}C chemical shifts. Since only one additional independent equation is needed in order to determine σ_{ax}^0 and σ_{eq}^0 with Eq. (3) and since this series of compounds runs from $x=1$ up to $x=5$, we can test this assumption by means of an overdetermined system of equations.

The best test for the pseudo-isotope character of the compounds $Fe(CO)_x(PF_3)_{5-x}$, however, is based on spin-spin coupling constants. Isotopic substitution of Y for X changes the spin-spin coupling constant J_{AX} to J_{AY}. The ratio of J_{AX} to J_{AY} is equal to the ratio of the gyromagnetic ratios of the X and Y nuclei. This ratio can be replaced by the ratio of the magnetic moments of nuclei if both isotopes have the same total spin I. This simple relationship holds because all electronic terms which usually influence the spin-spin coupling constant cancel. Real isotopes have very nearly identical electronic environments. Thus, real isotopes certainly show the same σ_i^0's in Eq. (3) since the a_i's are not influenced by isotopic substitution. Pseudoisotopes, on the other hand, have different ligand populations between axial and equatorial positions and therefore have different a_i's. Moreover, these a_i's usually change with temperature. Hence, the electronic environment of the carbon nuclei is certainly influenced by pseudo-isotopic substitution, as are also the ratios of the coupling constants. If the assumption of pseudo-isotopes is warranted, the ratio of the $^{13}C-{}^{31}P$ to the $^{31}P-{}^{31}P$ spin-spin coupling constants should be approximately equal to the ratio of the magnetic moments of the ^{13}C and ^{31}P nuclei.

$$\frac{J_{^{13}C\text{-}^{31}P}}{J_{^{31}P\text{-}^{31}P}} = \frac{\mu_{^{13}C}}{\mu_{^{31}P}} \qquad (6)$$

This relationship has been tested and proven accurate for the *cis*-coupling constants $J_{^{13}C-^{31}P}^{cis}$ and $J_{^{31}P-^{31}P}^{cis}$ for the compound $Fe(CO)_3(PF_3)_2$. The relationship also applies for the *vic*(120°) and *trans*(180°) spin-spin coupling constants. These compounds are therefore well suited as pseudo-isotopes for our purpose. Figure 1 shows the possible stereoisomers for $x=3$ and their symmetry classifications.

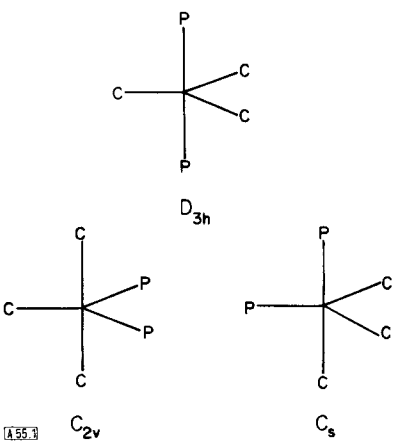


Fig. 1. Stereoisomers of $Fe(CO)_3(PF_3)_2$ and their symmetry classifications.

These stereoisomers cannot be separated due to the fast intramolecular isomerization process. However, the infrared spectra show bands due to the various stereoisomers, thus

setting an upper limit on the frequency of exchange. *Haas* and *Sheline*[11] made a band assignment for the CP stretching region based on force constant calculations (Table 1) and computed the mole fractions x_i of the isomers which are present at room temperature. The statistical populations a_{ax} and a_{eq} from Eq. (3) can easily be expressed in terms of these mole fractions. For $Fe(CO)_3(PF_3)_2$, *e.g.*, we obtain[*]

$$a_{ax} = 0.67\,X_{C_{2v}} + 0.33\,X_{C_s}$$
$$a_{eq} = X_{D_{3h}} + 0.33\,X_{C_{2v}} + 0.67\,X_{C_s} \qquad (7)$$

By measuring variable temperature infrared spectra for the compounds with $x=1$ up to $x=4$, a whole set of weighting factors a_{ax} and a_{eq} can be calculated. If time-averaged chemical shifts are determined for corresponding temperatures and compounds, a heavily overdetermined system of equations is obtained.

the NMR parameters, the chemical shifts as well as the spin-spin coupling constants, are time averaged and an overdetermined system of equations results which yields the true coupling constants and chemical shifts of the system which it would display in the absence of exchange.

The weighting factors are usually given by the mole fractions (or functions of the mole fractions) of the various possible stereoisomers. They are easily deduced from Fig. 1. So far we have only discussed variable temperature IR spectroscopy for the determination of the mole fractions x_i. This proves suitable as long as the exchange frequency is much slower than the IR line splitting $\Delta\nu$. Under these conditions the IR spectra display distinct species "in the absence of exchange". An alternative would be to study the Raman spectra. The selection rules of IR and Raman spectroscopy are different; consequently, the observation of both spectra offers an additional independent way for the determination of the x_i.

Table 1. Mole fractions for the different isomers of $Fe(CO)_5$ and $Fe(CO)_x(PF_3)_{5-x}$ at 25 °C.

Compound	Symmetry	Mole Fraction [%]	Frequency [cm^{-1}]
$Fe(CO)_5$	D_{3h}	100	2000
			2025
ax-$Fe(CO)_4PF_3$	C_{3v}	33	1993
			2092
eq-$Fe(CO)_4PF_3$	C_{2v}	67	2018
			1999
			2101
			2022
trans-$Fe(CO)_3(PF_3)_2$	D_{3h}	20.9	1986
			2059
cis-$Fe(CO)_3(PF_3)_2$	C_s	28.1	1992
			2071
			2019
vic-$Fe(CO)_3(PF_3)_2$	C_{2v}	51	2012
			2081
			2011
trans-$Fe(CO)_2(PF_3)_3$	D_{3h}	51	2006
cis-$Fe(CO)_2(PF_3)_3$	C_s	23.5	2052
			2006
vic-$Fe(CO)_2(PF_3)_3$	C_{2v}	25.5	1985
			2034
ax-$Fe(CO)(PF_3)_4$	C_{3v}	50	2037
eq-$Fe(CO)(PF_3)_4$	C_{2v}	50	2008

The observed coupling constants $\langle J_{CP}\rangle$ can be explained by using the experimentally determined mole fractions together with a set of coupling constants, J_{CP}^{trans}, J_{CP}^{vic} and J_{CP}^{cis}. For example, we would write for the compound with $x=3$ (cf. Fig. 1):

$$\langle J_{CP}\rangle = \tfrac{1}{6}[6\,X_{D_{3h}}J_{CP}^{cis} + X_{C_{2v}}(4J_{CP}^{cis} + 2J_{CP}^{vic}) + X_{C_s}(J_{CP}^{trans} + 2J_{CP}^{vic} + 3J_{CP}^{cis})] \qquad (8)$$

Likewise, we write for the phosphorus-phosphorus spin-spin coupling constants $\langle J_{PP}\rangle$ of the compound $Fe(CO)_3(PF_3)_2$ (Fig. 1):

$$\langle J_{PP'}\rangle = X_{D_{3h}}J_{PP'}^{trans} + X_{C_{2v}}J_{PP'}^{vic} + X_{C_s}J_{PP'}^{cis} \qquad (9)$$

Similar relationships can be written for all compounds with $x=1$—4 and all observed coupling constants. The $\langle J_{CP}\rangle$ coupling constants are obtained from ^{13}C-NMR spectra, whereas the $\langle J_{PP'}\rangle$, $\langle J_{FF'}\rangle$, $\langle J_{PF'}\rangle$ and $\langle J_{PF}\rangle$ coupling constants are obtained from ^{31}P- or ^{19}F-NMR spectra[12]. All

The observed ^{13}C chemical shifts are shown in Figure 2 as a function of temperature. A strong temperature effect is observed for both $Fe(CO)_3(PF_3)_2$ and $Fe(CO)_2(PF_3)_3$,

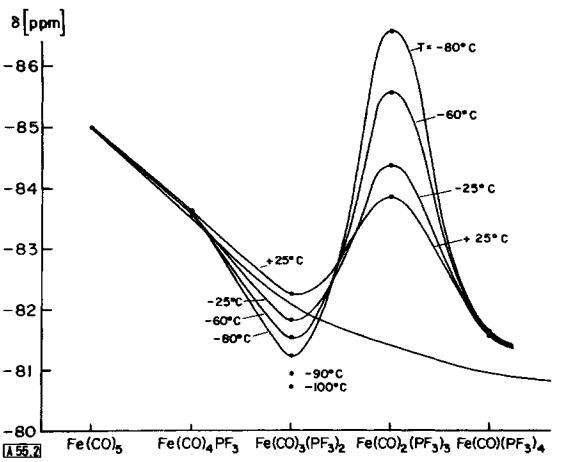


Fig. 2. ^{13}C chemical shift for the compounds $Fe(CO)_x(PF_3)_{5-x}$ as a function of temperature.

[*] It should be noted that, here, point groups are obtained by regarding the PF_3 groups as a single point. Thus, one structure of $Fe(CO)_3(PF_3)_2$ is the trigonal bipyramidal with point group D_{3h}. Obviously, the actual point group is "pseudo D_{3h}". This same simplification applies to other structures but does not affect the symmetry arguments.

whereas the remaining compounds of the series show at most a very small temperature dependence.

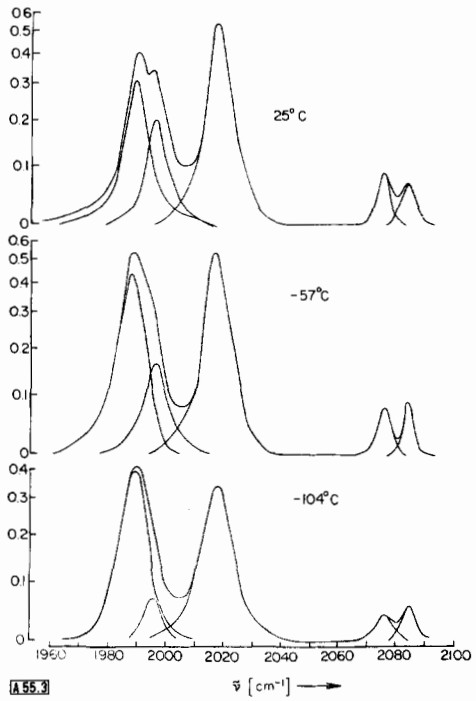


Fig. 3. IR spectra of $Fe(CO)_3(PF_3)_2$ at three different temperatures.

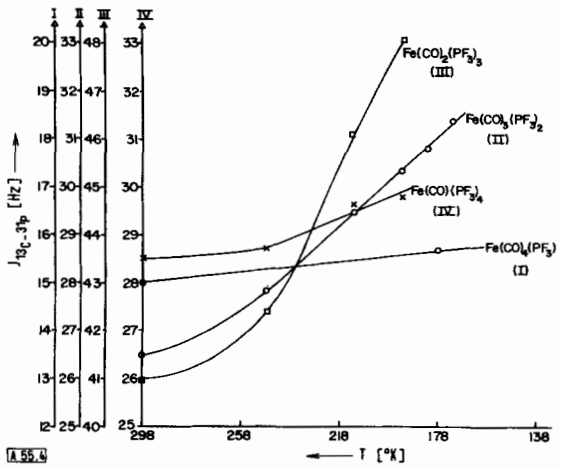


Fig. 4. Observed carbon-phosphorus spin-spin coupling constant $\langle J_{CP} \rangle$ as a function of temperature for the compounds $Fe(CO)_x(PF_3)_{5-x}$.

An analogous temperature effect is inferred from the IR data (cf. Fig. 3) and the $^{13}C-{}^{31}P$ spin-spin coupling constants (Fig. 4). The tendency appears to be the same for the $^{31}P-{}^{31}P$ spin-spin coupling constant $\langle J_{PP'} \rangle$. However, the magnitude of its increase with decreasing temperature is reversed, the biggest change being observed for $Fe(CO)_3(PF_3)_2$ followed by $Fe(CO)_2(PF_3)_3$. This was explained as resulting from different signs for the *trans*, *vic* and *cis* coupling constants of $^2J_{PP'}$[12, 13]. Indeed, a careful analysis using Eq. (9) of the coupling constant $\langle {}^2J_{PP'} \rangle$ in the nonrigid complexes belonging to the series $Fe(CO)_x(PF_3)_{5-x}$ reveals that an angular correlation function exists for $^2J_{PP'}$; in contrast to the normal NMR analysis for the $AA'X_3X'_3$ or $AA'A''X_3X'_3X''_3$ systems, one thus obtains relative signs of the coupling constants $^2J_{PP'}$[1, 14]. The discrepancy which appears to exist between the magnitudes of the coupling constants $^2J_{CP}$ and $^2J_{PP}$ in the case of $Fe(CO)_2(PF_3)_3$ and $Fe(CO)_3(PF_3)_2$ can be explained by inspection of Figures 5 and 6. It is immediately clear for both compounds that the D_{3h} structure is most stable followed by the C_{2v} and C_s structures, respectively. For the observed carbon phosphorus coupling constant this means that the weighting factors of J_{CP}^{trans} and J_{CP}^{vic} decrease in favor of J_{CP}^{cis}. Both changes have an additive effect on $\langle J_{CP} \rangle$. On the other hand, it means for $^2J_{PP'}$ that the weighting factor for $^2J_{PP'}^{vic}$ increases while those of $^2J_{PP'}^{trans}$ and $^2J_{PP'}^{cis}$ decrease. The disappearance of $^2J_{PP'}^{trans}$ in favor of $^2J_{PP'}^{vic}$ would cause the observed coupling constant $\langle J_{PP'} \rangle$ of $Fe(CO)_2(PF_3)_3$ to decrease in magnitude whereas the disappearance of $^2J_{PP'}^{cis}$ from equilibrium causes $\langle J_{PP'} \rangle$ to increase. Thus both changes almost cancel, resulting in only a small net change on the observed $\langle J_{PP'} \rangle$.

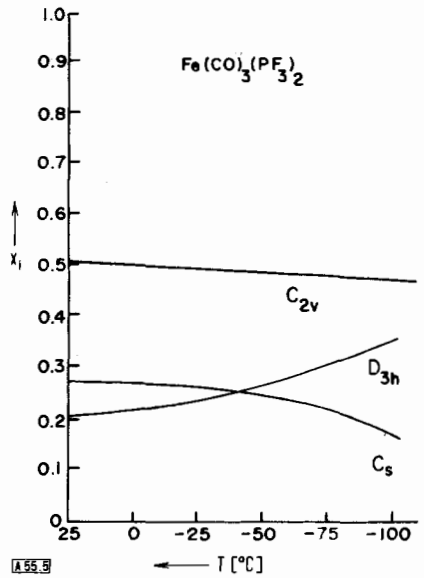


Fig. 5. Mole fractions of the stereoisomers of $Fe(CO)_3(PF_3)_2$ as a function of temperature.

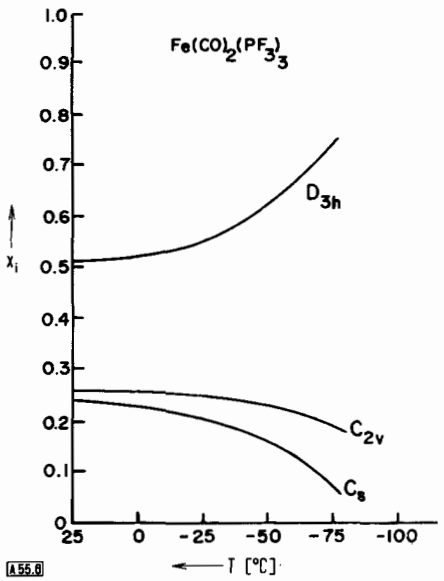


Fig. 6. Mole fractions of the stereoisomers of $Fe(CO)_2(PF_3)_3$ as a function of temperature.

The fact that spin-spin coupling constants can have different signs makes their use more difficult for studying nonrigid structures. If no effect is observed on changing the temperature,

it need not necessarily imply that the system is rigid; rather this could be due to a compensation of temperature effects. Therefore, it is of great importance, if a quantitative understanding of the variable temperature effect on NMR spectra of nonrigid systems is attempted, to study simultaneously the temperature effect on such parameters as the chemical shift and mole fractions obtainable from IR or Raman spectra.

Since the IR bands of the different stereoisomers (Fig. 1) in the CO stretching region are partially superimposed, a band stripping analysis was used to compute the band areas for the various overlapping bands (band analysis with Lorentzian curves (cf. Fig. 3).

The band assignment of the various stereoisomers can be tested from the temperature dependence of the IR spectra. Beer's law demands that the absorption area of a band due to one particular stereoisomer is proportional to its concentration in the mixture. Therefore, if the areas of two bands belonging to the same stereoisomer are plotted against each other, the resulting curve should be a straight line running through the origin of the coordinate system with a slope equal to the ratio of the extinction coefficients of the two bands. This method allows the assignment of pairs of bands belonging to the same stereoisomer. Consider for example the IR stretching region for the compound $Fe(CO)_3(PF_3)_2$ (Fig. 3). This figure clearly indicates that the bands at 2073 and 1993 cm^{-1} belong to the same isomer, as also the bands at 2081 and 2012 cm^{-1}. The remaining band at 1987 cm^{-1} can then be assigned immediately to the D_{3h} species, since this is the only symmetry species considered with a single allowed absorption band in the CO stretching region. This method cannot, however, differentiate between C_{2v} and C_s assignments for the two pairs of bands. This differentiation can be accomplished using the NMR data.

The temperature dependent IR spectra allow us to compute the mole fractions of the different stereoisomers in the mixture at each temperature[11]. The results for $Fe(CO)_3(PF_3)_2$ and $Fe(CO)_2(PF_3)_3$ are summarized in Figures 5 and 6. These mole fractions were inserted into Eq. (7) and yielded the statistical weighting factors a_{ax} and a_{eq} for each compound and temperature.

From the NMR studies, we obtain time-averaged chemical shifts for the various compounds at different temperatures. These, together with the corresponding statistical weighting factors a_{ax} and a_{eq} are used to determine $\delta\sigma^0=|\sigma^0_{ax}-\sigma^0_{eq}|$ employing Eq. (3). In the case of $Fe(CO)_2(PF_3)_3$, a temperature shift of 2.8 ppm was observed between +25 °C and −80 °C. This temperature shift yields $\delta\sigma^0=17.7$ ppm. Since we are dealing with an overdetermined system, we can calculate a mean value for $\delta\sigma^0$ as well as error limits: $\delta\sigma^0 = 17.7 \pm 1.5$ ppm. If this result is inserted in Eq. (5) we obtain for the mean lifetime $\tau_e=9.02\times10^{-11}$ s, which corresponds to an exchange frequency $\nu_e=1.1\times10^{10}\,s^{-1}$ at −20 °C. The accuracy in the measurement of T_2 almost entirely determines the error limit on ν_e. τ_e and ν_e are determined only as limits due to the theory on T_2-measurements. Thus we determined for τ_e an upper limit and for ν_e a lower limit.

By using Eq. (3) we not only obtain $\delta\sigma^0$ but also the magnitudes of the chemical shifts σ^0_{ax} and σ^0_{eq} individually. For $Fe(CO)_5$ we get $\sigma^0_{ax}=-95.6$, and $\sigma^0_{eq}=-77.9$ ppm, relative to benzene. This result has been interpreted as resulting from a greater amount of π back-bonding in the axial position as compared to the equatorial position[15].

3. Interpretation of Findings and Outlook

The flipping frequency, ν_e, of $1.1\times10^{10}\,s^{-1}$ is unexpectedly fast. In addition to determining the flipping frequency, other goals of such measurements are to find a mechanism for the exchange and to determine the energy barrier hindering the intramolecular ligand exchange. Determining the energy barrier E_a is usually achieved by variable temperature measurements of ν_e since according to the Arrhenius equation [Eq. (2)] a plot $\ln k$ *vs* $1/T$ yields E_a. In this case the rate of exchange ν_e corresponds to the rate of reaction k. The temperature range over which values of ν_e may be determined for $Fe(CO)_5$ is severely limited, since pentacarbonyliron freezes at −21 °C[10]. If one of the two unknowns in Eq. (2), ν_e^0 and E_a, can be estimated by an independent method the other can be calculated from a single measurement of ν_e. Therefore we want to try to estimate the magnitude of the frequency factor ν_e^0 by considering possible reaction paths.

The rapid intramolecular ligand exchange determined for $Fe(CO)_5$ has been observed in a great number of trigonal bipyramidal molecules, although the nature of the chemical bond in them varies considerably. One of the well studied examples is PF_5; indeed, all five coordinated phosphorus compounds show this phenomenon. Consequently, the most important feature appears to be geometry. According to *Gillespie*[16], the electron pair repulsion potential in five coordinated compounds is equally well minimized in either a trigonal bipyramid or a tetragonal pyramid; neither is energetically favored. By far the most stable configurations for tetra- or hexacoordinated compounds are the tetrahedron and octahedron, respectively. Both of these geometrical forms belong to a higher symmetry group, namely T_d and O_h, than either the trigonal bipyramid or the tetragonal pyramid which belong to the D_{3h} and C_{4v} groups, respectively. Therefore, one can consider the C_{4v} and D_{3h} structures as geometrical transition states with respect to the T_d or O_h structures. For example, the tendency to achieve either the octahedral or tetrahedral configuration is observed in PCl_5, which dissociates in the solid state:

$$2\,PCl_5 \rightarrow PCl_4^+ + PCl_6^-. \qquad (10)$$

However, in determining the stability, geometrical considerations are not as important as electronic considerations. In the case of metal carbonyls the most decisive factor is the "noble gas" rule. According to this rule, iron as a 3d transition metal tends to achieve the krypton shell. Since in the coordinate bond between CO and iron two electrons are contributed by each CO ligand group, iron(0) needs five CO groups in a mononuclear carbonyl in order to achieve the required 36 electrons of the krypton shell together with its own 26 electrons.

We will now attempt to describe the inversion process in $Fe(CO)_5$ by using a diffusion model involving a Schottky defect in conjunction with the symmetry considerations just presented and the Berry mechanism. Let us consider a layer of a crystal lattice with a Schottky defect. Diffusion of a vacancy occurs through the motion of an adjacent atom along a normal coordinate (diffusion coordinate). The probability that an adjacent atom will pass over a potential barrier ΔE is proportional to $\exp(-E_a/kT)$. If ν_0 is the characteristic

vibrational frequency corresponding to the diffusion coordinate, then the probability of a migration jump is, according to the Arrhenius equation

$$P = \nu_0 \exp[-E_a/kT] \qquad (11)$$

The probability P is called the jump frequency. The frequency factor ν_0 is a vibrational frequency in the IR region (10^{12} to 10^{14} Hz). In analogy with this diffusion model, we consider the C_{4v} structure as an octahedron with a Schottky defect, a vacancy. Similarly, the D_{3h} structure can be considered as a tetrahedron with a defect, in this case a superfluous ligand.

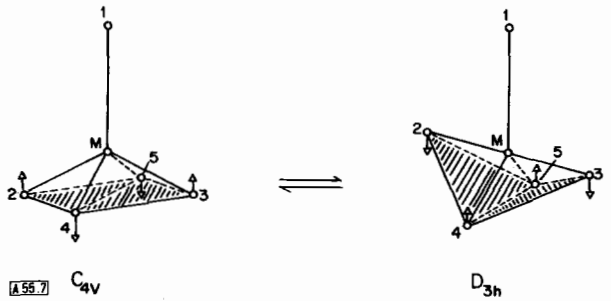


Fig. 7. "Berry-mechanism" for the ligand exchange in trigonal bipyramidal molecules using the C_{4v} and D_{3h} structures as transition states.

The Berry mechanism is presented in Fig. 7. A diffusion coordinate along which the octahedral vacancy in the C_{4v} structure can be filled, must be sought among the normal coordinates of the D_{3h} structure (Fig. 8). Previous investigations have failed to find a normal coordinate corresponding to the path of the Berry mechanism[17]. Since, however, a linear combination of normal modes again yields normal modes, we note that the normal coordinate corresponding to the combination $|\nu_6(E')-\nu_7(E')|$ yields the required diffusion path. Such a combination is usually called a beat frequency and we therefore call the resulting mechanism a beat mechanism. The combination $\nu_6(E')+\nu_7(E')$ results in distorted transition states (cf. Fig. 9) and is therefore excluded from our discussion.

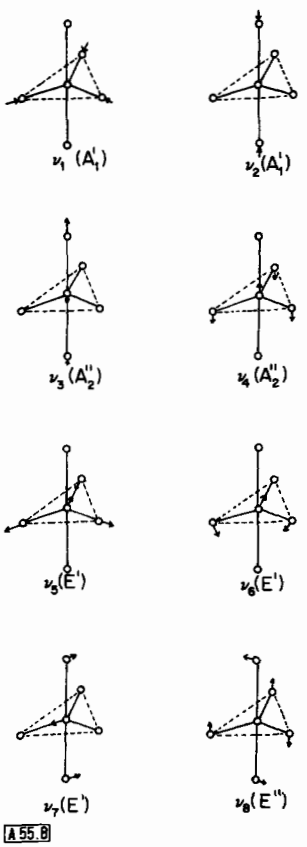


Fig. 8. Normal modes of vibration for the D_{3h} structure.

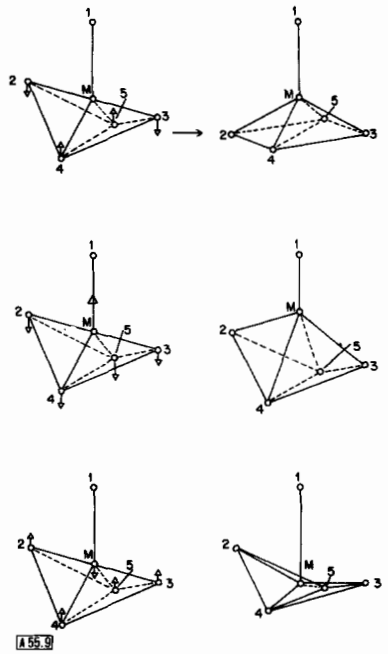


Fig. 9. Linear combination $\nu_6 \pm \nu_7$ of the D_{3h} structure leading to the transition states indicated on the right hand side of the figure. The (+)-combination leads to distorted high energy transition states, whereas the (−)-combination leads to the highly symmetrical and stable C_{4v} structure.

A diffusion coordinate for the transition $C_{4v} \rightarrow D_{3h}$ can be found if we examine the normal coordinates of the C_{4v} structure (Fig. 10): According to the correlation diagram in Fig. 11,

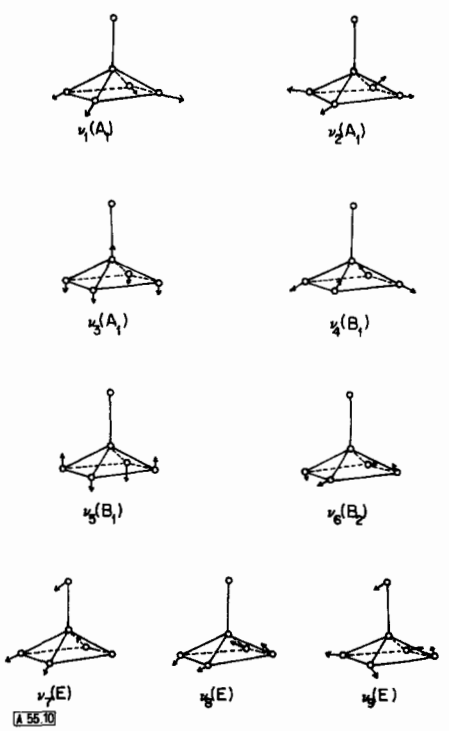


Fig. 10. Normal modes of vibration for the C_{4v} structure.

$\nu_5(B_1)$ of the C_{4v} structure connects with both $\nu_6(E')$ and $\nu_7(E')$ of the D_{3h} structure under angular distortion.

The relative values for $\nu_6(E')$ and $\nu_7(E')$ will differ in the general case. We assign the one with the lower frequency as ν_7, since the axial bending should occur easier than the equatorial bending. There is 120° between next neighbors in the equatorial plane compared to 180° in the axial plane. Symmetry demands that both frequencies become equal only under the C_{4v} "distortion". An identity of both frequencies anywhere else would be an accidental degeneracy and is indicated in Fig. 11 with the dashed horizontal line.

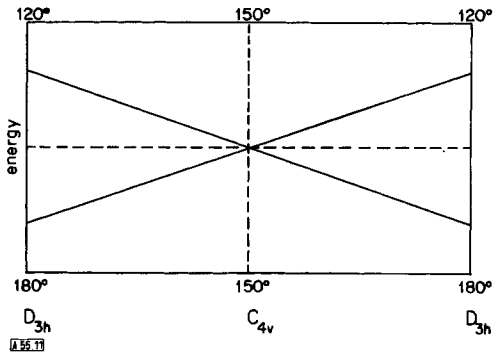


Fig. 11. Energy correlation diagram of angular distortion between $\nu_5(B_1)$ which corresponds to the C_{4v} structure and $\nu_6(E')$ and $\nu_7(E')$ which correspond to the D_{3h} structure.

As mentioned above the inversion frequency for the process $C_{4v}-D_{3h}$ can be described by an Arrhenius-type equation

$$1/\tau_{C_{4v}} = \nu_{C_{4v}\rightarrow D_{3h}} = \nu_5(B_1)\exp(-\Delta E_1/kT). \quad (12)$$

Similarly

$$1/\tau_{D_{3h}} = \nu_{D_{3h}\rightarrow C_{4v}} = \nu_{beat}(E')\exp(-\Delta E_2/kT) \quad (13)$$

where $\tau_{C_{4v}}$, $\tau_{D_{3h}}$ are the mean lifetimes of the C_{4v} and D_{3h} structures, respectively. A complete normal coordinate analysis of $Fe(CO)_5$ under the assumption of a D_{3h} structure has been carried out[18]. In that study $Fe(CO)_5$ was treated like a rigid molecule and the fact that it should also exhibit the C_{4v} structure was totally disregarded. Consequently, there exists the possibility that weak bands which were explained as combination bands or overtones are really due to the C_{4v} structure resulting in a possible misassignment. Nevertheless, we take ν_{beat} from these published results. The two bands considered here are calculated to be at 97 and 104 cm^{-1}, respectively. Consequently, we take ν_{beat} as 7 cm^{-1}. According to the correlation diagram (Fig. 11), $\nu_5(B_1)$ for the C_{4v} structure could be approximated as the average of these two frequencies. Therefore, $\nu_5(B_1)=100\,cm^{-1}$. Since the IR spectrum shows only the D_{3h} structure, we can write for the ratio of the concentrations of the two structural stereoisomers

$$C_{D_{3h}} \gg C_{C_{4v}} \quad (14)$$

Therefore, we conclude that the following relation holds for the corresponding lifetimes

$$\tau_{D_{3h}} \gg \tau_{C_{4v}} \quad (15)$$

The exchange frequency for the overall ligand inversion process for the D_{3h} structure is given by

$$1/\tau_e = \nu_e = \nu_{beat}/2\exp[-\Delta E_2/kT]. \quad (16)$$

The factor $^1/_2$ arises from the fact that the NMR cannot register an exchange between indistinguishable sites. From symmetry considerations we conclude that only half of all exchanges occur between distinguishable sites (Fig. 7). If we insert the experimentally determined ligand exchange frequency of $1.1\times10^{10}\,s^{-1}$ and the estimated value for ν_{beat}, we obtain for the energy barrier $\Delta E_2 = 7.8\cdot10^{-14}$ erg/mol = 1.13 kcal/mol.

Since the NMR experiment can only determine an upper limit for τ_e and a lower limit for ν_e, the calculated height of the energy barrier should be considered as the maximal possible value, *i.e.* $0\leqslant\Delta E_2\leqslant1.13$ kcal/mol. For the ligand exchange frequency in $Fe(CO)_5$ this means: $0.67\leqslant\nu_e\leqslant7.0$ cm^{-1}. For the exchange frequency between the C_{4v} and D_{3h} structures we find for $\Delta E = 0$ and $\Delta E = 1.13$ kcal/mol: $10.7\leqslant\nu_e\leqslant100\,cm^{-1}$.

This frequency is thus at least 14 times faster than the corresponding frequency for the $D_{3h}\rightarrow C_{4v}$ inversion. This is the reason why the IR spectrum shows only normal modes which are due to the D_{3h} structure. The "combination" or "overtones"[18], however, might possibly be explained as normal modes of the C_{4v} structure. These results are clearly consistent with the observation of a sharp IR spectrum for the D_{3h} structure and a time-averaged NMR spectrum, since the maximal exchange frequency is still small compared to the line splitting of 25 cm^{-1} in the CO stretching region (cf. Section 1) and on the other hand the activation energy is too small to slow it down considerably within the experimentally covered temperature range. The lifetimes of the C_{4v} structure are expected to be much shorter. Consequently, its IR spectrum is expected to be partly time-averaged but much weaker.

With time-averaging the number of lines actually observed is smaller than the number of lines deduced from group theory. Another effect of fast exchange for the IR spectra is "inversion splitting", first studied for the NH_3 molecule[19]. By far the most pronounced splitting has been found for the symmetrical bending mode of the ammonia molecule. The obvious reason is that the exchange coordinate is closely related to the normal coordinate of this vibrational mode. For $Fe(CO)_5$, the exchange occurs along an angular coordinate about the iron atom. Therefore, we expect inversion splittings to be important only for bending modes. For CO stretching modes we expect only time-averaging effects. Whereas time-averaging reduces the number of bands, "inversion splitting" increases the number of bands relative to the "no exchange" case.

This has a considerable impact on the matrix isolation technique where metal atoms are cocondensed at 4 °K together with CO gas diluted with Ar, resulting in the production of metal carbonyls and their fragments $M(CO)_x$, where $x = 1, 2, \ldots, n$. These species are usually identified by their IR spectra in the CO stretching region[20]. For the band assignment, the various species are treated as rigid, and group theory is applied in order to predict the number of lines due to a particular molecular fragment. As has been proven for NH_2, a molecular fragment of the ammonia molecule, this technique of band assignment becomes questionable. In its electronic ground state, NH_2 is a bent molecule (C_{2v}) and it behaves in this manner in electronic spectroscopy[21]. Relative to the much slower EPR and IR spectroscopy, how-

ever, it behaves like a linear molecule ($D_{\infty h}$), which is the average of two bent configurations[22]. Indeed, the ESR spectrum of NH_2 even at 4°K results from a "linear" molecule of symmetry $D_{\infty h}$. Similar ideas apply to $M(CO)_2$, where M is a transition metal, lanthanoid or actinoid. The molecular fragment $M(CO)_2$ would usually be expected to be bent (C_{2v})[20]. A fast pseudorotation of the fragment would display a linear configuration ($D_{\infty h}$). The C_{2v} structure would have two bands in the CO stretching region whereas the $D_{\infty h}$ species has only one band. Thus a method of band assignment, which depends importantly on the number of bands, could be misleading when the flipping frequency is fast enough. This study suggests then that a considerable amount of work is needed, possibly including measurement of flipping frequencies, to assure the correct band assignments for lanthanoid and actinoid carbonyls[20].

The surprisingly fast ligand exchange frequency determined for $Fe(CO)_5$ could also help to understand better the IR spectra of $M(CO)_5$ binary carbonyls (where M = Cr, Mo and W)[23]. The species initially prepared by the matrix-photolysis of the appropriate hexacarbonyls was believed to display the C_{4v} structure. The C_{4v} structure displays three bands in the CO stretching region and this was in fact observed. After warming the solid matrix to −170°C, the IR spectra showed only two bands, which were interpreted as being due to the D_{3h} structure. The surprisingly fast exchange which has been established for solid $Fe(CO)_5$ down to helium temperature throws doubt on the interpretation of the observed IR spectra. If ν_e is of the same order of magnitude in the group VIb pentacarbonyls as was found for $Fe(CO)_5$, then the observation of a C_{4v}-species between −196 and −170°C should be impossible. The $M(CO)_5$ photolysis fragments offer an opportunity for the formation of a relatively unstable complex, possibly with the solvent or N_2, at these low temperatures. Such a complex $M(CO)_5X$ would of course make impossible a ligand exchange process following the same type of beat mechanism formulated for $Fe(CO)_5$ in this study. If this complex decomposes, however, at slightly higher temperatures, the flip occurs instantly and what the CO stretching region shows, as in the case of $Fe(CO)_5$, is the D_{3h} structure.

The mean lifetime considered here can be compared to an angular correlation time which was measured for both $Ni(CO)_4$ and $Fe(CO)_5$[10]. The angular correlation time describes the angular reorientation of the entire molecule and is intimately related to the viscosity of a liquid. This reorientation is a random motion, whereas the mean lifetime τ_e is an angular correlation time for the intramolecular angular reorientation of ligand groups around the metal center and occurs only along well defined exchange paths. It is interesting to note that the frequencies and activation energies for both processes are of the same order of magnitude[10]. There appears to be little or no restriction for the angular motion of the ligands around the metal center although a strong interaction exists in the radical direction. Free movement of ligands presupposes an angular mobility of the binding electrons. The electrons occupy "delocalized" orbitals. They are certainly not as mobile as metal electrons in the bulk metal, but the small magnitude of the energy barrier hindering angular motion makes electron "tunneling" a very plausible process. One of the two binding electrons of a CO group may tunnel through a barrier to the adjacent equilibrium position forming a short-lived "bridging carbonyl". The noble gas rule will certainly not be violated. The tunneling of the second electron completes the formation of the C_{4v} structure. The mobility of the binding electrons was previously postulated for metal carbonyls and is consistent with many experimental observations[24].

Very recently, exchange frequencies have also been determined for solid $Fe(CO)_5$ down to helium temperature[25]. The exchange frequencies in the solid are also surprisingly fast (*ca.* 10^4 Hz) and show little temperature dependence. A plot of $\ln \nu_e$ *vs* $1/T$ yields an activation energy ΔE_2 of ≈ 0.9 kcal/mol, which is very similar to the value $0 \leqslant \Delta E_2 \leqslant 1.13$ kcal/mol determined in the measurements described here. This comparison lends strength to both measurements and suggests the existence of a similar very low energy barrier to intramolecular exchange for $Fe(CO)_5$ in both solid and liquid states.

Thanks are due to Dr. R. J. Clark and Dr. H. W. Spiess for many discussions concerning this problem and for carefully reviewing part of the arguments used in this manuscript.

Received: May 15, 1974 [A 55 IE]
German version: Angew. Chem. 87, 337 (1975)

[1] *J. W. Emsley, J. Feeney,* and *L. H. Sutcliffe:* High Resolution Nuclear Magnetic Resonance Spectroscopy, Vol. 1. Pergamon Press, London 1967.
[2] *H. Mahnke, R. J. Clark, R. Rosanske,* and *R. K. Sheline,* J. Chem. Phys. *60,* 2997 (1974).
[3] *F. A. Cotton, L. Kunczynski, B. L. Shapino,* and *L. F. Johnson,* J. Amer. Chem. Soc. *94,* 6191 (1972).
[4] *K. Noack,* Spectrochim. Acta *19,* 1925 (1963).
[5] *G. Bor,* Spectrochim. Acta *19,* 2065 (1963).
[6] *F. A. Cotton, A. Danti, J. S. Waugh,* and *R. W. Fessenden,* J. Chem. Phys. *29,* 1427 (1958).
[7] *R. Bramley, B. N. Figgis,* and *R. S. Nyholm,* Trans. Faraday Soc. *58,* 1893 (1962).
[8] *T. C. Farrar* and *E. D. Becker:* Pulse and Fourier Transform NMR: Introduction to Theory and Methods. Academic Press, New York 1971.
[9] *M. I. Davis* and *H. P. Hanson,* J. Phys. Chem. *69,* 3405 (1965).
[10] *H. W. Spiess* and *H. Mahnke,* Ber. Bunsenges. Phys. Chem. *76,* 990 (1972).
[11] *H. Haas* and *R. K. Sheline,* J. Chem. Phys. *47,* 2996 (1967).
[12] *H. Mahnke, R. J. Clark,* and *R. K. Sheline,* unpublished.
[13] *H. Mahnke,* Dissertation, Florida State University 1974.
[14] *R. K. Harris,* Can. J. Chem. *42,* 2275 (1964).
[15] *H. Mahnke, R. K. Sheline,* and *H. W. Spiess,* J. Chem. Phys. *61,* 55 (1974).
[16] *R. J. Gillespie* and *R. S. Nyholm,* Quart. Rev. Chem. Soc. *11,* 339 (1957).
[17] *L. C. Hoskins* and *R. C. Lord,* J. Chem. Phys. *46,* 2402 (1967).
[18] *L. H. Jones, R. S. McDowell, M. Goldblatt,* and *B. I. Swanson,* J. Chem. Phys. *57,* 2050 (1972).
[19] *W. J. Jones* in: Infrared Spectroscopy and Molecular Structure. Elsevier, Amsterdam 1963.
[20] *R. K. Sheline* and *J. L. Slater,* Angew. Chem. *87,* 332 (1975); Angew. Chem. internat. Edit. *14,* 309 (1975).
[21] *D. A. Ramsey,* Ann. N. Y. Acad. Sci. *67,* 485 (1957).
[22] *H. M. McConnell,* J. Chem. Phys. *29,* 1422 (1958).
[23] *I. W. Stoltz, G. R. Dobson,* and *R. K. Sheline,* J. Amer. Chem. Soc. *84,* 3589 (1962); *85,* 1013 (1963).
[24] *H. Haas,* Dissertation, Florida State University 1965.
[25] *H. W. Spiess* and coworkers, to be published.

Sulfur Atoms as Ligands in Metal Complexes

By Heinrich Vahrenkamp[*]

Dedicated to Professor Helmut Behrens on the occasion of his 60th birthday

The types of sulfur bonding—as sulfane or sulfide—encountered in the molecules of main-group elements are almost unknown in the chemistry of metal complexes, where the sulfur atoms function instead as two-electron donors by bridging two metal atoms, as four-electron donors by bridging three or four metal atoms, or as six-electron donors by incorporation between four metal atoms. In such complexes, the metal-metal bond can be modified over a wide range by chemical or electrochemical variation of the number of electrons present. The readiness with which polynuclear complexes containing metals and sulfur undergo redox reactions is also utilized by Nature in the active sites of some redox proteins.

1. Introduction

Transition metals and sulfur have an "affinity" for one another, as is discovered by every young chemist when willingly or unwillingly he meets the precipitation of metal sulfides. This also explains why combinations of d-elements with unsubstituted sulfur were known until recently almost exclusively in the form of the metal sulfides. The strong tendency for the formation of sulfidic solids follows from a qualitative picture of bonding. It can be seen most readily in the Pearson acid-base scale[1] where d^n-transition metal ions and sulfide ions are both classed as "soft" groups. Finer details include covalence contributions to, and back-bonding effects in, the metal-sulfur bond and the possibility of metal-metal interactions in sulfide structures[2].

Soluble metal complexes with unsubstituted sulfur as ligand are comparatively rare, however, since they also tend to revert to binary sulfides. Modern transition-metal chemistry with its possibilities for the stabilization of unusual bonding systems first provided a sufficient number of such complexes to justify a review article. Interest in these compounds is topical and their investigation has been stimulated by three factors: 1) The observation that the formation and catalytic activity of metal carbonyls are influenced, sometimes for the better, by sulfur impurities[3]; 2) the broad development of structural chemistry for the polynuclear metal-sulfur complexes[4]; and 3) the discovery that some redox-proteins contain transition-metal ions and "labile" sulfur in their active sites and that this sulfur can be liberated as H_2S by acids[5].

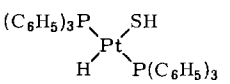
This review is an attempt to classify the known metal-sulfur complexes according to their structural chemistry, to discuss their synthesis and reactivity, and to present the most recent findings pertaining to their biochemical significance. Thiometalates of d^0-transition metals[6] and the incorporation of metals in sulfur rings[7] will not be considered since both topics have recently been surveyed elsewhere.

2. Structural Chemistry of the Complexes

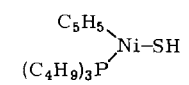
The analogy between oxygen and sulfur no longer holds in transition-metal chemistry. This is shown by the differing structures of oxides and sulfides and by the contrast between the large number of transition-metal aqua ions and the very few complexes with H_2S as the ligand[8, 9]; compound *(1)* is the sole recorded complex that has some degree of stability at room temperature[10]. Similarly, few complexes containing the SH group have been reported; *(2)*[11], *(3)*[12], and *(4)*[13] are the only known complexes containing terminal hydrogensulfide groups.

$C_5H_5(CO)_2Mn{-}SH_2$ *(1)*

$C_5H_5(CO)_3W{-}SH$ *(2)*

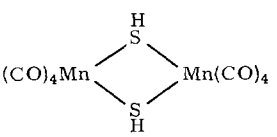


(3)

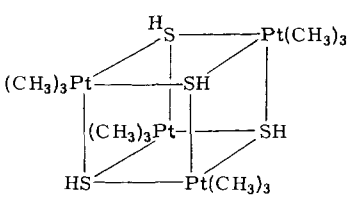


(4)

Even compounds with bridging SH groups, in which the reactivity of the sulfur has been reduced by coordination of its lone pairs, are hardly known; in $[(CO)_4Mn{-}SH]_2$ *(5)*[14] one lone pair on each sulfur atom is blocked, and in $[(CH_3)_3Pt{-}SH]_4$ *(6)*[15] both are blocked.



(5)



(6)

And yet even these complexes can decompose to form metal sulfides. Such decomposition is prevented only when the sulfur-containing ligand is present as an organic sulfur compound. Accordingly, numerous organosulfur complexes of the transition metals are known to exist[16, 17].

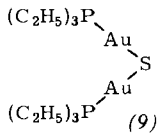
2.1. Metallosulfanes and Molecular Metal Sulfides

The situation for the simplest of sulfur complexes resembles that for the SH complexes: single metal-sulfur bonds do not suffice for stabilization against decomposition. Thus, compounds such as sulfanes of type *(7)* and sulfides of type *(8)* are hardly known in transition-metal chemistry, although they are normal in the main-group chemistry of sulfur.

[*] Prof. Dr. H. Vahrenkamp
Chemisches Laboratorium der Universität
78 Freiburg, Albertstrasse 21 (Germany)

$L_nM{-}S{-}ML_n$ (7) $L_nM{=}S$ (8) L = ligand, M = transition metal

They are found almost exclusively with d^{10}- and d^0-metals[6]; two proven examples are *(9)*[18] and *(10)*[19].



(9)

$Cl_4W{=}S$ *(10)*

The only reported example of such simple complexes in which the d-shell is neither filled nor empty is *(11)*[20].

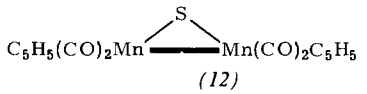
$[(CN)_5\overset{III}{C}o{-}S{-}S{-}\overset{III}{C}o(CN)_5]^{6-}$ *(11)*

Complex *(10)* and the numerous thiometalates of the d^0-species occupy a special position, insofar as the absence of d-electrons in these species (*e.g.* V^V, Mo^{VI}, Re^{VII}) precludes their behaving as typical transition elements but renders them more like main-group elements[6]. Furthermore, the metals cannot be regarded as soft acids in their high oxidation states.

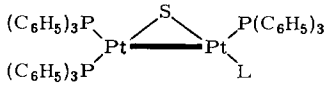
In the metallosulfanes *(7)* and sulfides *(8)* the sulfur behaves as a one- or two-electron donor toward the metal atoms. Its lone pairs are unused and reactive. This is probably the reason for the instability of other complexes of this type. Isolable complexes are obtained by surrounding the metal atom with π-acceptor ligands and by raising the coordination number of the sulfur and of the metal; the former measure implies resorting to the stabilizing principles of organometallic chemistry and the latter implies formation of polynuclear complexes, *i.e.* the occurrence of clusters, and thus an approximation to the stable state of solid metal sulfides.

2.2. Bridging Sulfur Atoms as Two-Electron Donors

The above concepts are implemented most readily in binuclear complexes in which a bridging sulfur atom spans a metal-metal bond to form an M_2S triangle. This triangle is also the simplest section from the lattice of a metal sulfide, *e.g.* the NiAs lattice; it occurs in the manganese complex *(12)*[21] and in the two platinum complexes *(13)*[22] and *(14)*[23, 24].

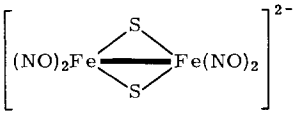


(12)

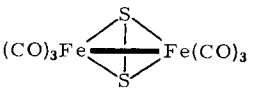


(13), L = $P(C_6H_5)_3$
(14), L = CO

The bonding system M_2S_2, in which two sulfur atoms span two metal atoms, is more common. This class includes the longest-known metal-sulfur complex, the red Roussain salt $K_2[Fe_2S_2(NO)_4]$[25]. The structure *(15)* of its anion was assumed by *Seel*[26] already in 1942 and was later confirmed by structure analysis of the red Roussain ethyl ester[27]; it is related to the structure *(16)*[28] of the complex $Fe_2S_2(CO)_6$[29, 30], which additionally displays an S—S bond.

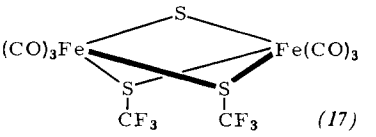


(15)



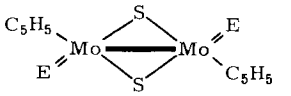
(16)

The stability of the M_2S_2 structural unit permits the additional appearance of metallosulfane and metal sulfide type bonds, *(7)* and *(8)*, which are otherwise uncommon for d"-metals; thus, the complex *(17)*[31] bears a certain resemblance to *(15)* and *(16)*.



(17)

Furthermore, among the Mo_2S_2 compounds both Mo=O[32] and Mo=S bonds[11] occur in terminal units, as shown by the almost identical structures *(18)*[33] and *(19)*[34].



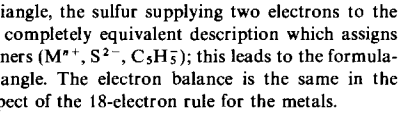
(18), E = O
(19), E = S

The above examples of M_2S_2 complexes are not isolated cases, for the discovery that several redox proteins contain iron, molybdenum, and "labile" sulfur (cf. Section 4) has meanwhile led to the preparation and crystallographic characterization of whole series of complexes containing the structural units Fe_2S_2[35–37] and Mo_2S_2[38–44] accompanied by naturally occurring ligands.

The assumption that the bridging sulfur in the M_2S triangle acts as a two-electron donor and thus that two M—S single bonds are present can be confirmed experimentally. The most convincing evidence comes from the M—S bond lengths: for example, in the molybdenum complexes *(18)* and *(19)* the Mo—S bridge bonds average 2.32 Å in length, whereas the length of the terminal Mo=S double bond in *(19)* is 2.14 Å[34]. If the bridging sulfur atom were a four-electron donor the bridging Mo—S bonds would have to be formulated as double bonds, which would contradict the experimental result[*]

Accordingly, in their complexes such as *(12)*, *(15)*, *(16)*, and *(17)* the metal atoms of the first transition series always attain 18 outer electrons—and the noble gas rule is thus fulfilled—if the bridging sulfur is counted as a two-electron donor. For molybdenum and platinum, however, even in complexes with π-acceptor ligands, an outer electron number of 16 is also common, and this is also so in the complexes *(13)*, *(14)*, *(18)*, and *(19)*.

[*] In the method of counting electrons used here all the bonding partners concerned in the covalent bonding system of these complexes are regarded as neutral particles. For example, the electrically neutral charge distribution *(a)* results for an Mo_2S triangle, the sulfur supplying two electrons to the bonding system. There is a completely equivalent description which assigns charges to the bonding partners (M^{n+}, S^{2-}, $C_5H_5^-$); this leads to the formulation *(b)* for the Mo_2S triangle. The electron balance is the same in the two cases, especially in respect of the 18-electron rule for the metals.



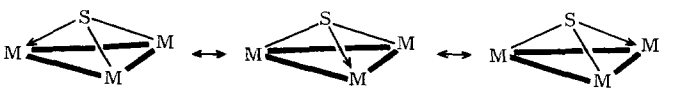
(a) *(b)*

The bridging-sulfur complexes described here cannot be classed among the sulfane derivatives *(7)* since the sulfur bridge occurs almost invariably together with a metal-metal bond and the angle at the bridging sulfur atom (about 75°) cannot be reconciled with the angle at sulfane-sulfur (about 105°). Thus, the metal-sulfur bond cannot be described independently of the metal-metal bonding (cf. Section 2.5). This three-center situation is similar to that for bridging CO groups[45], which also occur only in conjunction with metal-metal bonds and show no ketone character in either their structure or their bonding.

2.3. Sulfur Atoms as Threefold Bridges and Four-Electron Donors

This is the bonding situation specific to stable transition metal-sulfur complexes. As a four-electron donor, sulfur uses one of its lone pairs and forms three covalent bonds. The reactivity of the sulfur is thereby reduced and at the same time the M_3S structural unit represents a still closer approach to the structure of sulfidic solids. Furthermore, an M_3S atomic arrangement has a favorable geometry, for the three metals can interact with one another and, together with the remaining lone pair, provide approximate tetrahedral coordination for the sulfur. This type of bonding is so favorable that it permits enormous variations in the nature and electron configuration of the metals.

If the three metal atoms are the same the M_3S bonding system is normally symmetrical. Thus, there is no difference between the various bonds from the sulfur, as indicated by the individual resonance formulas of the valence-bond description *(20)*. It is justifiable, both qualitatively and quantitatively, to state that the sulfur contributes four electrons to three covalent bonds, without specifying the exact distribution of these electrons.

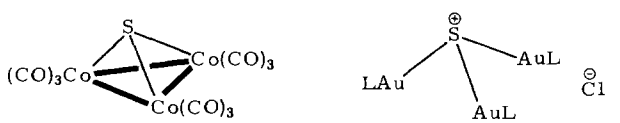


(20a) *(20b)* *(20c)*

When the sulfur is counted as a four-electron donor then for most of these complexes the 18-electron rule, the noble-gas rule of transition-metal chemistry, is fulfilled for all metals. The preference for the M_3S and also for the M_3S_2 structural unit—the latter bridged on both sides—is, however, so strong that some cases are also found in which the electronic configuration departs considerably from the 18-electron rule.

2.3.1. Complexes with the M_3S Structural Unit

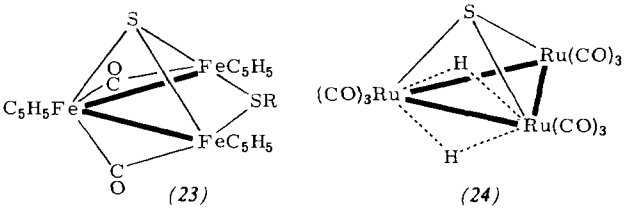
The M_3S structural unit can occur either with or entirely without metal-metal bonding; this is illustrated by the two symmetrical examples *(21)*[46] and *(22)*[18].



(21) *(22)*, L = $P(C_6H_5)_3$

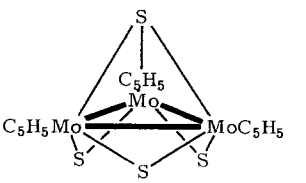
The Co_3S cluster is formed so readily that it is accessible *via* several routes[47–50] and can occur in widely differing structures[46, 51–53].

Somewhat more complicated bonding occurs in the thiol-bridged iron complex *(23)*[54], whose crystal structure has been elucidated[55], and in the ruthenium hydride *(24)*[56, 57].



(23) *(24)*

Finally, the Mo_3S_4 complex *(25)*, which occurs both as a cation and as a neutral complex[11, 58], contains a combination of twofold and threefold bridging sulfur atoms.

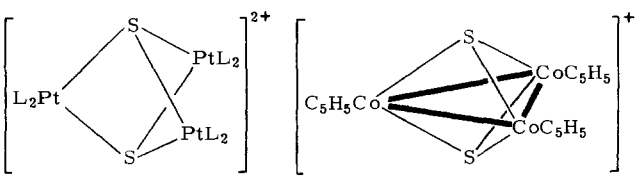


(25)

In this compound there are four sulfur atoms situated at the corners of a tetrahedron; they leave room for a fourth metal atom which, together with the three molybdenum atoms, would span a tetrahedron inverse to this. Together they would provide a M_4S_4-cubane (cf. Fig. 2) seven-eighths of which is complete in the Mo_3S_4 cluster *(25)*.

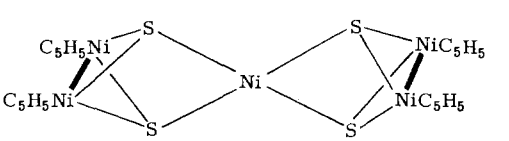
2.3.2. Complexes with the M_3S_2 Structural Unit

There are also examples of various degrees of metal-metal bonding among the M_3S_2 complexes. The extremes are the cations *(26)* without metal-metal bonds[22] and *(27)* with strong metal-metal interaction[59].



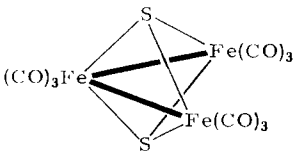
(26), L = $P(CH_3)_2C_6H_5$, $As(CH_3)_2C_6H_5$ *(27)*

The tendency for the formation of these complexes is high and the $(C_5H_5)_3M_3S_2$ system represented by *(27)* occurs in several variants[59–62]; one of these is the pentanuclear nickel complex *(28)*, which exhibits two M_3S_2 skeletons sharing a single corner.

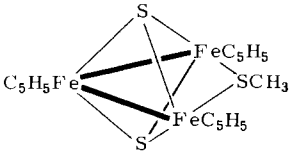


(28)

The longest-known member of this group is enneacarbonyl-triiron disulfide *(29)*, which is a representative of classical Hieber carbonyl chemistry and can be formed in a variety of ways[29, 63–65] and whose structure[66] with its two metal-metal bonds has an isoelectronic analog in the complex *(30)*[67].



(29)

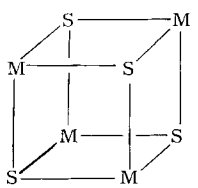


(30)

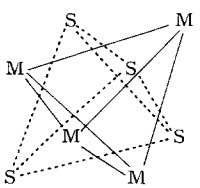
In all these complexes a unit of three metal atoms, which alone would not be stable, is doubly clamped together by the sulfur atoms.

2.3.3. Complexes with the M_4S_4-Cubane Skeleton

The arrangement of four metal atoms and four sulfur atoms in a cubane cluster has a particularly favorable geometry, for it permits the optimal M_3S bonding for the sulfur while satisfying the metal's demand for bonding to several sulfur atoms. In the M_4S_4-cubane each sulfur atom is bonded to three metal atoms, and each metal atom to three sulfur atoms; moreover, metal-metal interaction is also possible. Alternatively the cubane skeleton can be described as a double tetrahedron: one tetrahedron of metal atoms and another of sulfur atoms interpenetrate in inverse arrangement. The formulas *(31)* (cubane) and *(32)* (double tetrahedron) in which the atoms have the same arrangement illustrate the two methods of description.



(31)



(32)

If one interprets the full lines in *(31)* and *(32)* as denoting chemical bonds, then *(31)* represents the case with minimal and *(32)* the case with maximal metal-metal bonding. These cases occur in $[(C_5H_5)CoS]_4$[68] and $[(NO)FeS]_4$[69]; very many intermediate types are possible (cf. Section 2.5).

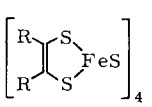
In the cubane clusters the greatest variety is shown by the cyclopentadienyl complexes $[(C_5H_5)MS]_4$ with M = Cr[70], Mo[71], Fe[72, 73], and Co[68, 74]. The metal introduced most frequently into M_4S_4-cubane geometry is iron. Fe_4S_4 structures with four different ligand systems are now known; the compound types are *(33)*[72, 73], *(34)*[69], *(35)*[75, 76], and *(36)*[77, 78].

$[(C_5H_5)FeS]_4$

(33)

$[(NO)FeS]_4$

(34)



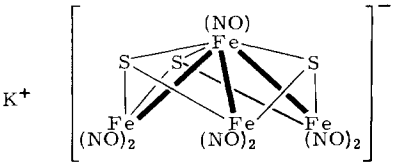
(35)

$[(RS)FeS]_4^{2-}$

(36)

This variety is confirmed by the finding that iron also occurs with Fe_4S_4-cubane geometry in Nature (cf. Section 4.1).

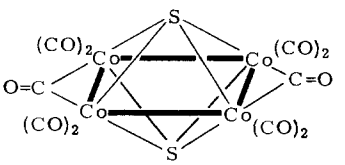
Finally, the black Roussain salt $K[Fe_4S_3(NO)_7]$ *(37)*[25, 26, 79] is an incomplete cubane whose Fe_4S_3 structure is reminiscent of the Mo_3S_4 situation in *(25)*.



(37)

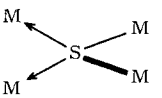
2.4. Sulfur Atoms as Bridges between Four Metal Atoms

So far only one case is known of a sulfur atom located as a four-electron donor above a plane containing four metal atoms, namely the complex $Co_4S_2(CO)_{10}$[3, 48, 49] having structure *(38)*[80].



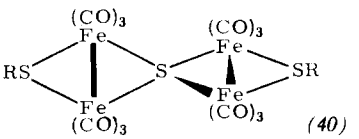
(38)

In all the other examples containing sulfur as a fourfold bridge the sulfur lies in a "tetrahedral hole" between four metal atoms. The sulfur no longer has any lone pairs because all six of its valence electrons are required for the four metal-sulfur bonds. The bonding relationships can be represented schematically as *(39)*, which, however, like *(20)*, is a crude simplification of the mostly symmetrical bonding system.



(39)

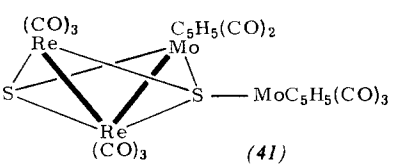
This type of complex exists in the iron compound *(40)* with R = CH_3[81] or R = *tert*-C_4H_9[82], whose structures are related to those of *(16)*[28] and $[(CO)_3Fe—SR]_2$[83], respectively.



(40)

Other complexes contain the SM_4 structural group as part of a complicated bonding skeleton, the arrangement of the metal atoms around the sulfur corresponding only roughly to a tetrahedron. Examples are the complex *(41)*[4] with two different metals and the two rhenium complexes shown in Figure 1. The two last-mentioned complexes are structurally related in that the Re_4S_3 nucleus of $S_3Re_6(CO)_{22}$ *(42)*[84] represents an incomplete cubane which is complete in $S_4Re_8(CO)_{32}$ *(43)*[85], for which an Mn analog exists[86].

Two interesting complexes that tend more toward conventional inorganic chemistry are $SM_4[S_2As(CH_3)_2]_6$ *(44)* with



(41)

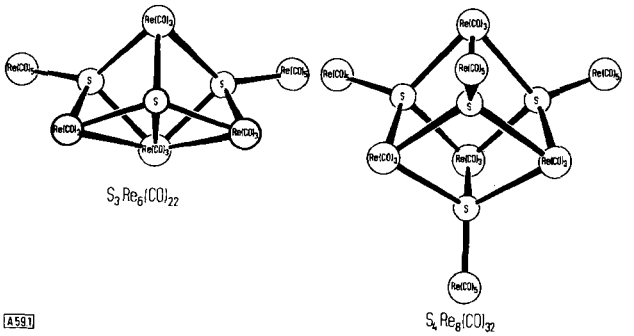


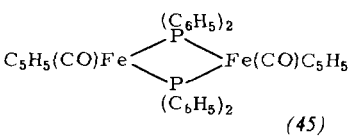
Fig. 1. Schematic structures of the complexes *(42)* and *(43)*.

M = Co or Zn[87], whose SM_4 nucleus corresponds to the OM_4 nucleus in the structures derived from basic beryllium acetate[88]. In all the SM_4 complexes with the exception of *(38)* the coordination of the sulfur with four metal atoms corresponds to that in zinc sulfide, *i.e.* to a typical solid. Since the metal atoms in the cubane *(36)* are also surrounded tetrahedrally by four sulfur atoms, molecular sulfur complexes do in fact exist in which the bonding approaches or corresponds to that found in solid-state chemistry. However, no molecules are yet known in which the sulfur atoms are surrounded by six metal atoms, as in most of the transition-metal sulfides.

2.5. Modification of Metal-Metal Bonds

MO calculations for multinuclear transition-metal complexes with basic bridging atoms (P, As, S, Se)[69, 89, 90] by means of the parameter-free model of *Fenske* and *Hall*[91] have shown that the HOMOs and LUMOs[*] in these complexes have predominating metal-atom character and reflect bonding, nonbonding, or antibonding metal-metal interactions. These calculations provide the supplementary explanation of why such enormous variation in the bonding between the metal atoms can arise in the base-bridged multinuclear complexes of which the sulfur-bridged systems are a special case; for on the basis of the MO scheme a change in the number of electrons in the complex primarily affects the metal-metal bond while scarcely affecting the bond from the metal to the bridging atom, which is the actual stabilizing element of the polynuclear complex.

A convincing experimental example is provided by the phosphido-bridged complex *(45)*[89, 92].

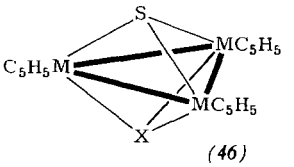


(45)

This must be formulated as a neutral complex without an Fe—Fe bond, because its HOMO is a σ*-orbital with respect to the interaction between the two iron atoms. Oxidation to $(45)^{1+}$ removes an electron from the σ*-orbital, and oxidation to $(45)^{2+}$ transforms the σ*-orbital into the LUMO, with the result that in $(45)^{1+}$ a half and in $(45)^{2+}$ a whole Fe—Fe bond is present. This is confirmed by the Fe—Fe interatomic distances: they amount to 3.49 Å in *(45)*, 3.12 Å in $(45)^{1+}$, and 2.78 Å in $(45)^{2+}$.

[*] HOMO = highest occupied molecular orbital, LUMO = lowest unoccupied molecular orbital.

The chemistry described here for complexes of the transition metals with sulfur contains many examples of this variability of metal-metal bonding. For example, the metal-metal separations in the complexes $(27)^{1+}$[59], $(33)^{1+}$[93], $(33)^{2+}$[94], and $[(C_5H_5)CoS]_4^{+}$[68] are smaller than in the corresponding neutral complexes, since metal-metal antibonding electrons are removed on oxidation. Still more impressive is a comparison of the complexes in which the number of electrons is changed by chemical modification. This modification may consist in the replacement of ligands or of metal atoms, as can be seen, *e.g.*, in the series of complexes *(46)*[59, 61].



(46)

In such a process replacement of the cobalt atoms by nickel atoms changes the total number of electrons by 3, and the four-electron donor sulfur supplies two more electrons than the CO group, a two-electron donor. The metal-metal bond lengths respond dramatically to variations in the number of electrons, while a qualitative MO consideration shows the electrons involved to be antibonding electrons[59, 61]. The numerical values are listed in Table 1.

Table 1. Structural data of complexes $(C_5H_5M)_3SX$ *(46)*.

Complex	Antibonding electrons	Average M—M distance [Å]
$(C_5H_5Co)_3S(CO)$	0	2.45
$(C_5H_5Co)_3S_2^{+}$	1	2.53
$(C_5H_5Co)_3S_2$	2	2.69
$(C_5H_5Ni)_3S_2$	5	2.80

According to the electron count the CO-bridged cobalt complex permits three metal-metal bonds, which are in fact observed. For the Ni_3S_2 complex, however, the count shows five excess electrons; their antibonding character is shown by the very weak Ni—Ni interaction.

Further experimental proof of the metal-metal bonding character of the highest occupied orbitals in such complexes has been provided for compound *(21)*. This complex contains an unpaired electron. A single-crystal ESR study[95] has shown that this electron is to be found in an antibonding A_2 orbital formed from metal d-orbitals. This is confirmed by the structurally similar complex $FeCo_2S(CO)_9$ *(47)*[96], in which a cobalt atom of *(21)* is replaced by iron and from which the antibonding electron is thus absent. Accordingly the metal-metal separation in *(47)* is 0.08 Å shorter than in *(21)*[97].

Aesthetically the deepest impression is imparted by variation in metal-metal bonding in the cubane complexes $[(C_5H_5)MS]_4$. In this series $[(C_5H_5)CoS]_4$[68] should be formulated without any metal-metal bond, since the cyclopentadienyl ligands and the sulfur atoms provide sufficient electrons to complete the 18-electron configuration of each cobalt atom. In the iron compound $[(C_5H_5)FeS]_4$[72, 73], however, there is one electron too few for each iron atom. This is compensated by formation of one metal-metal bond per iron atom, a total of two iron-iron bonds in the cubane, and the electron balance thus restored. Similarly, for $[(C_5H_5)MnS]_4$ two metal-metal

bonds per manganese atom are to be expected, making a total of four in the cubane; this complex is not yet known, but its electron count is approximated by the two complexes $[(C_5H_5)FeS]_4^{2+}$[94] and *(35)*$^{2-}$[76], which have the expected structure. Finally, in $[(C_5H_5)MoS]_4$[71] three metal-metal bonds per molybdenum atom are necessary for all the atoms to attain the noble-gas configuration; accordingly, here the metal atoms form a tetrahedral cluster of type *(32)*. Figure 2 surveys the structural changes in these cubanes.

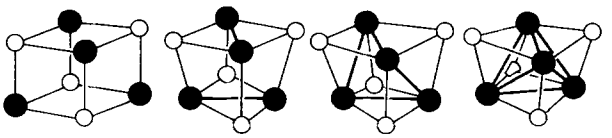


Fig. 2. Structures of M_4S_4 nuclei in the cubane complexes $[(C_5H_5)MS]_4$ with M = Co, Fe, Mn (hypothetical), and Mo. The cyclopentadienyl groups are situated symmetrically on each metal atom.

3. Synthesis and Reactivity

The chemical properties of the transition metal-sulfur complexes have hitherto been largely unexplored, perhaps because many of the complexes result from unusual reactions of unusual reactants and the yields are often low. Nevertheless, the tendency for their formation is illustrated by the fact that transition metals can abstract sulfur atoms from the most varied sulfur compounds.

In only few cases[18, 22, 36, 49, 63, 78, 98, 99] can H_2S or sulfide ions serve as starting materials for the complexes. More often the complexes are formed by the reaction of carbonylmetal derivatives with sulfur[3, 47, 48, 61, 69, 70, 72, 74, 96] or sulfur-transfer agents such as episulfides[11, 32, 64] or disulfanes[31, 49, 50, 54, 72]. From among the unusual sources of sulfur atoms we may mention thiocyanate[21, 81], carbonyl sulfide[23], and *tert*-butylsulfur diimide[60, 69]; in this context the manifold methods of forming the carbonyl-sulfide complexes of iron[29, 30, 63–65, 81, 82] and cobalt[3, 47–50, 53, 96] are especially striking. Most of these preparations are accompanied by the formation of metal sulfide. Stoichiometry can be given only very rarely, and reaction mechanisms never.

One possibility of directed synthesis is to introduce the sulfur as a functional derivative containing removable substituents. The simplest example would be H_2S, but this is too reactive and does not react unambiguously. In a few cases by using bis(trimethyltin) sulfide it was possible to transfer sulfur atoms by successive fission of tin-sulfur bonds with carbonylmetal halides[4, 85, 86], but even then obscure reaction courses could not always be avoided[58, 84, 86].

The thermal stability of the complexes of the transition metals and sulfur, which in some cases is quite high, is an advantage that has hitherto hardly been exploited for investigations of reactivity. Only redox reactions have been studied in detail[36, 37, 59, 68, 69, 75–78, 89, 93, 94]. The effects of altering the number of electrons have been described in Section 2.5, and replacement of CO groups by phosphanes[100, 101] has also been mentioned.

In some cases the sulfur complexes themselves served as the starting materials for the synthesis of related compounds. For instance, the pentanuclear nickel complex *(28)* was formed on decomposition of the trinuclear $(C_5H_5)_3Ni_3S_2$[62], and the cubane $[(C_5H_5)MoS]_4$ (cf. Fig. 2) was obtained by introducing a C_5H_5Mo group into the incomplete cubane *(25)*[71]. Other reactions of this kind are certainly possible, but isolation of the polynuclear structure from the complex reaction mixture would probably be difficult.

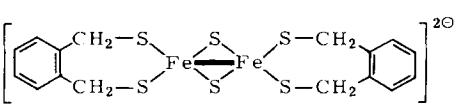
4. Biochemical Aspects

The popularization of inorganic biochemistry that resulted from the demand for social relevance in science has also brought certain aspects of metal-sulfur complex chemistry into the forefront of interest. This applies to verification of the complementary nature of the metal and the "labile" sulfur long known as individual constituents of many proteins, and also to the resulting attempts to determine the structure and function of the inorganic part of these proteins[5, 102]. For the most thoroughly investigated systems, namely those of iron and molybdenum, it can be said that we are approaching an understanding of their action. Here the initial difficulties have now been overcome, *e. g.* the oversimplified models proposed by inorganic chemists and the lack of chemical information about the complicated proteins available to biologists.

4.1. Ferredoxin Models

The ferredoxin problem stands out in the extensive literature about iron-sulfur proteins[37, 103–105]. The ferredoxins, proteins containing an even number of iron and "labile" sulfur atoms, are used by many organisms as electron-transfer agents. In view of the considerations in Section 2.5 it seems reasonable to assume that the redox center of these proteins lies in an iron-sulfur cluster, and there has been no lack of attempts to find this redox center and to imitate it in simple compounds. For a long time a handicap of these model investigations was that the isolable Fe_2S_2 and Fe_4S_4 complexes contained the stabilizing π-acceptor ligands which do not occur in Nature. Only very recently could models be developed for which a claim of similarity to Nature is justified.

In Fe_2S_2-ferredoxins each iron atom is known to be bound not only to the "labile" sulfide-sulfur atoms but also to two sulfur atoms of cysteine members of the polypeptide chain. This bonding eliminates almost all the known Fe_2S_2 complexes as model substances[35, 37, 104]. Compound *(48)* is the sole such complex in which the iron atoms are bonded only to sulfur and tetracoordinated[36].

$[(C_2H_5)_4N]_2^{\oplus}$  *(48)*

(48) corresponds to the natural material in its electronic spectra, Mössbauer spectra, and magnetic properties; only the redox potentials are different, because they do not depend only on the immediate coordination sphere of the iron[37, 104].

In contrast to the Fe_2S_2 system, the crystal structures of natural Fe_4S_4 redox proteins are already known. In all three cases they contain cubane-like $(-Cys-S-)_4Fe_4S_4$ structural units[106, 107]. Figure 3 illustrates the very symmetrical structure of the ferredoxin from *Peptococcus aerogenes*, with its two Fe_4S_4-cubane units[107]. Thus, the known simple Fe_4S_4

complexes[69, 72, 73, 75] are again excluded as model substances, even though they are excellent redox systems[90, 108–110]; nevertheless, discussion of the electronic structure of these complexes[69, 90] shows that the bonding differs from that in the natural system.

Only the synthesis and precise physicochemical investigation of the model compounds *(36)*, especially $[(C_6H_5—CH_2S)FeS]_4^{2-}$, provide an adequate approximation to the natural state[77, 78, 111–113]. The complexes *(36)* are comparable in all their spectra with the Fe_4S_4-ferredoxins. In particular, they also exhibit electron delocalization in the various oxidation stages; this means, for example, that the two Fe^{II} and two Fe^{III} ions formally required in the molecules $[(RS)FeS]_4^{2-}$ cannot be distinguished. However, it should be mentioned that the structural elucidation and the imitation of these ferredoxins by models still does not explain their mode of action, and especially their mode of electron transfer[107].

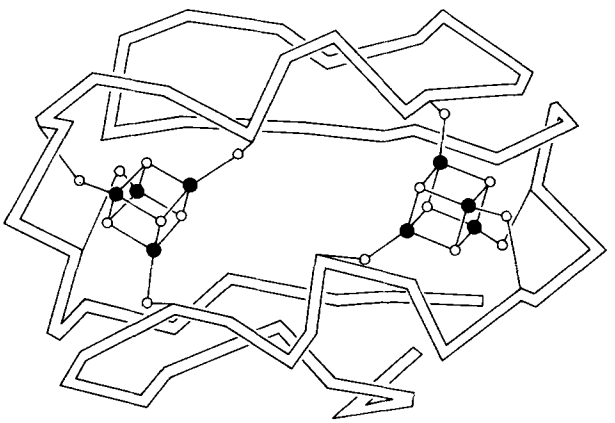
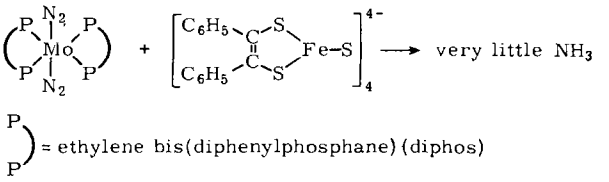


Fig. 3. The polypeptide chain and $[(RS)FeS]_4$ units in the ferredoxin from *Peptococcus aerogenes*.

4.2. Models of Molybdenum Enzymes

The biochemistry of molybdenum has not yet afforded such detailed information as in the case of iron[114, 115]. Molybdenum is known essentially to occur in redox enzymes such as xanthine oxidase, aldehyde oxidase, nitrate reductase, and nitrogenase together with sulfur-containing ligands and perhaps also "labile" sulfur. However, caution must be exercised in discussing sulfur-bridged molybdenum complexes such as *(18)* and similar systems[33, 38–44, 98, 99] proposed as model substances.

Owing to the eminent industrial importance of nitrogen fixation[116], particular interest attaches to the enzyme nitrogenase, which converts nitrogen into ammonia under normal conditions. Purification and investigation showed it to consist of two proteins[117, 118]. One of these contains two iron and two "labile" sulfur atoms, and the other one molybdenum and about 16 iron and "labile" sulfur atoms. Thus, sulfur-bridged Mo_2 complexes are excluded, although the iron and sulfur contents are reminiscent of the ferredoxins. Since the nitrogen uptake of the enzyme no longer occurs in the absence of molybdenum, it seems likely that the molybdenum is required for binding of the nitrogen molecule, and the iron-sulfur units for delivery of the reduction equivalents. While this hypothesis has not yet been verified by enzyme studies, it has already been tested in a model experiment with a molybdenum-N_2 complex and a ferredoxin analog[119]:



A similar reaction was attempted with $[(C_2H_5S)FeS]_4^{3-}$[120], but the ammonia yields were always very low and could not even be confirmed in one case[121].

Summarizing, investigation of nitrogenase has not yet advanced to the stage of close cooperation between biology and inorganic chemistry characterizing the ferredoxin problem.

5. Outlook

This progress report, which covers the literature up to the middle of 1974, finds the chemistry of the metal-sulfur complexes in a transitional state. Whereas the main emphasis has hitherto been placed on finding new structural characteristics, interest is now passing to the preparation of such structures and to the study of their practical importance. The ease with which transition-metal compounds undergo redox reactions without changing their chemical composition, as shown by polynuclear complexes in general and by metal-sulfur clusters in particular, could be important in this connection, and should provide a stimulus not only to biochemistry but also to catalysis research. Finally, the question of how far the stabilizing bonding principles in sulfidic solids are retained in the molecular compounds containing transition-metals and sulfur provides a challenge to both the theoretical and the practical chemist.

Our own research reported in this article was supported by the Deutsche Forschungsgemeinschaft and the National Science Foundation. My colleagues and co-workers Dr. V. A. Uchtman, Dr. P. J. Vergamini, and Dipl.-Chem. V. Küllmer participated in this work. The author is grateful to Professor L. F. Dahl of the University of Wisconsin for stimulating these studies and for many vigorous discussions. Prof. L. F. Dahl, Prof. E. O. Fischer, and Dr. W. P. Fehlhammer kindly placed some unpublished results at our disposal.

Received: September 11, 1974 [A 59 IE]
German version: Angew. Chem. 87, 363 (1975)
Translated by Express Translation Service, London

[1] *R. G. Pearson*, J. Amer. Chem. Soc. *85*, 3533 (1963).
[2] *J. Jellinek* in *G. Nickless:* Inorganic Sulphur Chemistry. Elsevier, Amsterdam 1968.
[3] *L. Marko, G. Bor*, and *G. Almasy*, Chem. Ber. *94*, 847 (1961).
[4] *P. J. Vergamini, H. Vahrenkamp*, and *L. F. Dahl*, J. Amer. Chem. Soc. *93*, 6326 (1971).
[5] *M. N. Hughes:* The Inorganic Chemistry of Biological Processes. Wiley, London 1972.
[6] *E. Diemann* and *A. Müller*, Coord. Chem. Rev. *10*, 79 (1973).
[7] *M. Schmidt*, Angew. Chem. *85*, 474 (1973); Angew. Chem. internat. Edit. *12*, 445 (1973).
[8] *F. Fehér* in *J. J. Lagowski:* The Chemistry of Nonaqueous Solvents, Vol. III. Academic Press, New York 1970.
[9] *J. Jander* and *Ch. Lafrenz:* Wasserähnliche Lösungsmittel. Verlag Chemie, Weinheim 1968.
[10] *W. Strohmeier* and *J. F. Guttenberger*, Chem. Ber. *97*, 1871 (1964).
[11] *W. Beck, W. Danzer*, and *G. Thiel*, Angew. Chem. *85*, 625 (1973); Angew. Chem. internat. Edit. *12*, 582 (1973).
[12] *D. Morelli, A. Segre, R. Ugo, G. La Monica, S. Cenini, F. Conti*, and *F. Bonati*, Chem. Commun. *1967*, 524.

[13] *M. Sato, F. Sato, N. Takemoto,* and *K. Iida,* J. Organometal. Chem. *34,* 205 (1972).
[14] *W. Beck, W. Danzer,* and *R. Höfer,* Angew. Chem. *85,* 87 (1973); Angew. Chem. internat. Edit. *12,* 77 (1973).
[15] *R. Graves, J. M. Homan,* and *G. L. Morgan,* Inorg. Chem. *9,* 1592 (1970).
[16] *S. E. Livingstone,* Quart. Rev. Chem. Soc. *19,* 386 (1965).
[17] *E. W. Abel* and *B. C. Crosse,* Organometal. Chem. Rev. *2,* 443 (1967).
[18] *C. Kowala* and *J. M. Swan,* Aust. J. Chem. *19,* 547 (1966).
[19] *M. G. B. Drew* and *R. Mandyczewsky,* J. Chem. Soc. *A 1970,* 2815.
[20] *H. Siebert* and *S. Thym,* Z. Anorg. Allg. Chem. *399,* 107 (1973).
[21] *E. O. Fischer* and *R. Schneider,* unpublished results; cf. *R. Schneider,* Dissertation, Technische Universität München 1968.
[22] *J. Chatt* and *D. M. P. Mingos,* J. Chem. Soc. *A 1970,* 1243.
[23] *M. C. Baird* and *G. Wilkinson,* J. Chem. Soc. *A 1967,* 865.
[24] *A. C. Skapski* and *P. G. H. Troughton,* J. Chem. Soc. *A 1969,* 2772.
[25] *J. Roussain,* Ann. Chim. Phys. *(3) 52,* 285 (1858).
[26] *F. Seel,* Z. Anorg. Allg. Chem. *249,* 308 (1942).
[27] *J. T. Thomas, J. H. Robertson,* and *E. G. Cox,* Acta Crystallogr. *11,* 599 (1958).
[28] *C. H. Wei* and *L. F. Dahl,* Inorg. Chem. *4,* 1 (1965).
[29] *W. Hieber* and *J. Gruber,* Z. Anorg. Allg. Chem. *296,* 91 (1958).
[30] *W. Hieber* and *H. Beutner,* Z. Naturforsch. *15b,* 324 (1960).
[31] *J. Grobe* and *F. Kober,* Z. Naturforsch. *24b,* 1346 (1969).
[32] *P. M. Treichel* and *G. R. Wilkes,* Inorg. Chem. *5,* 1182 (1966).
[33] *D. L. Stevenson* and *L. F. Dahl,* J. Amer. Chem. Soc. *89,* 3721 (1967).
[34] *A. Liu, B. Fähnrich,* and *W. P. Fehlhammer,* unpublished.
[35] *A. Terzis* and *R. Rivest,* Inorg. Chem. *12,* 2132 (1973); *G. T. Kubas, T. G. Spiro,* and *A. Terzis,* J. Amer. Chem. Soc. *95,* 273 (1973).
[36] *J. J. Mayerle, R. B. Frankel, R. H. Holm, J. A. Ibers, W. D. Phillips,* and *J. F. Weiher,* Proc. Nat. Acad. Sci. U.S. *70,* 2499 (1973).
[37] *S. J. Lippard,* Accounts. Chem. Res. *6,* 282 (1973).
[38] *G. N. Schrauzer, V. P. Mayweg,* and *W. Heinrich,* J. Amer. Chem. Soc. *88,* 5174 (1966).
[39] *L. Ricard, J. Estienne,* and *R. Weiss,* Inorg. Chem. *12,* 2182 (1973).
[40] *D. H. Brown* and *J. A. D. Jeffreys,* J. C. S. Dalton *1973,* 732.
[41] *B. Spivack* and *Z. Dori,* J. C. S. Dalton *1973,* 1173.
[42] *B. Spivack* and *Z. Dori,* J. C. S. Chem. Comm. *1973,* 909.
[43] *B. Spivack, A. P. Gaughan,* and *Z. Dori,* J. Amer. Chem. Soc. *93,* 5265 (1971).
[44] *M. G. B. Drew* and *A. Kay,* J. Chem. Soc. *A 1971,* 1851.
[45] *E. W. Abel* and *F. G. A. Stone,* Quart. Rev. Chem. Soc. *23,* 325 (1969).
[46] *C. H. Wei* and *L. F. Dahl,* Inorg. Chem. 6, 1229 (1967).
[47] *L. Marko, G. Bor,* and *E. Klumpp,* Chem. Ind. London *1961,* 1491.
[48] *L. Marko, G. Bor, E. Klumpp, B. Marko,* and *G. Almasy,* Chem. Ber. *96,* 955 (1963).
[49] *E. Klumpp, L. Marko,* and *G. Bor,* Chem. Ber. *97,* 926 (1964).
[50] *E. Klumpp, G. Bor,* and *L. Marko,* Chem. Ber. *100,* 1451 (1967).
[51] *D. L. Stevenson, V. R. Magnuson,* and *L. F. Dahl,* J. Amer. Chem. Soc. *89,* 3727 (1967).
[52] *C. H. Wei* and *L. F. Dahl,* J. Amer. Chem. Soc. *90,* 3977 (1968).
[53] *G. Natile, S. Pignataro, G. Innorta,* and *G. Bor,* J. Organometal. Chem. *40,* 215 (1972).
[54] *R. J. Haines, J. A. de Beer,* and *R. Greatrex,* J. Organometal. Chem. *55,* C 30 (1973).
[55] *C. P. Boysen, J. D. Sinclair,* and *L. F. Dahl,* unpublished; cf. ref. [90].
[56] *A. J. Deeming, R. Ettore, B. F. G. Johnson,* and *J. Lewis,* J. Chem. Soc. *A 1971,* 1797.
[57] *E. Sappa, O. Gambino,* and *G. Cetini,* J. Organometal. Chem. *35,* 375 (1972).
[58] *P. J. Vergamini, H. Vahrenkamp,* and *L. F. Dahl,* J. Amer. Chem. Soc. *93,* 6327 (1971).
[59] *P. D. Frisch* and *L. F. Dahl,* J. Amer. Chem. Soc. *94,* 5082 (1972).
[60] *S. Otsuka, A. Nakamura,* and *T. Yoshida,* Inorg. Chem. 7, 261 (1968); Liebigs Ann. Chem. *719,* 54 (1968).
[61] *H. Vahrenkamp, V. A. Uchtman,* and *L. F. Dahl,* J. Amer. Chem. Soc. *90,* 3272 (1968).
[62] *H. Vahrenkamp* and *L. F. Dahl,* Angew. Chem. *81,* 152 (1969); Angew. Chem. internat. Edit. *8,* 144 (1969).
[63] *W. Hieber* and *O. Geisenberger,* Z. Anorg. Allg. Chem. *262,* 15 (1950).
[64] *R. B. King,* Inorg. Chem. *2,* 326 (1963).
[65] *R. Havlin* and *G. R. Knox,* J. Organometal. Chem. *4,* 247 (1965).
[66] *C. H. Wei* and *L. F. Dahl,* Inorg. Chem. *4,* 493 (1965).
[67] *J. D. Sinclair* and *L. F. Dahl,* unpublished; cf. ref. [90].
[68] *G. L. Simon* and *L. F. Dahl,* J. Amer. Chem. Soc. *95,* 2164 (1973).
[69] *R. S. Gall, C. T. W. Chu,* and *L. F. Dahl,* J. Amer. Chem. Soc. *96,* 4019 (1974).
[70] *E. O. Fischer* and *K. Ulm,* unpublished results; cf. *K. Ulm,* Dissertation, Universität München 1961.
[71] *L. F. Dahl,* Lecture, VIth Int. Conf. Organometal. Chem., Amherst, Mass. (USA), August 1973.
[72] *R. A. Schunn, C. J. Fritchie,* and *C. T. Prewitt,* Inorg. Chem. *5,* 892 (1966).
[73] *C. H. Wei, G. R. Wilkes, P. M. Treichel,* and *L. F. Dahl,* Inorg. Chem. *5,* 900 (1966).
[74] *V. A. Uchtman* and *L. F. Dahl,* J. Amer. Chem. Soc. *91,* 3756 (1969).
[75] *A. L. Balch,* J. Amer. Chem. Soc. *91,* 6962 (1969).
[76] *I. Bernal, B. R. Davis, M. L. Good,* and *S. Chandra,* J. Coord. Chem. *2,* 61 (1972). Improved structural data are mentioned by *Dahl et al.* [90].
[77] *T. Herskovitz, B. A. Averill, R. H. Holm, J. A. Ibers, W. D. Phillips,* and *J. F. Weiher,* Proc. Nat. Acad. Sci. U.S. *69,* 2437 (1972).
[78] *B. A. Averill, T. Herskovitz, R. H. Holm,* and *J. A. Ibers,* J. Amer. Chem. Soc. *95,* 3523 (1973).
[79] *G. Johansson* and *W. N. Lipscomb,* Acta Crystallogr. *11,* 594 (1958).
[80] *C. H. Wei* and *L. F. Dahl,* unpublished.
[81] *J. M. Coleman, A. Wojcicki, P. J. Pollick,* and *L. F. Dahl,* Inorg. Chem. *6,* 1236 (1967).
[82] *J. A. de Beer* and *R. J. Haines,* J. Organometal. Chem. *24,* 757 (1970).
[83] *L. F. Dahl* and *C. H. Wei,* Inorg. Chem. *2,* 328 (1963).
[84] *P. J. Vergamini* and *L. F. Dahl,* unpublished.
[85] *V. Küllmer* and *H. Vahrenkamp,* unpublished experiments.
[86] *H. Vahrenkamp,* Chem. Ber. *103,* 3580 (1970).
[87] *D. Johnstone, J. E. Fergusson,* and *W. T. Robinson,* Bull. Chem. Soc. Jap. *45,* 3721 (1972).
[88] *A. J. Burn* and *G. W. Smith,* Chem. Commun. *1965,* 394.
[89] *B. K. Teo, M. B. Hall, R. F. Fenske,* and *L. F. Dahl,* J. Organometal. Chem. *70,* 413 (1974).
[90] *L. F. Dahl, J. D. Sinclair,* and *B. K. Teo* in *E. A. Koerner von Gustorf:* The Organic Chemistry of Iron, in press.
[91] *M. B. Hall* and *R. F. Fenske,* Inorg. Chem. *11,* 768 (1972).
[92] *N. G. Conelly, L. F. Dahl,* and *J. D. Sinclair,* cited by *P. D. Frisch, M. K. Lloyd,* and *J. A. McCleverty,* J. C. S. Dalton *1973,* 2268.
[93] *Trinh-Toan, W. P. Fehlhammer,* and *L. F. Dahl,* unpublished.
[94] *Trinh-Toan, B. K. Teo, J. A. Ferguson, T. J. Meyer,* and *L. F. Dahl,* unpublished.
[95] *C. E. Strouse* and *L. F. Dahl,* Discuss. Faraday Soc. *47,* 93 (1969).
[96] *S. A. Khattab, L. Marko, G. Bor,* and *B. Marko,* J. Organometal. Chem. *1,* 373 (1964).
[97] *D. L. Stevenson, C. H. Wei,* and *L. F. Dahl,* J. Amer. Chem. Soc. *93,* 6027 (1971).
[98] *B. Spivack* and *Z. Dori,* Chem. Commun. *1970,* 1716.
[99] *A. Kay* and *P. C. H. Mitchell,* J. Chem. Soc. *A 1970,* 2421.
[100] *W. Hieber* and *A. Zeidler,* Z. Anorg. Allg. Chem. *329,* 92 (1964).
[101] *K. Burger, L. Korecz,* and *G. Bor,* J. Inorg. Nucl. Chem. *31,* 1527 (1969).
[102] *L. E. Bennet,* Progr. Inorg. Chem. *18,* 1 (1973).
[103] *J. C. M. Tsibris* and *R. W. Woody,* Coord. Chem. Rev. *5,* 417 (1970).
[104] *R. Mason* and *A. Zubieta,* Angew. Chem. *85,* 390 (1973); Angew. Chem. internat. Edit. *12,* 390 (1973).
[105] *W. Lovenberg:* Iron-Sulfur Proteins. Academic Press, New York 1973.
[106] *C. W. Carter, J. Kraut, S. T. Freer, R. A. Alden, L. C. Sieker, E. T. Adman,* and *L. H. Jensen,* Proc. Nat. Acad. Sci. U.S. *69,* 3526 (1972).
[107] *E. T. Adman, L. C. Sieker,* and *L. H. Jensen,* J. Biol. Chem. *248,* 3987 (1973).
[108] *W. D. Phillips, M. Poe, C. C. McDonald,* and *R. B. Bartsch,* Proc. Nat. Acad. Sci. U.S. *67,* 682 (1970).
[109] *J. A. Ferguson* and *T. J. Meyer,* Chem. Commun. *1971,* 623.
[110] *R. B. Frankel, W. M. Reiff, I. Bernal,* and *M. L. Good,* Inorg. Chem. *13,* 493 (1974).
[111] *M. A. Bobrick, L. Que jr.,* and *R. H. Holm,* J. Amer. Chem. Soc. *96,* 285 (1974).
[112] *R. H. Holm, W. D. Phillips, B. A. Averill, J. J. Mayerle,* and *T. Herskovitz,* J. Amer. Chem. Soc. *96,* 2109 (1974).
[113] *R. H. Holm, B. A. Averill, T. Herskovitz, R. B. Frankel, H. B. Gray, O. Siiman,* and *F. J. Grunthaner,* J. Amer. Chem. Soc. *96,* 2644 (1974).
[114] *J. T. Spence,* Coord. Chem. Rev. *4,* 475 (1969).
[115] *R. C. Bray* and *J. C. Swann,* Struct. Bonding *11,* 107 (1972).
[116] *J. Chatt* and *G. J. Leigh,* Chem. Soc. Rev. *1,* 121 (1972).
[117] *G. Nakos* and *L. E. Mortenson,* Biochim. Biophys. Acta *229,* 431 (1971); *H. Dalton, J. A. Morris, M. A. Ward,* and *L. E. Mortenson,* Biochemistry *10,* 2066 (1971).
[118] *G. Nakos* and *L. E. Mortenson,* Biochemistry *10,* 455 (1971).
[119] *E. E. van Tamelen, J. A. Gladysz,* and *J. S. Miller,* J. Amer. Chem. Soc. *95,* 1347 (1973).
[120] *E. E. van Tamelen, J. A. Gladysz,* and *C. R. Brület,* J. Amer. Chem. Soc. *96,* 3020 (1974).
[121] *J. Chatt, C. M. Elson,* and *R. L. Richards,* J. C. S. Chem. Comm. *1974,* 189 (1974).

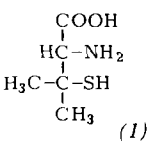
D-Penicillamine—Production and Properties

By Wolfgang M. Weigert, Heribert Offermanns, and Paul Scherberich[*]

The non-naturally occurring amino acid D-penicillamine, originally only of interest as a key substance in the structural elucidation and total synthesis of penicillins is gaining increasing importance as a therapeutic, particularly in the long-term treatment of rheumatoid arthritis. D-Penicillamine which previously was obtained semi-synthetically by degradation of penicillins can now be totally synthesized using a new process which starts from isobutyraldehyde, sulfur, ammonia, and hydrogen cyanide and yields the racemate which is then selectively resolved. The biochemical behavior of D-penicillamine—chelate formation with heavy metal ions, cleavage of disulfide bridges, and condensation with aldehyde groups—affords information related to its therapeutic activity.

1. Introduction

In 1943, during their investigations on the structural elucidation of penicillins, *Abraham et al.*[1, 2] ("The Oxford Group") found all penicillins to give a common degradation product which, in ignorance of its exact structure, was called "penicillamine" because of the presence of an amino group in the molecule. The β,β-dimethylcysteine structure *(1)* postulated by *Cornforth*[1] was later confirmed by the "Oxford Group" on investigation of its reactions and synthesis[1].



(1)

"Penicillamine" is levorotatory in alkine solution and, with respect to its absolute configuration, belongs to the D-series of amino acids. The correct chemical name for "penicillamine" is D-(−)-2-amino-3-mercapto-3-methylbutyric acid. Common synonyms are: D-(−)-β,β-dimethylcysteine; D-(−)-β-mercaptovaline; and D-(−)-2-amino-3-mercaptoisovaleric acid. In this report the substance will be called D-penicillamine.

D-Penicillamine *(1)* was at first solely of interest as a key substance in the structural elucidation of penicillins and as a central building block in their total synthesis[3, 4]. In 1956, D-penicillamine, which itself possesses no antibiotic activity, was first introduced into medicine as a chelating agent to accelerate the elimination of physiological heavy metals present in high, non-physiological concentrations (therapy of Wilson's disease) and non-physiological heavy metals (antidote in heavy metal poisoning)[5, 6].

D-Penicillamine is becoming increasingly important as a basis therapeutic in rheumatoid arthritis (chronic polyarthritis)[7–9]. Further new indications for D-penicillamine, *e. g.* chronic aggressive hepatitis[10–13] and multiple sclerosis[14], are becoming apparent.

Only pure D-penicillamine is of therapeutic importance as the racemate and the L-isomer are toxic. Further differences between D- and L-penicillamine lie in their antagonistic activity towards vitamin B_6 and their molecular biological behavior (see Section 4.3).

[*] Dr. W. M. Weigert, Dr. H. Offermanns, and Dr. P. Scherberich
Degussa
6 Frankfurt/Main 1, Postfach 2644 (Germany)

2. Manufacture of D-Penicillamine

D-Penicillamine can be manufactured either semi-synthetically by degradation of penicillins or completely synthetically *via* the racemate. Production from penicillins has been considerably improved in the last few years[15]. A new process for the manufacture of fully-synthetic D-penicillamine *via* the racemate and its resolution ("Asinger process") is now also being carried out industrially. Both processes produce highly pure D-penicillamine which is then used as the active ingredient in drug manufacture[*].

2.1. Manufacture of D-Penicillamine by Degradation of Penicillins

On degradation of penicillins [*e. g.* penicillin G *(2)*, Scheme 1]both the β-lactam ring and the thiazolidine ring are opened. The β-lactam ring is best cleaved in the presence of alkali; the resulting penicilloic acid *(3)* is decarboxylated to penilloic acid *(4)*. As a 2-monosubstituted thiazolidine-4-carboxylic acid, *(4)* is relatively stable to hydrolysis. Thus cleavage to D-penicillamine *(1)* and the aldehyde *(5)* requires removal of one or both of the decomposition products from the hydrolysis equilibrium.

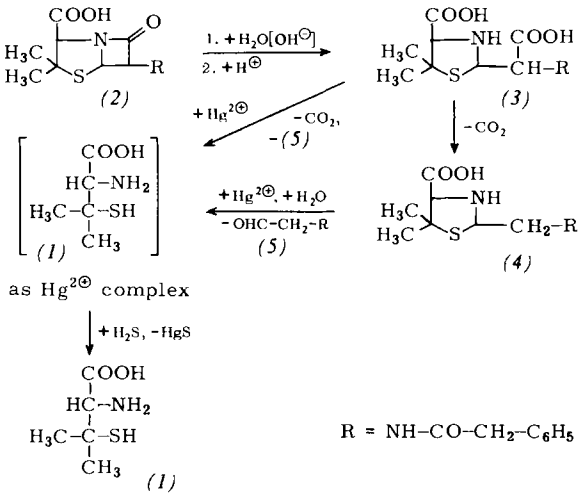
Preferably *(1)* is converted into the sparingly soluble 1:1 or 2:1-D-penicillamine-mercury(II) complexes and separated from the readily soluble product *(5)*[15, 16] (see Section 4.1 for the structure of the complexes).

Treatment with hydrogen sulfide liberates *(1)* from the mercury complex, mercuric sulfide being formed as by-product. Compound *(3)* can also be cleaved directly by mercuric salts. In this variant, decarboxylation and thiazolidine ring opening proceed simultaneously.

In another process the D-penicillamine-mercury 1:1 complex is kept in solution by addition of acid and the aldehyde *(5)*, after reaction with a carbonyl reagent, *e. g.* hydrazine or hydroxylamine, is separated by extraction with an inert organic solvent which is immiscible with water[17].

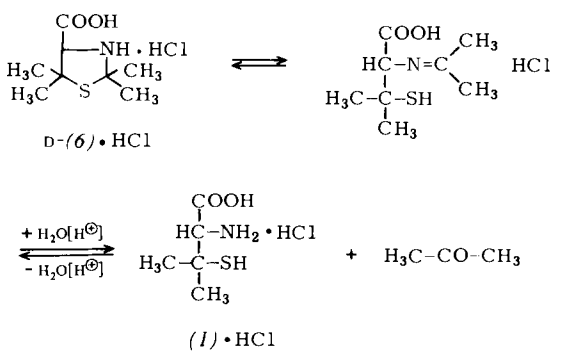
The use of other heavy metal salts in place of the expensive and toxic mercury salts has been recommended[18]. Without the use of heavy metal salts, *(3)* and *(4)* can be converted into D-penicillamine using 5,5-dimethyl-1,3-cyclohexanedione (dimedon)[19] or 4-hydroxycoumarin[20].

[*] D-Penicillamine (semisynthetic): Metalcaptase® (Knoll AG, Ludwigshafen/Heyl & Co, Berlin); D-penicillamine (fully synthetic): Trovolol® (Chemiewerk Homburg, Frankfurt (Main)/Bayer AG, Leverkusen).



Scheme 1

Purification of *(1)* is most suitably carried out by conversion into the hydrogen chloride of D-2,2,5,5-tetramethylthiazolidine-4-carboxylic acid *(6)*. This latter product *(6)* is also known as "D-penicillamine-acetone adduct" or "isopropylidene-D-penicillamine" due to the ease with which it can be reconverted into acetone and *(1)*[30, 31].

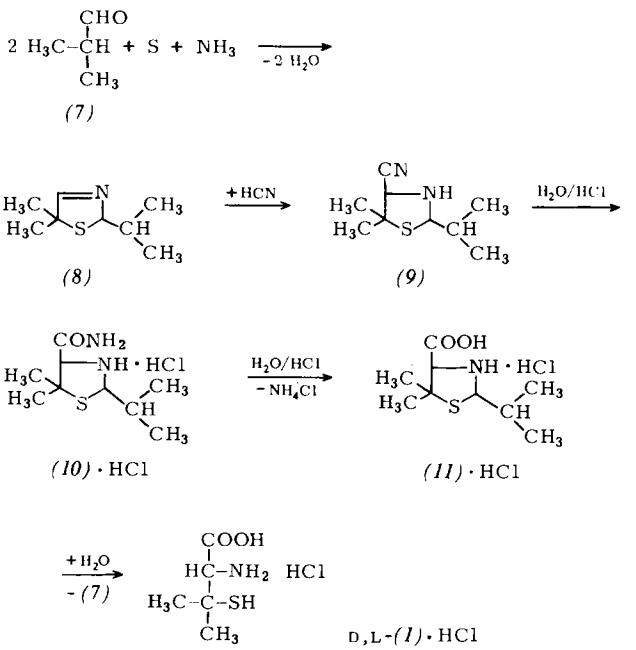


2.2. Manufacture of D-Penicillamine *via* the Racemate

The new fully synthetic process for the manufacture of D,L-penicillamine *via* 3-thiazoline starting from isobutyraldehyde, sulfur, ammonia, and hydrogen cyanide, and the new procedure for obtaining pure D-penicillamine from the racemate without the inevitable production of the L-isomer are based on the fundamental work of *Asinger et al.*[21–24] and have been developed by Degussa/Chemiewerk Homburg[*] to technical maturity[25]. Apart from this technique, which is an alternative to the hydrolysis of penicillins, there are several other procedures for the production of D,L-penicillamine and resolution of the racemate which were primarily developed in connection with the structural elucidation and total synthesis of penicillins during World War II. A description of these methods will be dispensed with here as a detailed review is already available[1]. However, we shall discuss two new synthetic routes, one of which starts from isocyanoethyl acetate and the other utilizes a modified Strecker synthesis.

2.2.1. Synthesis of D,L-Penicillamine *via* 3-Thiazoline

The simultaneous reaction of sulfur and ammonia with isobutyraldehyde *(7)* affords 2-isopropyl-5,5-dimethyl-3-thiazoline *(8)* in *ca.* 80% yield if the resulting water is azeotropically removed (see Scheme 2). Benzene, toluene, cyclohexane, chloroform, or preferably an excess of isobutyraldehyde itself can be used as the azeotropic partner[26]. The 3-thiazoline *(8)* itself is purified by rectification (b.p. 68—70°C/12 torr).



Scheme 2

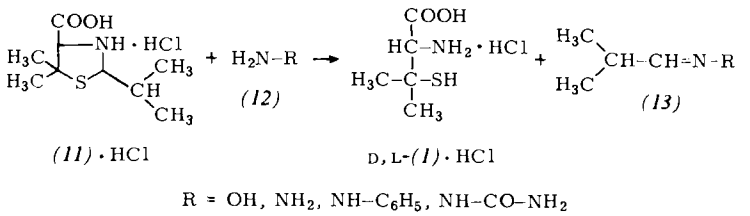
Anhydrous hydrogen cyanide adds across the azomethine group of *(8)* to form 2-isopropyl-5,5-dimethylthiazolidine-4-carbonitrile *(9)* almost quantitatively. The hydrogen cyanide itself can be introduced either as a liquid or as a gas, or actually generated within the reaction mixture itself, for example from sodium cyanide and acids. If addition of HCN is carried out in an inert solvent, *e.g.* diethyl ether or petroleum ether, *(9)* can be isolated in crystalline form (m.p. ≈30°C) by cooling the reaction mixture. It is also possible to work in the absence of solvent and continue directly with the crude nitrile *(9)*.

In order to convert *(9)* into D,L-penicillamine the nitrile group must be saponified to a carboxyl group and the thiazolidine ring opened[27]. This is preferably carried out in several steps: *(9)* dissolved *e.g.* in methanol containing sufficient water to form the amide is treated with hydrogen chloride at 50—65°C. 2-Isopropyl-5,5-dimethylthiazolidine-4-carboxamide hydrogen chloride *(10)*·HCl is then obtained in crystalline form. *(10)*·HCl is subsequently hydrolyzed by refluxing with 10—20% hydrochloric acid to form 2-isopropyl-5,5-dimethylthiazolidine-4-carboxylic acid hydrogen chloride *(11)*·HCl[28]. Use of gaseous hydrogen chloride can be avoided by converting *(9)* into *(10)*·HCl by treatment with at least 30% aqueous hydrochloric acid at 40—70°C[29].

As a 2-monosubstituted thiazolidine derivative, *(11)*·HCl is extremely stable to hydrolytic ring opening[30, 31]. However it is possible to quantitatively convert *(11)*·HCl into D,L-penicillamine hydrogen chloride if the isobutyraldehyde *(7)* formed is azeotropically steam distilled out of the hydrolysis equilibrium[27]. In a variant of this procedure[32] the isobutyraldehyde is converted with a carbonyl reagent *(12)*, *e.g.* hydroxylamine, hydrazine, phenyl hydrazine, or semicarb-

[*] Degussa/Chemiewerk Homburg (Pharmaceutical Division of Degussa).

azide in aqueous solution into a derivative *(13)* which can be isolated by extraction with an inert organic solvent, *e.g.* toluene or chloroform, which is immiscible with water.



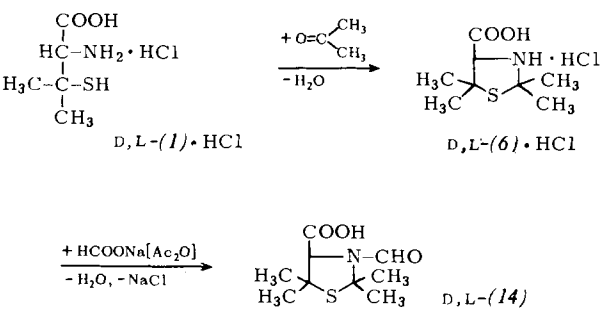
(11) · HCl D,L-*(1)* · HCl

R = OH, NH_2, NH–C_6H_5, NH–CO–NH_2

These methods for ring cleavage of *(11)* · HCl afford an aqueous solution of D,L-penicillamine hydrogen chloride containing ammonium chloride originating from saponification of the nitrile.

The D,L-penicillamine or its hydrogen chloride need not be isolated; after evaporation of the water it is preferable to react the D,L-penicillamine hydrogen chloride, with acetone in an organic solvent, *e. g.* toluene, which is immiscible with water. In this way crystalline D,L-2,2,5,5-tetramethylthiazolidine-4-carboxylic acid hydrogen chloride, D,L-*(6)* · HCl is obtained in admixture with ammonium chloride. From this mixture D,L-penicillamine can be isolated in the pure form or converted into a suitable derivative for resolution.

A new procedure[33] using sodium formate in the presence of acetic anhydride in an organic solvent not miscible with water can be used to advantage for converting D,L-*(6)* · HCl into the corresponding *N*-formyl derivative D,L-*(14)* and permits removal of inorganic salts. The D,L-3-formyl-2,2,5,5-tetramethylthiazolidine-4-carboxylic acid D,L-*(14)*, obtained in high yield and in excellent purity, is well suited for enantiomerization (see Section 2.2.3).



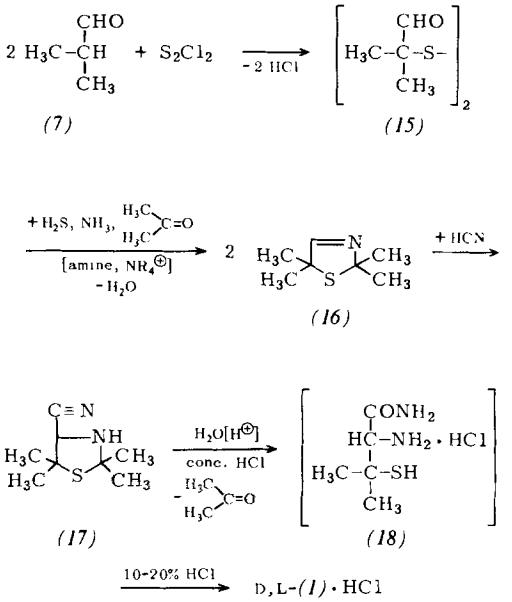
D,L-*(1)* · HCl D,L-*(6)* · HCl

D,L-*(14)*

Using a variant of this technique, D,L-penicillamine can also be prepared from 2,2-dialkyl-5,5-dimethyl-3-thiazolines, and preferably from 2,2,5,5-tetramethyl-3-thiazoline *(16)* (Scheme 3). *(16)* cannot be obtained from isobutyraldehyde *(7)* in one step. For the preparation of *(16)*, isobutyraldehyde is initially reacted with disulfur dichloride to give 2,2'-dithiodiisobutyraldehyde *(15)*[34]. Simultaneous treatment of a mixture of *(15)* and acetone with hydrogen sulfide gas and ammonia gas furnishes *(16)*[35] in satisfactory yields provided that the reaction is carried out in the presence of amines and ammonium salts[36].

The nitrile *(17)* obtained by addition of hydrogen cyanide can be easily hydrolyzed to D,L-penicillamine hydrogen chloride without isolating the intermediate *(18)*[37].

This process does not require a steam distillation or use of a carbonyl reagent for ring cleavage since *(17)* is a 2,2-disubstituted thiazolidine derivative and thus undergoes facile hydrolytic cleavage[31]. Saponification of *(17)* to D,L-*(1)* · HCl has considerable advantages over the previously described pathway *via* the ester of tetramethylthiazolidine-4-carboxylic acid[21]. However, the ease of ring opening in *(17)* does not compensate for the disadvantage of the more complicated synthesis of the thiazoline *(16)* itself.

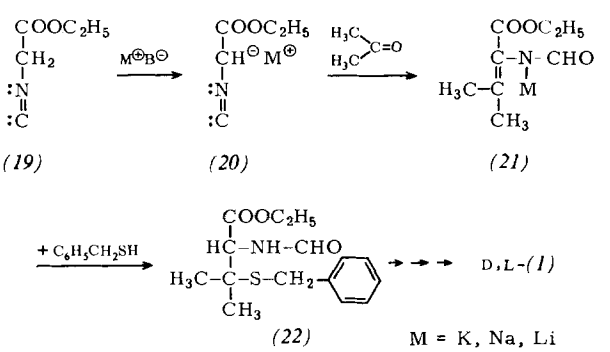


(7) *(15)* *(16)* *(17)* *(18)* D,L-*(1)* · HCl

Scheme 3

2.2.2. Synthesis of D,L-Penicillamine by Other Recent Methods

A general synthesis of *S*-benzyl-*N*-formylcysteines which is also suitable for the manufacture of D,L-*S*-benzyl-*N*-formylpenicillamine developed by *Schöllkopf* and *Hoppe*[38] starts from ethyl isocyanoacetate (see Scheme 4).



(19) *(20)* *(21)* *(22)* M = K, Na, Li D,L-*(1)*

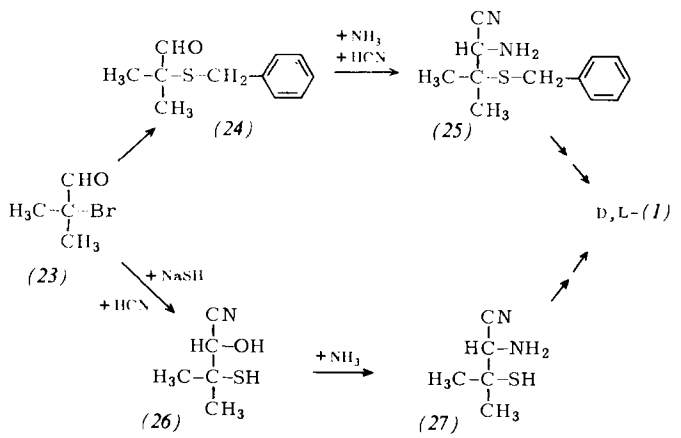
Scheme 4

Metalation of ethyl isocyanoacetate *(19)* by potassium *tert*-butoxide, sodium hydride, or *n*-butyllithium in tetrahydrofuran, and subsequent reaction of the metalated ester *(20)*

with acetone gives the metalated α-formylaminoacrylate *(21)* Treatment of *(21)* with thiobenzyl alcohol and hydrolysis with potassium hydroxide solution yields the ester *(22)* which can be selectively hydrolyzed to D,L-*S*-benzyl-*N*-formylpenicillamine or hydrolytically deformylated and then debenzylated to D,L-penicillamine.

D,L-Penicillamine can also be prepared by a kind of Strecker synthesis[39] (see Scheme 5) in which α-bromoisobutyraldehyde *(23)* is reacted with the sodium salt of thiobenzyl alcohol to give α-benzylthioisobutyraldehyde *(24)*. This product reacts with hydrogen cyanide and ammonia to form the nitrile *(25)*, which can be converted by hydrolysis and debenzylation into D,L-penicillamine in moderate yield.

According to *Ugi* and *Böttner*[40] α-hydroxy-β-mercaptoisovaleronitrile *(26)* can be obtained from α-bromoisobutyraldehyde by reaction with sodium hydrogen sulfide and hydrogen cyanide (see Scheme 5). *(26)* is converted by ammonia into *(27)*, which according to *Böttner*[41] can be saponified to D,L-penicillamine.



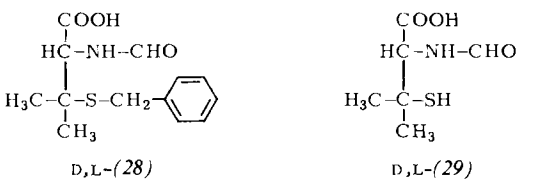
Scheme 5

The methods described in this section do not generally afford pure D,L-penicillamine but rather a derivative suitable for resolution.

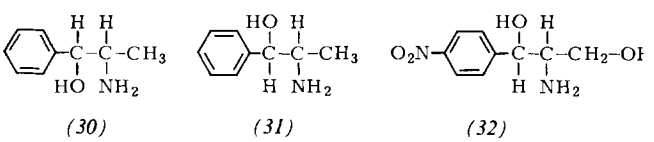
2.2.3. Isolation of D-Penicillamine from the Racemate

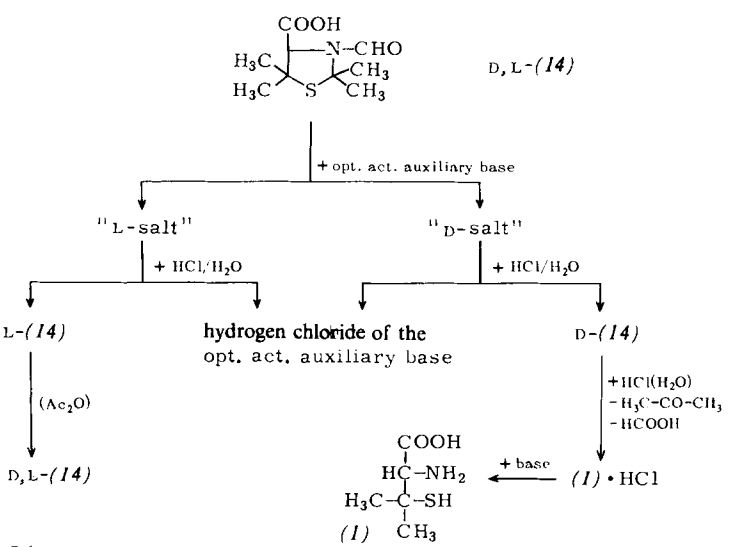
Owing to the widely differing biological properties of the optical antipodes of penicillamine (see Sections 1 and 4.3) it is necessary to quantitatively remove the undesirable L-isomer.

Optical resolution of D,L-penicillamine is performed by the classical method of transforming optical antipodes into diastereoisomers. Thus suitable derivatives of D,L-penicillamine are converted into the diastereomeric salts with alkaloids or other optically active auxiliary bases. Resolution is performed with *N*-acyl derivatives of D,L-penicillamine and of D,L-*S*-benzylpenicillamine as well as with the *N*-acyl derivatives of the condensation products of D,L-penicillamine with carbonyl compounds, especially D,L-3-formyl-2,2,5,5-tetramethylthiazolidine-4-carboxylic acid, D,L-*(14)*. The first racemic resolution was achieved by the previously mentioned "Oxford Group"[42] who resolved D,L-*S*-benzyl-*N*-formylpenicillamine, D,L-*(28)* using the alkaloid brucine. D,L-*N*-Formylpenicillamine, D,L-*(29)* and D,L-*(14)* can also be enantiomerized with brucine[43, 44].



Other bases used in the racemic resolution of D,L-penicillamine are thebaine[45], quinidine[46], cinchonidine[46], (−)-ephedrine[44, 46], and (+)-pseudoephedrine[46]. Regarding the need to quantitatively remove the therapeutically undesirable L-penicillamine, the above optical bases are not wholly suitable for obtaining pure D-penicillamine because in some cases the salts of L-penicillamine derivatives crystallize from the solution first. This is a disadvantage since the diastereoisomer which crystallizes out first always possesses the higher purity[47, 48]. Moreover, the yields are unsatisfactory. For an economically viable separation of the antipodes the very expensive or highly toxic alkaloids can hardly be considered. L-





Scheme 6

Lysine[49], (−)-norephedrine *(30)*[50], (−)-pseudonorephedrine *(31)*[51], and D-(−)-*threo*-2-amino-1-(*p*-nitrophenyl)-1,3-propanediol *(32)*[52] are most suitable as auxiliary bases. These bases are preferentially reacted with D,L-*(14)* according to Scheme 6.

In all cases the amine salts of the D-penicillamine derivatives ("D-salts") are obtained as the more insoluble diastereoisomers. In suitable solvents the solubility differences between the diastereoisomeric salts are so large that quantitative removal of the L-penicillamine derivative becomes feasible. The "D-salts" are preferentially treated with dilute hydrochloric acid in the cold to form the water-soluble hydrogen chloride of the optical base and the sparingly water-soluble D-penicillamine derivative D-*(14)*. On deformylation and ring opening D-*(14)* furnishes pure D-penicillamine · HCl, which can be converted into free D-penicillamine *(1)* with, for example, triethylamine in an alcohol.

The amine salt of the L-penicillamine derivative ("L-salt") retained in the mother liquor on resolution is likewise cleaved with dilute hydrochloric acid to give L-3-formyl-2,2,5,5-tetramethylthiazolidine-4-carboxylic acid L-*(14)*. This product is quantitatively racemized, for example, on refluxing in toluene containing catalytic quantities of acetic anhydride[53], and subjected to renewed resolution. It is thus possible—apart from the losses inevitably incurred by processing—to quantitatively obtain D-penicillamine from the racemic penicillamine derivatives. The optically active adjuvant bases can be almost completely recovered.

3. Physical Properties and Analysis of D-Penicillamine

D-Penicillamine *(1)* is a colorless crystalline powder with a weak odor typical of sulfur-containing amino acids, and a characteristic taste. It is relatively soluble in water but less so in alcohols and almost insoluble in ether, chloroform, carbon tetrachloride, and aliphatic or aromatic hydrocarbons.

(1) melts with decomposition at 202—206 °C (Mettler FP melting point apparatus, starting temperature 195 °C, heating rate 2°/min).

Qualitative identification of *(1)* is based on the reaction with iodine solution (decolorized due to oxidation of the SH group), ninhydrin (blue-violet color), phosphortungstic acid (deep blue color), and acetone (colorless precipitate)[54].

Quantitative determination is best carried out by titration against mercuric acetate solution in the presence of diphenylcarbazone as indicator[54]. Traces of impurities, *e. g.* D-penicillamine disulfide *(39)* may be detected either by TLC or, after silylation, by GLC.

In 1 N sodium hydroxide solution [5 g *(1)* in 100 ml] *(1)* is levorotatory. The pure compound *(1)* to be used as a drug constituent should have an optical rotation of −62.5 to −63.5° (at 20 °C in sodium D light = 589 nm). D-Penicillamine prepared according to the "Asinger process" is identical in its physical, spectroscopic, and chemical properties with the material obtained from penicillin. The stereochemical equivalence of the fully and semi-synthetic D-penicillamine can be confirmed by precision polarimetry and ORD spectroscopy. No traces of the L-isomer can be detected in either semi-synthetic or fully-synthetic D-penicillamine used in drugs formulation by present-day physical methods.

The optical purity can also be confirmed[56] by tests with *E. coli* bacteria, whose growth is selectively inhibited by L-penicillamine[55]. Again no difference was found between semi-synthetic and fully-synthetic D-penicillamine.

4. Biochemical Properties of D-Penicillamine

The biochemical properties of D-penicillamine are primarily based on three types of reaction in which the amino and mercapto groups are principally involved:

1) Chelate formation with heavy metal ions; 2) exchange reactions with low molecular and high molecular weight disulfides; 3) condensation with aldehydes.

4.1. Chelate Formation

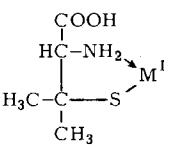
D-Penicillamine is a strong complexing agent and reacts with the majority of heavy metal ions, particularly with those with an affinity for S, to form chelates[57]. While D-penicillamine forms only a 1:1 complex of type *(33)*, *e. g.*, with $Cu^{\oplus}$ ions[58-61], it forms not only 1:1 complexes of types *(33)* and *(34)* but also 2:1 *(35)* or sometimes 3:1 complexes[59-63] with other heavy metal ions.

Depending on the number of functional groups involved in complex formation D-penicillamine functions as a bidentate *(33)* or tridentate ligand *(34)*.

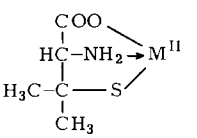
Of the physiological metal ions which participate in complex formation with D-penicillamine, copper, zinc, iron, cobalt, manganese, and nickel deserve mention.

The therapeutic activity of D-penicillamine in the treatment of Wilson's disease is based upon chelate formation with protein-bound copper and its rapid excretion[59, 64, 65]. A similar mode of activity is assumed in for example the treatment of sclerodermia[66] and schizophrenia[67, 68] with D-penicillamine.

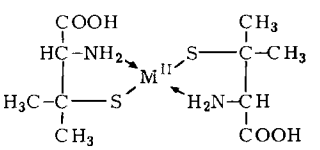
Chelate formation is also the basis for the antidote action of D-penicillamine in heavy metal poisoning, *e. g.* by mercury or lead compounds[69-71].



(33)



(34)



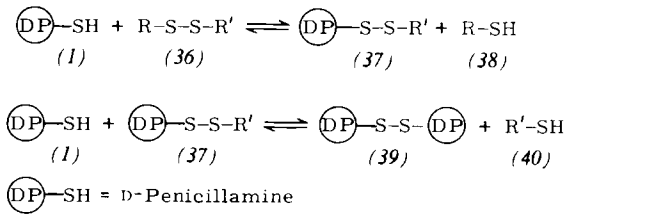
(35)

Undesirable side effects caused by elimination of zinc or other biometals can be avoided by substitution[72].

4.2. Exchange Reactions with Disulfides

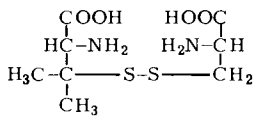
D-Penicillamine *(1)* can react with disulfides *(36)* in organisms according to Scheme 7[73-75]; the mixed disulfide of D-penicillamine *(37)* and the free thiol *(38)* are formed.

(37) can react further with D-penicillamine to give D-penicillamine disulfide *(38)* and the thiol *(40)*.



Scheme 7

The formation of the mixed disulfide *(41)* from D-penicillamine and L-cysteine and of the symmetrical disulfide *(39)* is decisive for the treatment of cystinuria and the associated formation of urinary calculus (cystine stones)[73, 76]. D-Penicillamine disulfide *(39)* and D-penicillamine L-cysteine disulfide *(41)* are much more soluble than cystine and are thus eliminated.

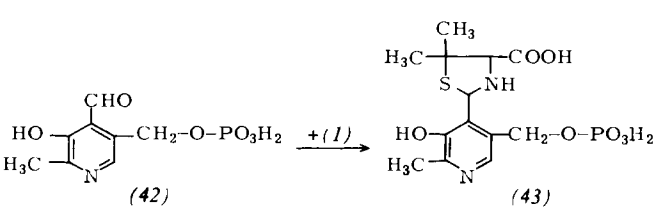


(41)

Similar exchange reactions can also take place with proteins linked intermolecularly through S—S bridges, *e. g.* immunoglobulins, pathological macroglobulins (rheumatic factors) which play an important role in the pathogenesis of rheumatoid arthritis[77–80]. It is suspected that the macroglobulins lose their pathogenic properties through depolymerization according to Scheme 7. This is partly the reason for the use of D-penicillamine in cases of rheumatoid arthritis. The depolymerizing activity of D-penicillamine on macroglobulins was confirmed by *in vitro* experiments[81, 82].

4.3. Reactions with Aldehydes

D-Penicillamine reacts with the aldehyde group of pyridoxal 5'-phosphate *(42)* to form the thiazolidine derivative *(43)*[83–85].

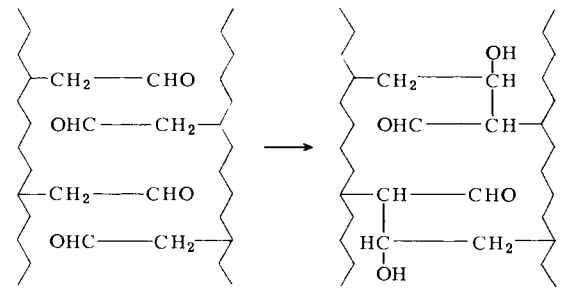


(42) *(43)*

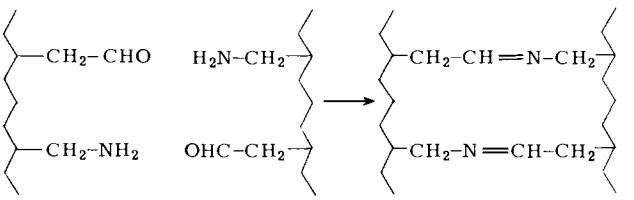
The co-enzyme *(42)* which is formed in the organism from vitamin B_6 plays an important role in amino acid metabolism, in the synthesis of coenzymes, as well as in the biosynthesis of hormones such as adrenalin.

Both isomers of penicillamine possess an anti-vitamin B_6 effect, that of the L-isomer being considerably stronger than that of *(1)*[86, 87]. For this reason, the therapy with D-penicillamine of high stereochemical purity is of particular importance. Vitamin B_6 deficiency symptoms caused by treatment with D-penicillamine are relatively rare and can be corrected by the simultaneous administration of vitamin B_6[88–90]. However, it appears that there is no direct correlation between the reaction of D-penicillamine with *(42)* and its therapeutic activity.

The crosslinking of collagen fibers (tropocollagens) soluble in physiological saline solution to insoluble precollagens plays an important roll in sclerodermia[91–93], chronic aggressive hepatitis[10], and rheumatoid arthritis[94]. The formation of insoluble precollagens is probably initiated by enzymatic oxidation of the ε-amino groups of lysine residues to aldehyde groups. It is assumed that the aldehyde groups are crosslinked *via* aldol condensations (Scheme 8) or by the formation of azomethine bridges (Scheme 9)[95–97].



Scheme 8



Scheme 9

D-Penicillamine reacts with the aldehyde groups of the soluble collagens forming thiazolidines and thus inhibits crosslinking[58, 97].

In contrast to other sulfur-containing amino acids, *e.g.* cysteine D-penicillamine is relatively stable in the organism, and thus its therapeutic activity is fully displayed. It is primarily converted by oxidation or exchange reactions according to Scheme 7 into the disulfides *(39)* and *(41)* and eliminated in this form[98]. Unlike L-penicillamine, D-penicillamine cannot be incorporated into proteins or inhibit protein synthesis[99–101].

Received: September 23, 1974 [A 57 IE]
German version: Angew. Chem. 87, 372 (1975)

[1] *H. T. Clarke, J. R. Johnson,* and *R. Robinson,* The Chemistry of Penicillin. Princeton University Press, Princeton 1949, p. 455.
[2] *E. P. Abraham, E. Chain, W. Baker,* and *R. Robinson,* Nature *151,* 107 (1943).
[3] *J. C. Sheehan* and *K. H. Henery-Jogan,* J. Amer. Chem. Soc. *79,* 1262 (1957); *81,* 3089 (1959).
[4] *O. Süs,* Liebigs Ann. Chem. *559,* 92 (1948); *561,* 31 (1948); *564,* 55 (1949); *568,* 129 (1950); *569,* 153 (1950); *571,* 201 (1951).
[5] *J. M. Walshe,* Lancet *1956,* I, 25.
[6] *J. M. Walshe,* Amer. J. Med. *21,* 487 (1956).
[7] Die Behandlung der Rheumatoiden Arthritis mit D-Penicillamin. Symposion, Berlin, Jan. 1973; "Der Rheumatismus", Vol. 42, Steinkopff-Verlag, Darmstadt 1974.
[8] *I. A. Jaffe,* Ther. Ber. Bayer *45,* (2), 121 (1973).
[9] *F. M. Andrews, D. N. Golding, A. M. Freemann, J. R. Golding, A. T. Day, A. G. S. Hill, A. V. Camp, E. Lewis-Faning,* and *W. H. Lyle,* Lancet *1973,* 275.
[10] *M. Alexander* and *M. Kludas,* München. Med. Wochenschr. *111,* 847 (1969).

[11] *J. Lange, K. Schumacher*, and *H. P. Witscher*, Deut. Med. Wochenschr. *96*, 139 (1971).
[12] *J. Lange, K. Schumacher*, and *H. P. Witscher*, Med. Welt *22*, 1880 (1971).
[13] *E. Wildhirt*, Therapiewoche *1973*, 3.
[14] *W. Danielczyk*, Therapiewoche *1973*, 4704.
[15] *M. Bock*, DOS 2114329 (1971). Heyl & Co.
[16] *E. Ridgway, J. N. Green*, and *N. M. Cross*, Brit. Pat. 854339 (1960), Distillers Co.
[17] *A. R. Restivo, F. A. Dondzila*, and *H. Murphy, Jr.*, US-Pat. 3281461 (1963), Squibb & Sons.
[18] *U. Eberhard, J. Depner*, and *J. Schaumann*, GDR-Pat. 80921 (1969).
[19] *U. Eberhardt, J. Depner*, and *J. Schaumann*, GDR-Pat. 82718 (1970).
[20] *K. Fucik*, CSSR-Pat. 127553 (1966).
[21] *F. Asinger, E.-Ch. Witte, H. Offermanns*, and *M. Ghyczy:* Jahrbuch 1967, Landesamt für Forschung des Landes NRW. Westdeutscher Verlag, Köln 1967.
[22] *F. Asinger* and *H. Offermanns*, Angew. Chem. *79*, 953 (1967); Angew. Chem. internat. Edit. *6*, 907 (1967).
[23] *M. Ghyczy*, Dissertation, Technische Hochschule Aachen 1968.
[24] *R. Gluzek*, Dissertation, Technische Hochschule Aachen 1972.
[25] Europachemie 1972, 290.
[26] *F. Asinger, H. Offermanns*, and *M. Ghyczy*, DOS 1795299 (1968), Degussa; US-Pat. 3700683; Brit. Pat. 1272865.
[27] *F. Asinger, H. Offermanns*, and *M. Ghyczy*, DOS 1795297 (1968), Degussa; Brit. Pat. 1272866.
[28] *F. Asinger, H. Offermanns*, and *M. Ghyczy*, DOS 2032952 (1970); DOS 2123232 (1971), both Degussa.
[29] *F. Asinger, H. Offermanns*, and *R. Gluzek*, DOS 2156601 (1971), Degussa.
[30] See [1], p. 926.
[31] *R. Riemschneider* and *G. A. Hoyer*, Z. Naturforsch. *18b*, 25 (1963).
[32] DOS 2142336 (1971), Degussa.
[33] *P. Scherberich* and *W.-D. Pfeifer*, DOS 2335990 (1973), Degussa.
[34] *W. D. Niederhauser*, US-Pat. 2580695 (1952), Rohm & Haas.
[35] *F. Asinger, M. Thiel*, and *H. G. Hauthal*, Liebigs Ann. Chem. *615*, 70 (1958).
[36] *F. Asinger, H. Offermanns, W.-D. Pfeifer, P. Scherberich*, and *G. Schreyer*, DOS 2254701 (1972), Degussa.
[37] DOS 2163810 (1971), Degussa.
[38] *U. Schöllkopf* and *D. Hoppe*, Liebigs Ann. Chem. *1973*, 799.
[39] See [1], p. 466.
[40] *I. Ugi* and *E. F. Böttner*, Liebigs Ann. Chem. *670*, 83 (1963).
[41] *E. F. Böttner*, Präp. Pharmaz. *5*, (2), 24 (1969).
[42] See [1], p. 462.
[43] See [1], p. 467.
[44] *W. M. Duffin* and *S. Wilkinson*, Brit. Pat. 585413 (1947), Wellcome.
[45] See [1], p. 463.
[46] *P. Mozingo, J. F. McPherson*, and *K. Folkers*, US-Pat. 2539854 (1951), Merck & Co.
[47] *H. D. Jakubke* and *H. Jeschkeit:* Aminosäuren, Peptide, Proteine. Akademie-Verlag, Berlin 1969.
[48] *L. F. Fieser* and *M. Fieser:* Organic Chemistry. Reinhold, New York.
[49] *R. Fahnenstich, J. Heese*, and *H. Offermanns*, DOS 2304054 (1973), Degussa.
[50] *F. Asinger, R. Gluzek, W. v. Bebenburg*, and *H. Offermanns*, DOS 2138122 (1971); DOS 2258411 (1972), both Degussa.
[51] *P. Scherberich*, DOS 2304055 (1973), Degussa.
[52] *P. Scherberich*, DOS 2362687 (1973), Degussa.
[53] *W. M. Duffin* and *S. Wilkinson*, Brit. Pat. 585436 (1947), Wellcome.
[54] The United States Pharmacopeia, 18th Revision, 1970, p. 476.
[55] *R. M. Blair* and *H. V. Aposhian*, Biochim. Biophys. Acta *30*, 214 (1958).
[56] *P. Chandra*, Rheumatismus *42*, 113 (1974).
[57] *C. A. McAuliffe* and *S. G. Murray*, Inorg. Chim. Acta *6*, 103 (1972).
[58] *E. Schiffmann* and *G. R. Martin*, Arch. Biochem. Biophys. *138*, 226 (1970).
[59] *J. Peisach* and *W. E. Blumberg*, Mol. Pharmacol. *5*, 200 (1969).
[60] *M. L. Sharma* and *L. D. Tuck*, Amer. Chem. Soc., 158th Meeting 1969, Abstr. Papers, Medi 59.
[61] *G. Tisman, J. Peisach*, and *V. Herbert*, J. Clin. Invest. *50*, 93a (1971).
[62] *G. R. Lenz* and *A. E. Martell*, Biochemistry *3*, 745 (1964).
[63] *D. A. Doornbos*, Pharm. Weekblad *103*, 1213 (1968).
[64] *M. L. Leu, G. T. Strickland*, and *S. J. Yeh*, J. Lab. Clin. Med. *77*, 438 (1971).
[65] *J. B. Tu, R. Q. Blackwell*, and *R. H. Watten*, Metabolism *14*, 653 (1965).
[66] *M. E. Nimni* and *L. A. Bavetta*, Science *150*, 905 (1965).
[67] *H. Helmchen, H. Hippius, J. Hoffmann*, and *H. Selbach*, Nervenarzt *38*, 218 (1967).
[68] *G. A. Nicolson, A. C. Greiner, W. J. G. MacFarlane*, and *R. A. Baker*, Lancet *1966* I, 344.
[69] *A. Goldberg, J. A. Smith*, and *A. C. Lochhead*, Brit. Med. J. *1963*, 1270.
[70] *O. R. Klimmer*, Arch. Toxikol. *24*, 15 (1968).
[71] *L. Magos* and *T. Stoytcher*, Brit. J. Pharmacol. *35*, 121 (1969).
[72] *C. C. Pfeiffer, J. Cawley, V. Iliev*, and *E. H. Jenney*, Clin. Pharmacol. Ther. *12*, 299 (1971).
[73] *J. C. Crawhall, E. F. Scowen*, and *R. W. E. Watts*, Brit. Med. J. *1963*, 588.
[74] *G. Gorin, G. Doughty*, and *R. Gideon*, J. Chem. Soc. *B 1967*, 729.
[75] *M. Tabachnick, H. N. Eisen*, and *B. Levine*, Nature *174*, 701 (1954).
[76] *G. S. Stokes, J. T. Potts, Jr., M. Lotz*, and *F. C. Bartter*, Clin. Sci. *35*, 467 (1968).
[77] *J. J. Constanzi, C. A. Coltman jr., D. A. Clark, J. J. Tennenbaum*, and *D. Criscuolo*, Amer. J. Med. *39*, 163 (1965).
[78] *G. Virella*, Experientia *27*, 94 (1971).
[79] *E. Prohaska, W. Schwägerl*, and *H. Jesserer*, Klin. Wochenschr. *43*, 141 (1965).
[80] *I. A. Jaffe*, Ann. Rheum. Dis. *22*, 71 (1963).
[81] *H. Mathies* and *H. Gaedicke*, Klin. Wochenschr. *45*, 849 (1967).
[82] *W. Schneider*, München. Med. Wochenschr. *10*, 531 (1967).
[83] *V. Du Vigneaud, E. J. Kuchinskas*, and *A. Horvath*, Arch. Biochem. Biophys. *69*, 130 (1957).
[84] *D. F. Evered, B. M. C. Hargreaves*, and *Z. H. M. Verjee*, Biochem. J. *111*, 15 P (1969).
[85] *G. Hasenbank, F. Körber*, and *P. Siegmund*, Hoppe-Seylers Z. Physiol. Chem. *349*, 310 (1968).
[86] *I. A. Jaffe, K. Altman*, and *P. Merryman*, J. Clin. Invest. *43*, 1869 (1964).
[87] *F. Körber, G. Hasenbank*, and *P. Siegmund*, Z. Klin. Chem. Klin. Biochem. *6*, 58 (1968).
[88] *E. Costa* and *P. Greengard*, Psychopharmacol. Bull. *7*, 30 (1971).
[89] *D. P. Rose*, J. Clin. Pathol. *25*, 17 (1972).
[90] *V. R. Ott* and *K. L. Schmidt*, Internist *15*, 328 (1974).
[91] *R. Bluestone, R. Graham*, and *V. Holloway*, Ann. Rheum. Dis. *29*, 153 (1970).
[92] *A. Böni, K. Pavelka*, and *M. Kludas*, München. Med. Wochenschr. *111*, 1580 (1969).
[93] *E. D. Harris* and *A. Sjoerdsung*, Lancet *1966* II, 996.
[94] *U. S. Müller, H. Wagner, W. Wirth, G. Junge-Hülsing*, and *W. H. Hauss*, Arzneim.-Forsch. *21*, 679 (1971).
[95] *E. J. Miller, S. R. Pinnell, G. R. Martin*, and *E. Schiffmann*, Biochem. Biophys. Res. Commun. *26*, 132 (1967).
[96] *S. R. Pinnell, G. R. Martin*, and *E. J. Miller*, Science *161*, 475 (1968).
[97] *K. Deshmukh* and *M. E. Nimni*, J. Biol. Chem. *244*, 1787 (1969).
[98] *P. Wei* and *A. Sass-Kortsack*, Gastroenterology *58*, 288 (1970).
[99] *A. Wacker, P. Chandra*, and *E. Heyl*, Arzneim.-Forsch. *16*, 825 (1966).
[100] *A. Wacker, E. Heyl*, and *P. Chandra*, Arzneim.-Forsch. *21*, 971 (1971).
[101] *G. Tisman, V. Herbert, L. T. Go*, and *L. Brenner*, Proc. Soc. Exp. Biol. Med. *139*, 355 (1972).

Prostaglandins

By Wilhelm Bartmann[*]

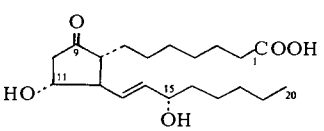
The prostaglandins are lipid-soluble C_{20}-carboxylic acids containing a five-membered ring, several oxygen functions, and at least one double bond. They are found in animal organisms where they stimulate, *inter alia*, the smooth muscle. In the last decade more has been learned about the occurrence, biosynthesis, metabolism and pharmacological properties of the prostaglandins. Analytical methods for their determination, and syntheses for the naturally occurring prostaglandins and their synthetic analogs have been developed. In this report, an attempt is made to show why new knowledge has dramatically stimulated pharmaceutical research in this field.

1. Introduction

In 1965 there appeared in this journal an article dealing primarily with the structural elucidation and biosynthesis of prostaglandins[1]. In the same year some 60 other publications on prostaglandins appeared in the literature. It is estimated that about four papers are now being published each day on these natural products; in the following report, therefore, no attempt has been made to compile a bibliography of prostaglandin research, since numerous excellent reviews, some already in book-form, are available on special aspects of the prostaglandins[2–8].

Generalizing, from the standpoint of the pharmaceutically orientated chemist there have so far been three major phases of development in prostaglandin research:

1. The period of structural elucidation which culminated in 1966 with a joint publication by the research teams of *Bergström et al.* and *van Dorp et al.* on the determination of the absolute configuration of prostaglandin E_1 *(1)*[9].



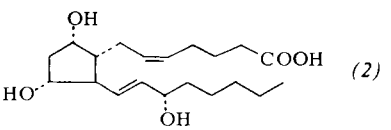
(1)

(1) Prostaglandin E_1 (PGE_1)=(−)-11α,15(*S*)-dihydroxy-9-oxo-13-*trans*-prostenoic acid [**]

2. The synthetic phase in which, from 1965 to 1973, the basic scientific problems of the total synthesis were solved.

3. The molecular-biological phase in which, initially in 1964[10] and intensified since about 1970, the multitudinous, and apparently contradictory, physiological properties of the prostaglandins began to be understood, through the recognition of their molecular biological role in nature (see for example Ref. [7]).

A fourth phase—that of a broad employment of naturally occurring prostaglandins or their synthetic analogs in medicine—has, despite the intensive worldwide efforts of the pharmaceutical industry, not yet got underway if one disregards the single example of the marketing of $PGF_{2\alpha}$ *(2)* as an abortifacient[11].



(2)

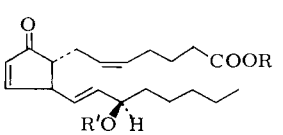
(2) Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$)=(−)-9α,11α,15(S)-trihydroxy-5-*cis*-13-*trans*-prostadienoic acid.

In spite of a certain disillusionment, interest in the prostaglandins continues undiminished—on the one hand because of the ubiquity of these natural products, which are structurally and biogenetically related to the long chain fatty acids, and on the other hand because of their manifold biological properties.

2. Occurrence

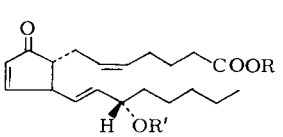
Prostaglandins have been detected in almost all animal organs, albeit in small and tissue-dependent quantities[12]. All investigations carried out so far would suggest that they are synthesized by an enzyme complex, prostaglandin synthetase[13], at the active site and are then rapidly deactivated[14] by another specific enzyme.

Prostaglandins of the A-series or their esters occur in relatively large quantities in a Carribean coral—both in the physiologically inactive (15*R*)-form *(3)* as well as in the active (15*S*)-form *(4)*[15].



(3)

(3a), R = R' = H
(3b), R = CH_3, R' = CH_3CO



(4)

(4a), R = R' = H
(4b), R = CH_3, R' = CH_3CO

Up to 1.5 % by weight of a mixture of several prostaglandins has been isolated from the cortex of wet frozen horny corals *Plexaura homomalla*. This naturally occurring source is already being commercially exploited[16]. The prostaglandins A so obtained serve as starting material for other natural and synthetic prostaglandins.

From results published in the literature so far it would appear doubtful that this biological source will acquire the same degree of importance for the industrial production of prostaglandins as the isolation of the diosgenins from dioscorea species has for the partial synthesis of steroid hormones.

[*] Dr. W. Bartmann
Hoechst AG, Pharma Synthese
623 Frankfurt (M) 80, Postfach 800320 (Germany)

[**] For the structure of other prostaglandins and their nomenclature see also formulas *(2)*, *(4)*, *(7)*, and *(47)* and Ref. [6].

The physiological role played by prostaglandins occurring in marine organisms is as yet unclear[15]; equally unclear is their mode of formation in these lower forms of life[17]. While prostaglandins are known to occur in a very early stage of evolution in the animal kingdom they have not been demonstrated with certainty in the plant kingdom[18].

Prostaglandin-synthetase has been found in a broad spectrum of species including primates, pigs, sheep, and rats down to fishes, mussels and lobsters, thus indicating that the prostaglandins have a basic regulatory function[13].

3. Analysis

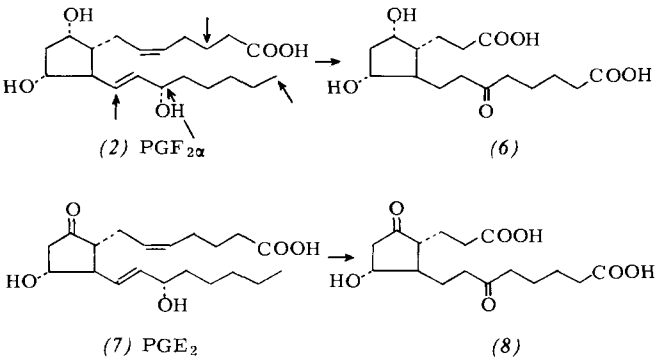
The determination of prostaglandin-synthetase activities and prostaglandin concentrations in tissue is prerequisite for an understanding of the physiological role of prostaglandins. There are, for example, hypotheses which postulate a basic causal interrelation between prostaglandin tissue levels that vary from the norm, and certain types of illnesses (see Section 6).

The determination of prostaglandins normally produced in various tissues abounds in difficulties. The prostaglandins are rapidly deactivated; for example 43% of PGE_1 *(1)* is converted into less polar metabolites[20] after a single passage through the kidney of a dog, while up to 95% of the prostaglandins E_1 *(1)*, E_2 *(7)* and $F_{2\alpha}$ *(2)* are metabolized after a single passage through the lungs of cats, dogs or rabbits[19]. There are also indications that prostaglandin synthetase is stimulated during work-up of the prostaglandins from animal tissues[13, 27], and that prostaglandin levels are simulated which are never met with under "normal conditions".

The relatively expensive, complicated and time-consuming chemical-analytical techniques for the work-up of tissues, and the isolation and concentration of prostaglandins in the presence of comparatively large quantities of lipids and fatty acids having similar physical parameters form the subjects of numerous publications in which the detection of prostaglandins by means of gas chromatography of special derivatives[21], gas chromatography combined with mass spectrometry[22–24], radioimmunoassay[25] and the enzymatic test[26] are reported. It would appear that the most reliable method to date for the determination of "normal" prostaglandin levels in blood plasma is that of the mass spectrometric determination of prostaglandin metabolites[27]. After having laid down the foundations for the determination of prostaglandin concentrations under normal and pathological conditions the standardization and reduction in cost of the analytical methods will in all probability stimulate research into ways of using the determination of prostaglandin concentrations as a diagnostic method.

4. Metabolism

The only essential difference in the metabolism of the prostaglandins and that of the long chain fatty acids lies in the two initial and—for the deactivation—rate-determining steps. The stereospecific 15(*S*)-hydroxyprostaglandin dehydrogenase oxidizes the alcohol function to a ketone, the 13-14-prostaglandin reductase hydrogenates the double bond, and then β- and ω-oxidation follow. Scheme 1 outlines the metabolism of $PGF_{2\alpha}$ *(2)*[28] and PGE_2 *(7)*[29] to the dicarboxylic acids *(6)* and *(8)*, respectively, in humans (for additional metabolites see Refs. [30, 31]).



Scheme 1. Metabolism of prostaglandins $PGF_{2\alpha}$ *(2)* and PGE_2 *(7)* to 19-carboxy-9α,11α-dihydroxy-15-oxo- *(6)* and 19-carboxy-11α-hydroxy-9,15-dioxo-2,3,4,5-tetranorprostenoic acid *(8)*. The arrows in *(2)* indicate the sites of the enzymatic attack.

A therapeutic target is to find ways of slowing down the deactivation of prostaglandins. Considering the ubiquitous occurrence of prostaglandins, the metabolizing enzyme should if possible be locally inhibited. The synthesis of antagonists which displace the prostaglandins from the receptor will be dealt with more closely in Section 5.

In this connection one has also to think of the synthetic prostaglandin analogs, in which the known biochemical degradation reactions can be inhibited or slowed down by suitable structural variations.

5. Biosynthesis

If there is a deficiency or over-production of local hormones[32]—prostaglandins have been defined as such—ways are sought to stimulate or inhibit their biosynthesis, respectively.

In 1964 two laboratories reported that unsaturated fatty acids are precursors of prostaglandins[33, 34] and in 1965 that both oxygen atoms on the ring of the primary prostaglandins E and F originate from the same oxygen molecule[35, 36]. The reaction is catalized by a multienzyme complex, prostaglandin synthetase, which requires several cofactors for the oxidative rearrangement of the essential fatty acids into prostaglandins. Concepts about the mechanistic course of the reaction were developed in 1966[37] and 1967[38][*].

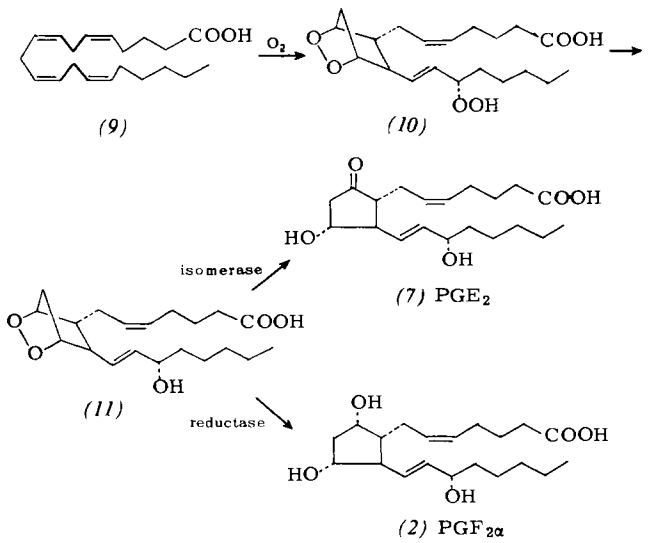
In 1973 previously postulated intermediates of the enzymatic synthesis of prostaglandins E from polyunsaturated fatty acids, were isolated[42–44].

The biosynthesis proceeds in accordance with previously developed concepts in at least three sequential reaction steps. The twofold attack of oxygen is followed by a reduction and isomerization, or a further reduction.

Scheme 2 illustrates these steps.

Of considerable importance from a pharmaceutical standpoint is, on the one hand, *Vane*'s discovery that this biosynthesis can be inhibited by non-steroid anti-inflammatory drugs such as aspirin or indomethacin and, on the other hand, the observations made by numerous research teams that prostaglandins

[*] Details on the elucidation of the biosynthesis can be found in the reviews cited under Refs. [39—41].



Scheme 2. The biosynthesis of prostaglandin E_2 *(7)* and $F_{2\alpha}$ *(2)* from arachidonic acid *(9)*.

or their precursors cause fever and pain and bring about inflammation[32]. The inhibition of prostaglandin synthetase by non-steroid anti-inflammatory agents, as for example in the experimental procedures of *Takeguchi* and *Sih*[45], already forms the basis of a test used in the search for new anti-inflammatory agents. Prostaglandins exercise different activities in different tissues of a given animal species. For example, in the stomach they apparently have a protective function against the overproduction of gastric acids[46]. It is thus understandable why ulcers are observed on administration of high dosages of non-steriod anti-inflammatory drugs, as are occasionally necessary for example for the treatment of rheumatic illnesses.

The problem of finding a non-steroid anti-rheumatic therapeutic which does not adversely affect the stomach is thus basically difficult to solve.

Prostaglandin synthetases from different tissues exhibit varying sensitivity toward medicaments having aspirin-like activity. Herein lies the explanation for the existence of antipyretics similar to aspirin but without an anti-inflammatory component[32]. The complex problem—prostaglandins and production of pain, inflammation, fever—especially rheumatism and peptic ulcers—will be the subject of investigations for years to come, both in basic research institutes and in more practically orientated scientific laboratories of drug houses.

6. Pharmacological Activity

6.1. Abortive and Luteolytic Activity

Despite their close "association" with cyclic AMP *(vide infra)*, prostaglandins exhibit a number of biological qualities that—in contrast to cyclic AMP, which so far has not found a use in medicine—may prove to be of practical value. In the first place one has to consider local applications based on the influence of prostaglandins upon the smooth muscle.

$PGF_{2\alpha}$ and its synthetic analogs are currently being tested throughout the world as abortificiants in the second trimester of pregnancy; they are described by several schools of medicine as the agents of choice[5].

Prostaglandins cannot yet compete, however, with methods currently in use for the induction of abortion in the first and third trimester of pregnancy.

Fundamental investigations which should answer the question of whether $PGF_{2\alpha}$ is a luteolytic hormone in mammals led to positive results on working with ewes[47]. Ovulation can also be induced by $PGF_{2\alpha}$ or its synthetic analogs in cows, mares and sows. Thus a practical application of prostaglandins in the synchronization of oestrus in herds of animals is a distinct possibility[48].

The often discussed question whether prostaglandins can supplement steroids in birth control—a question which is at the same time coupled with the question whether $PGF_{2\alpha}$ is a luteolytic hormone in primates—requires further fundamental research before it can be answered.

6.2. Bronchospasmolytic Activity

Another activity, particularly of prostaglandins of the E and A series, illustrates once again the apparent contradictory biological properties of the prostaglandins. In biological experiments these prostaglandins are recognized by their spasmogenic activity on the isolated smooth muscle, *e.g.*, on the isolated stomach of the rat (Fig. 1).

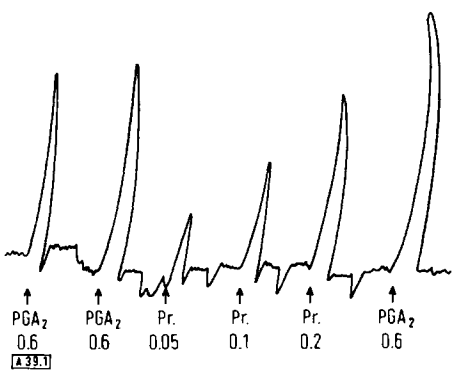


Fig. 1. Dosage-dependent contracting activity of the synthetic prostaglandin (±)-10,11-dihydro-PGA_1 (Pr) *(13a)* on isolated strips of rat stromach compared with natural PGA_2 *(47)*. The figures indicate concentrations in µg/ml.

However these prostaglandins have a relaxing effect on the smooth muscle of the bronchial tract thus suggesting that they or their synthetic analogs might be suitable for the treatment of the acute asthmatic crisis.

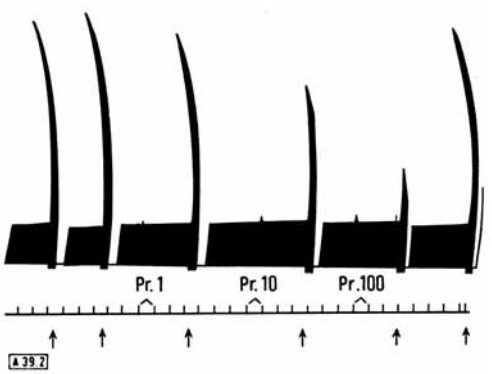


Fig. 2. Dosage-dependent depression of bronchial spasms in guinea pigs induced by 4 µg histamine/kg as a function of the quantity of (±)-10,11-dihydro-PGA_1 (Pr) *(13a)*. The figures represent doses in ng/animal. 1 Subdivision = 1 minute.

Fig. 2 illustrates how bronchial spasms produced by histamine in guinea pigs can be dosage-dependently depressed by pretreatment with (±)-10,11-dihydro-PGA_1 *(13a)*. The transient activity of prostaglandins due to their rapid metabolization is advantageous in this case; for example, repeated administration of this bronchospasmolytic does not lead to an accumulation of the active substance.

6.3. Inhibition of Gastric Secretion

Regulation of gastric secretion by prostaglandins could possibly be used in the treatment of hyperacidity, and perhaps prostaglandin derivatives can be used in ulcer therapy[49].

It has not definitely been proven that the influence of prostaglandins on gastric secretion is due primarily to a change in the blood circulation through the gastric mucosa[50].

6.4. Cardiovascular Activity and Blood Pressure

The hypotensive and simultaneous diuretic and sodium diuretic activity of renally produced prostaglandins is of fundamental interest in basic investigations concerning the treatment of essential hypertension[51, 52]. The hypothesis that prostaglandins of the A or E series are natural antagonists of the pressor peptides angiotension I or II seems to be confirmed.

In this context the question whether PGA_2 *(47)* or PGE_2 *(7)* is the—hypothetical—renal, sodium diuretic and antihypertensive hormone[53, 54] is of secondary importance, from the standpoint of the synthetic chemist. The properties of prostaglandin analogs—and only such compounds could be of practical value in the treatment of essential hypertension if they can be given orally and demonstrate a prolonged activity—do not always correspond quantitatively to the naturally occurring parent substances, particularly in the A and E series.

The possible role which the essential fatty acids may play in the prophylaxis of circulatory diseases could be derived from the fact that they are biogenetic precursors of the prostaglandins[55, 56].

In principle it is possible to extend the transient—lasting at the most ten minutes—hypotensive activity of the natural prostaglandins E and A by the synthesis of suitable derivatives, and it is also possible to replace, at least in animal experiments, the intravenous administration by oral administration[57]. Continued investigations with prostaglandins will undoubtedly lead to practical results in the treatment of hypertension, although when and in what form cannot be predicted.

A large number of other physiological properties are still the subject of fundamental research and therefore are currently of more interest to the biologist than to the chemist, who is looking for criteria which will allow him to modify basic principles provided by nature in such a way that selected properties can be optimized and others suppressed. In this connection one should remember the numerous modifications of the steriod skeleton which have led to the development of new drugs.

7. Structure—Activity Relationships

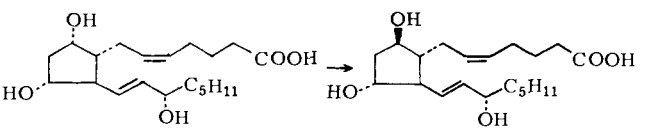
In order to produce drugs having the desired activity, structure-activity relationships must first be clarified. Qualitative differences (for one organ in one animal species) can easily be recognized in the case of naturally occurring prostaglandins of the E and F series; for example prostaglandin $F_{2\alpha}$ *(2)* exercises a spasmogenic activity on the bronchial muscle whereas PGE_2 *(7)* exhibits spasmolytic activity[58].

It has not yet been possible to decide whether the difference in physiological activity between the prostaglandins E and A—probably pharmaceutically useful—is of a qualitative or quantitative nature. The qualitative differences between the prostaglandins of the E and F series can also be confirmed by molecular biological investigations[59]. It remains to be seen whether intermediates in the biosynthesis possess particular activities which the relatively stable end-products, the prostaglandins, lack. Although we are still a long way from compiling a catalog of structure-activity relationships it is possible on the basis of the available biological results to assume that prostaglandins are not unspecific surface-active agents but rather that they require for their activity definite structures, definite configurations and possibly even definite conformations.

This can be illustrated by a few examples.

1. All investigations on structural variations published so far in the literature suggest that the characteristic activity of natural prostaglandins, *i.e.*, the influence upon the tone of the smooth muscle, is associated with a cyclopentane ring bearing at least one oxygen function.

2. The spatial arrangement of the oxygen substituents is important for the type of activity; thus, for example, the bronchospasmogenic properties of $PGF_{2\alpha}$ *(2)* are transformed into bronchospasmolytic properties on configurational inversion of the substitutents on C^9[60].



(2) $PGF_{2\alpha}$ *(12)*

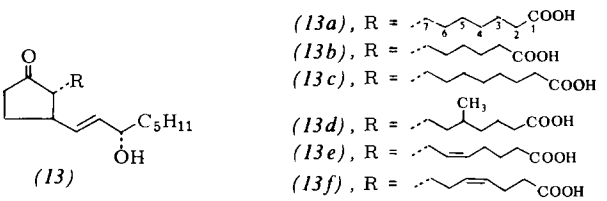
3. The length of the side chain carrying the carboxylic group in compounds of the 10,11-dihydro-PGA_1 type *(13)* is important for optimal activity. For example, lengthening or shortening of this chain by only one methylene group drastically reduces the spasmogenic activity[61].

4. The conformation of this side chain also influences the activity.

If, for example, a proton on the 2-, 3-, 4-, 5-, or 6-position of 10,11-dihydroprostaglandin A, *(13a)*, a compound which is closely related in structure and biological properties to naturally occurring PGA_1, is substituted by a methyl group—a procedure in which the lipophilic nature of the 2-, 3-, 4-, 5-, or 6 substituted molecules being compared remains essentially unaltered while steric relationships change, then the maximum spasmogenic activity as measured on the isolated stomach of the rat is obtained with the 5-methyl compound *(13d)*[61]. A possible explanation for this is that in the 5-methyl compound the zig-zag arrangement of the side chain, which has been proven for a natural crystalline prostaglandin by X-ray analysis[62] and has been required for solutions of prostaglandins[63], is the least disturbed. In its spasmogenic activity, however, the 5-methyl compound is considerably less active than 10,11-dihydroprostaglandin A_1 *(13a)*. However,

a final statement will only be possible after a separation of racemates and diastereomers.

On going from 10,11-dihydroprostaglandin A_2 *(13e)* to its double-bond isomer 7-[2-(3-hydroxy-1-*trans*-octenyl)-5-oxocyclopentyl]-4-*cis*-heptenoic acid *(13f)* a clear separation of the hypotensive and spasmogenic activities of *(13e)* is achieved. *(13f)* does not reduce the blood pressure whereas its spasmogenic activity is comparable to that of *(13e)*[61].



These results lead to the indirect conclusion that for prostaglandins there are specific receptors at the site of activity which are sensitive to stereochemical changes and that receptors from tissues of different organs are influenced to different extents by structural and configurational changes in the prostaglandins interacting with them.

8. Receptors

Proof of the existence of special prostaglandin binding proteins, which are receptors for prostaglandin E, has been obtained in isolated mouse ovaries[64], in rat stomach[65], in the liver[66], in thyroid glands[68] and in the luteal cells of several animal species[67]. Furthermore, these experiments lead to the hypothesis that such receptors are localized in cell membrane. The extensive investigations by *Sutherland*[69] have shown that the adenyl cyclase which is localized in the cell membrane controls the tissue levels of cyclic AMP, the "second messenger".

The interaction between cyclic AMP and prostaglandins was first observed as long ago as 1964[10]. Today, we have evidence that the activity of prostaglandin E on the above mentioned receptors is based upon its influence on the level of cyclic AMP, and is in general coupled with an increased synthesis of this material.

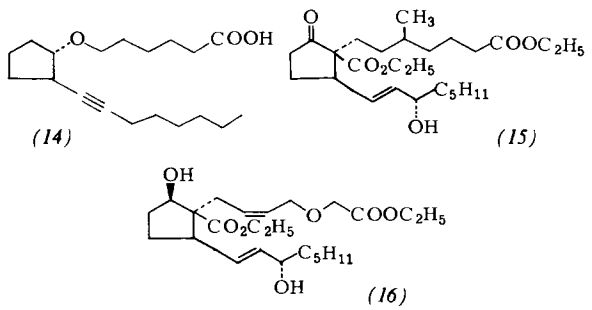
A receptor for $PGF_{2\alpha}$ in luteal cells of sheep has recently been detected[70]. In physiological concentrations, however, $PGF_{2\alpha}$ does not influence the level of cyclic AMP, but probably that of cyclic GMP[59].

A general hypothesis which unequivocally regards the prostaglandins as a link in an information chain, does not as yet exist. However, the stimulation of progesterone synthesis in the ovaries of mice can probably be regarded as an activity of the "messenger PGE_2"[64].

9. Prostaglandin Antagonists

Other compounds apart from naturally occurring prostaglandins can attack the prostaglandin receptors and either competitively or non-competitively inhibit their activity.

Compounds structurally related to natural prostaglandins, are the 7-oxaprostaglandins *(14)*[71]. These compounds competitively inhibit the spasmogenic activity of prostaglandins and can also displace PGE_2 *(7)* from the receptor[64]. 8-Ethoxycarbonyl-10,11-dihydroprostaglandins A *(15)* and *(16)* have recently been synthesized and these inhibit the spasmogenic activity of natural prostaglandins to a greater extent than do the 7-oxaprostaglandins[61].

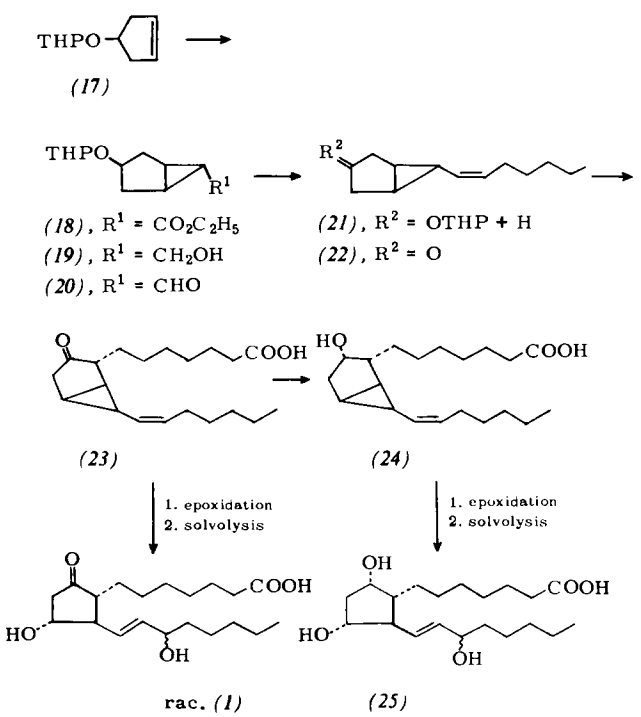


Further examples of prostaglandin antagonists are dibenzoxazine derivatives and polyphloretin phosphate[*].

The prostaglandins E stimulate the production of cyclic AMP in rat brain homogenates. This stimulation is inhibited by morphine[73]. Morphine does not, however, inhibit prostaglandin biosynthesis. Further experiments are necessary to clarify the question of whether this is a true antagonism and whether the analgesic activity of certain centrally attacking analgesics can be solely derived from their properties as prostaglandin antagonists.

10. Chemistry of the Prostaglandins

While the physiological role of prostaglandins and their potential therapeutical usefulness are still the subject of basic



Scheme 3. The most important steps in the synthesis of rac. prostaglandin E_1 *(1)* and $F_{1\alpha}$ *(25)* after *Just* and *Simonovitch* [74]. THP = Tetrahydropyranyl.

[*] Detailed information on substances which inhibit the activity of prostaglandins and on their therapeutic potentialities, may be found in Ref. [72].

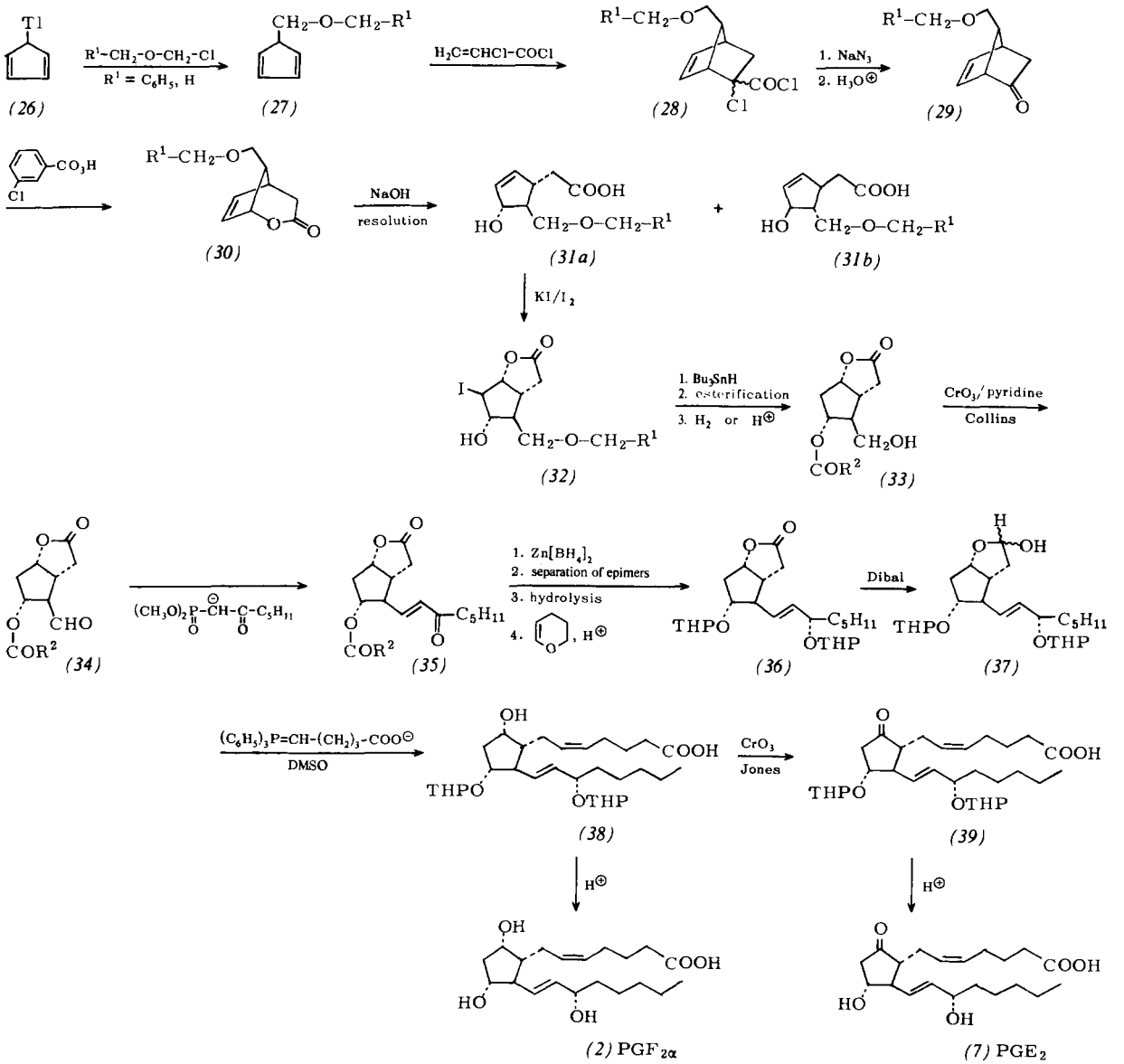
research, despite countless publications, the scientific problems of the synthesis have been fundamentally solved.

The first total synthesis of the prostaglandins E_1 and $F_{1\alpha}$ was reported by *Just* and *Simonovitch* in 1967[74]; although its reproduction initially produced problems, it formed the basis for extensive synthetic work by the Upjohn company, who, from 1968 to 1973, published modifications of the original principles of the synthesis[75–77]. The fundamental step in the *Just* synthesis consisted in a stereospecific opening of a cyclopropyl oxide of *(23)* in which the α-hydroxy group in position 11 together with the *trans* double bond in position 13—14 were stereospecifically introduced, whereas epimers were obtained on C^{15}. The essential steps of the synthesis are illustrated in Scheme 3.

The first synthesis of an optically active prostaglandin was accomplished by *Corey* at Havard University in 1969[79], about one year after he had reported the total synthesis of the racemates of the prostaglandins E_1 and F_1[78].

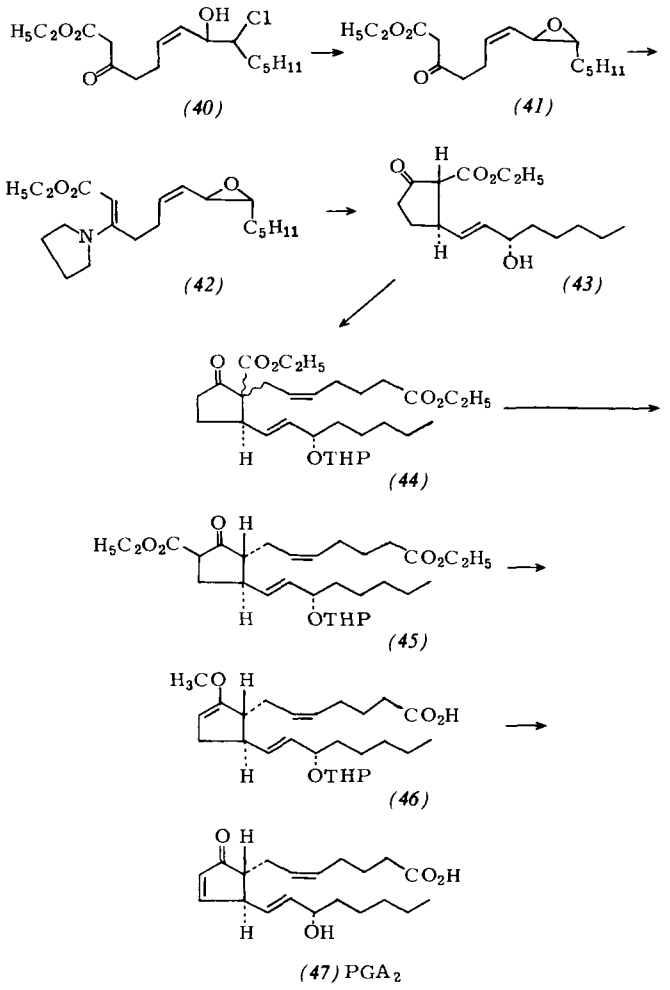
The important synthesis described by the Harvard group[80], by which primarily prostaglandins of the E_2 and $F_{2\alpha}$ series together with a number of non-natural analogs can be synthesized, uses the Diels-Alder reaction as the initial step. This synthesis has been developed in industrial laboratories up to pilot plant production. Starting with the intermediate *(28)*, obtained by the Diels-Alder reaction just mentioned, a synthon *(34)* is built up containing four of five chiral centers of $PGF_{2\alpha}$. Resolution of the optical antipodes is also possible at an early stage (Scheme 4)[80].

As the introduction of the *trans* double bond in the lower side chain using the Horner-Emmons-Wittig reaction *(34)*→*(35)* and the introduction of the *cis* double bond in the upper side chain using a variation of the Wittig reaction *(37)*→*(38)* proceed stereospecifically, the only non-stereospecific reaction of this synthesis was, initially, the reduction of the 15-keto compound *(35)* to the corresponding alcohol. However, using special reducing agents this reaction could also be carried out stereoselectively[81]. This synthesis has been varied and extended, not only in the laboratories of Harvard University but also in several industrial laboratories. For example, new ways have been described for the production of the intermediate *(34)*[82–84].



Scheme 4. Synthesis of prostaglandin $F_{2\alpha}$ *(2)* and E_2 *(7)* according to *Corey et al.* [80]. THP = Tetrahydropyranyl, Dibal = Diisobutylaluminum hydride.

Lack of space prevents commenting on all the previously published total prostaglandin syntheses. Of the syntheses whereby also the *S*-configuration of the OH group on C^{15} could be stereospecifically introduced, mention must be made of the total synthesis of prostaglandin A_2 *(47)* by *Mathieu et al.* (Roussel-Uclaf), the essential stage of which consists of an intramolecular S_N2' reaction in which the asymmetric carbon atoms are introduced into positions 12 and 15 (Scheme 5)[85].



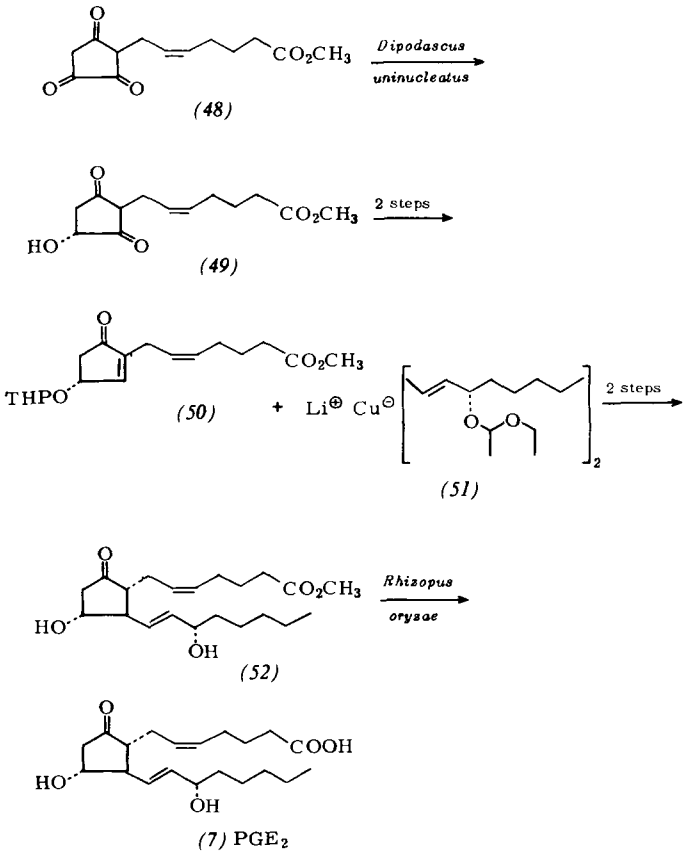
Scheme 5. Synthesis of prostaglandin A_2 *(47)* according to *Mathieu et al.* [85]. THP = Tetrahydropyranyl.

Both the Syntex group[87] and *Sih*[86] of the University of Wisconsin almost simultaneously reported the synthesis of prostaglandins using the conjugated addition of organocopper compounds to substituted cyclopentenones.

As illustrated in reaction Scheme 6, *Sih*[86] used an additional microbiological reduction and a microbiological esterification in his stereospecific total synthesis.

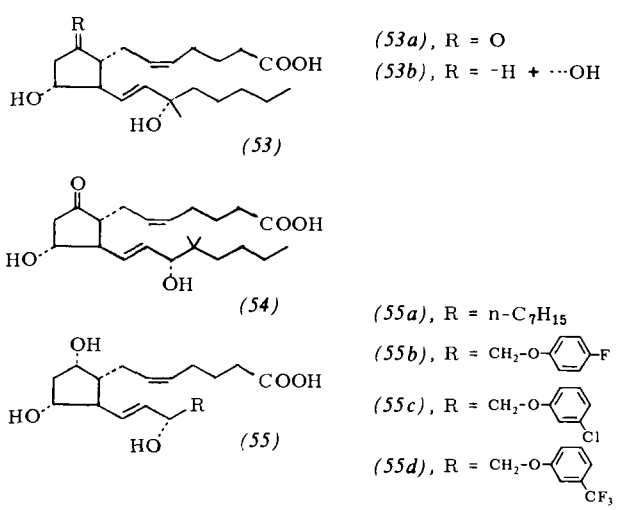
Synthetic work on prostaglandins is at present concentrated in industry, which is less interested in the stereospecific total synthesis of the natural products than in syntheses which can produce a series of structural and configurational analogs.

With such synthetic analogs the aim is to achieve a) a split of the pharmacological activities and b) in general a prolongation of certain activities. 15-Methyl-$PGF_{2\alpha}$ *(53b)*, 15-methyl-PGE_2 *(53a)* and 16,16-dimethyl-PGE_2 *(54)*[49, 88] are substances which, as a result of a hindered or totally suppressed attack of 15(*S*)-prostaglandin dehydrogenase, are metabolized more slowly and, as a result of their increased half-life, are



Scheme 6. Synthesis of prostaglandin E_2 *(7)* according to *Sih* [86]. THP = Tetrahydropyranyl.

better abortificiants and inhibitors of gastic secretion than the unsubstituted compounds. Analogs of $PGF_{2\alpha}$ *(55a)*—*(55d)*[48] exhibit in animal experiments an increased luteolytic activity. It is understandable that economic considerations conflict with the optimal exchange of information in this field.



11. Closing Remarks

Bearing in mind the amount of information to be covered, the selection in this paper of individual aspects of prostaglandin research has, to a certain extent, been somewhat arbitrary. This limitation, however, does not affect the statement that

from the extensive research being carried out on this class of natural products substantial progress in medicine, pharmacy and chemistry can be expected.

I wish to thank Dr. Babej for providing me with experimental biological results and Dr. Kunstmann for a critical review of the manuscript.

Received: August 30, 1974 [A 39 IE]
German version: Angew. Chem. 87, 143 (1975)

[1] *B. Samuelsson*, Angew. Chem. 77, 445 (1965); Angew. Chem. internat. Edit. 4, 410 (1965).
[2] *P. W. Ramwell* and *J. E. Shaw:* "Prostaglandins". Ann. N. Y. Acad. Sci. *180*, 1—568 (1971).
[3] *S. Bergström* and *S. Bernhard:* Advances in the Biosciences 9. International Conference on Prostaglandins, Vienna, September 1972. Pergamon, Oxford, and Vieweg, Braunschweig 1973.
[4] *M. F. Cuthbert:* The Prostaglandins, Pharmacological and Therapeutic Advances. William Heinemann Medical Books, London 1973.
[5] *E. M. Southern:* The Prostaglandins, Clinical Application in Human Reproduction. Futura Publ. Comp., New York 1972.
[6] *P. W. Ramwell:* The Prostaglandins. Plenum Press, New York 1973.
[7] *R. H. Kahn* and *W. E. M. Lands:* Prostaglandins and Cyclic AMP. Academic Press, New York 1973.
[8] *T. O. Oesterling, W. Morozowich*, and *T. J. Roseman*, J. Pharm. Sci. *61*, 1861 (1972).
[9] *D. H. Nugteren, D. A. van Dorp, S. Bergström, M. Hamberg*, and *B. Samuelsson*, Nature *212*, 38 (1966).
[10] *D. Steinberg, M. Vaughan, P. J. Nestel, O. Strand*, and *S. Bergström*, J. Clin. Invest. *43*, 1533 (1964).
[11] Dinoprost®, Upjohn & Co.
[12] *S. Bergström, L. A. Carlson*, and *J. R. Weeks*, Pharmacol. Rev. *20*, 1 (1968).
[13] *E. J. Christ* and *D. A. van Dorp* in [3], p. 35.
[14] *S. H. Ferreira* u. *J. R. Vane*, Nature *216*, 868 (1967).
[15] *A. J. Weinheimer* and *R. L. Spraggins*, Tetrahedron Lett. *1969*, 5185; *W. P. Schneider, R. D. Hamilton*, and *L. E. Rhuland*, J. Amer. Chem. Soc. *94*, 2122 (1972), and literature cited therein.
[16] Chem. Unserer Zeit 7, 95 (1973), and literature cited therein.
[17] *E. J. Corey* and *W. N. Washburn*, J. Amer. Chem. Soc. 96, 934 (1974).
[18] *M. Attrep, K. A. Attrep*, and *J. M. Mariani*, Lipids *8*, 484 (1973).
[19] *P. J. Piper, J. R. Vane*, and *H. J. Wyllie*, Nature *225*, 600 (1970).
[20] *J. Nakano*, Brit. J. Pharmacol. *40*, 317 (1970).
[21] *P. W. Ramwell* and *E. G. Daniels* in *G. V. Marinetti:* Lipid Chromatographic Analysis. Vol. 2. Marcel Dekker, New York 1969, p. 313.
[22] *K. Green* in [3], p. 91.
[23] *U. Axen, L. Baczynskyj, D. J. Duchamp, K. T. Kirton*, and *J. F. Zieserl, Jr.* in [3], p. 109.
[24] *K. Gréen, E. Gangström, B. Samuelsson*, and *U. Axen*, Anal. Biochem. *54*, 434 (1973).
[25] *L. Levine, R. M. Gutierrez-Cernosek*, and *H. V. Vunakis* in [3], p. 71.
[26] *E. Änggård, F. M. Matzchinsky*, and *B. Samuelsson*, Science *163*, 479 (1969).
[27] *B. Samuelsson* in [3], p. 7.
[28] *E. Granström* and *B. Samuelsson*, J. Amer. Chem. Soc. *91*, 3398 (1969).
[29] *B. Samuelsson, E. Granström, K. Gréen*, and *M. Hamberg* in [2], p. 138.
[30] *M. Hamberg* and *M. Wilson* in [3], p. 39.
[31] *E. Granström* in [3], p. 49.
[32] *J. R. Vane* in [3], p. 395.
[33] *S. Bergström, H. Danielsson*, and *B. Samuelsson*, Biochim. Biophys. Acta *90*, 207 (1964).
[34] *D. A. van Dorp, R. K. Beerthuis, D. H. Nugteren*, and *H. Vonkeman*, Biochim. Biophys. Acta *90*, 204 (1964).
[35] *R. Ryhage* and *B. Samuelsson*, Biochem. Biophys. Res. Commun. *19*, 279 (1965).
[36] *D. H. Nugteren* and *D. A. van Dorp*, Biochim. Biophys. Acta *98*, 654 (1965).
[37] *D. H. Nugteren, R. K. Beerthuis*, and *D. A. van Dorp*, Rec. Trav. Chim. Pays-Bas *85*, 405 (1966).
[38] *B. Samuelsson*, Progr. Biochem. Pharmacol. *3*, 59 (1967).
[39] *B. Samuelsson*, Progr. Biochem. Pharmacol. *5*, 109 (1969).
[40] *W. Lands, R. Lee*, and *W. Smith* in [2], p. 107.
[41] *B. Samuelsson:* Biosynthesis and Metabolism of Prostaglandins. Seminaire Inserm, Prostaglandins 1973. Editions Inserm, Paris 1973, p. 21.
[42] *M. Hamberg* and *B. Samuelsson*, Proc. Nat. Acad. Sci. USA *70*, 899 (1973).
[43] *D. H. Nugteren* and *E. Hazelhof*, Biochim. Biophys. Acta *326*, 448 (1973).
[44] *M. Hamberg, J. Svensson, T. Wakabayashi*, and *B. Samuelsson*, Proc. Nat. Acad. Sci. USA *71*, 345 (1974).
[45] *C. Takeguchi* and *C. J. Sih*, Prostaglandins *2*, 169 (1972).
[46] See, *inter alia*, *I. H. M. Main* in [4], p. 287.
[47] *J. A. McCracken, B. Barcikowski, J. C. Carson, K. Gréen*, and *B. Samuelsson* in [3], p. 599.
[48] *D. Binder, J. Bowler, E. D. Brown, N. S. Crossley, J. Hutton, M. Senior, L. Slater, P. Wilkinson*, and *N. C. A. Wright*, Prostaglandins *6*, 87 (1974).
[49] *A. Robert, B. Nylander*, and *S. Andersson*, Life Sci. *14*, 533 (1974).
[50] *I. H. M. Main* and *B. J. R. Whittle*, Brit. J. Pharmacol. *49*, 428 (1973).
[51] *J. B. Lee* in [6], p. 133.
[52] *J. Nakano* in [6], p. 239.
[53] *J. B. Lee:* The Prostaglandins and the Regulation of Systemic Blood Pressure and Sodium and Water Homeostasis. Seminaire Inserm, Prostaglandins 1973, Editions Inserm, Paris 1973, p. 161.
[54] *D. A. Terragno, J. C. Strand, D. A. Pacholczyk*, and *J. C. McGiff:* Prostaglandin E_2, an Intrarenal Hormone. Seminaire Inserm, Prostaglandins 1973, Editions Inserm, Paris 1973, p. 207.
[55] *W. Förster*, Deut. Gesundheitsw. *27*, 2264 (1972).
[56] *M. Cohen, J. Sztokalo*, and *E. Hinsch*, Life Sci. *13*, 317 (1973).
[57] Farbwerke Hoechst, unpublished results.
[58] *M. F. Cuthbert* in [4], p. 253.
[59] *F. A. Kuehl, Jr.*, Prostaglandins *5*, 325 (1974).
[60] *M. E. Rosenthale, A. Dervinis, J. Kassarich, A. Blumenthal*, and *M. I. Gluckman*, Prostaglandins *3*, 767 (1973).
[61] Farbwerke Hoechst, unpublished results.
[62] *S. Abrahamsson*, Acta Crystallogr. *16*, 409 (1963).
[63] *J. R. Hoyland* and *L. B. Kier*, J. Med. Chem. *15*, 84 (1972).
[64] *F. A. Kuehl, Jr., V. J. Cirillo, E. A. Ham*, and *J. L. Humes* in [3], p. 155.
[65] *O. V. Miller* and *W. E. Magee* in [3], p. 83.
[66] *M. Smigel* and *S. Fleischer*, Fed. Proc. *32*, 454 (1973).
[67] *Ch. V. Rao*, Prostaglandins *4*, 567 (1973).
[68] *W. V. Moore* and *J. Wolff*, J. Biol. Chem. *248*, 5705 (1973).
[69] See, *e.g.*, *E. W. Sutherland*, Science *177*, 401 (1972).
[70] *W. S. Powell, S. Hammarström*, and *B. Samuelsson*, Eur. J. Biochem. *41*, 103 (1974).
[71] *J. Fried*, Nature *223*, 208 (1969).
[72] *J. H. Sanner*, Arch. of Intern. Med. *133*, 133 (1974).
[73] *H. O. Collier* and *A. C. Roy*, Nature *248*, 24 (1974).
[74] *G. Just* and *C. Simonovitch*, Tetrahedron Lett. *1967*, 2093.
[75] *G. Just, C. Simonovitch, F. H. Lincoln, W. P. Schneider, U. Axen, G. B. Spero*, and *J. E. Pike*, J. Amer. Chem. Soc. *91*, 5364 (1969).
[76] *W. P. Schneider, U. Axen, F. H. Lincoln, J. E. Pike*, and *J. L. Thompson*, J. Amer. Chem. Soc. *91*, 5372 (1969).
[77] *R. C. Kelly, V. Van Rheenen, I. Schletter*, and *M. D. Pillai*, J. Amer. Chem. Soc. *95*, 2746 (1973).
[78] *E. J. Corey, N. H. Anderson, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas*, and *R. E. K. Winter*, J. Amer. Chem. Soc. *90*, 3245 (1968).
[79] *E. J. Corey, I. Vlattas*, and *K. Harding*, J. Amer. Chem. Soc. *91*, 535 (1969).
[80] *E. J. Corey, Th. K. Schaaf, W. Huber, U. Koelliker*, and *N. M. Weinshenker*, J. Amer. Chem. Soc. *92*, 397 (1970).
[81] *E. J. Corey, S. M. Albonico, U. Koelliker, T. K. Schaaf*, and *R. K. Varma*, J. Amer. Chem. Soc. *93*, 1491 (1971), and literature cited therein.
[82] *R. B. Woodward, J. Gosteli, I. Ernest, R. J. Friary, G. Nestler, H. Raman, R. Sitrin, Ch. Suter*, and *J. K. Whitesell*, J. Amer. Chem. Soc. *95*, 6853 (1973).
[83] *J. K. Sutherland* and *T. R. Peel*, J. C. S. Chem. Comm. *1974*, 151.
[84] *E. J. Corey, J. S. Bindra, A. Grodski*, and *Th. K. Schaaf*, J. Amer. Chem. Soc. *95*, 7522 (1973).
[85] *J. Martel, E. Toromanoff, J. Mathieu*, and *G. Nomine*, Tetrahedron Lett. *1972*, 1491.
[86] *J. B. Heather, R. Sood, P. Price, G. P. Peruzzotti, S. S. Lee, L. F. H. Lee*, and *J. Sih*, Tetrahedron Lett. *1973*, 2313.
[87] *F. S. Alvarez, D. Wren*, and *A. Prince*, J. Amer. Chem. Soc. *94*, 7823 (1972).
[88] *N. Wiqwist, F. Béguin, M. Bygdeman*, and *M. Toppozada* in [3], p. 831.

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

Cationic Carbyne-Metal Complexes—Tetracarbonyl-*trans*-(trimethylphosphane)(methylcarbyne)chromium(I) Tetrahaloborates from Tetracarbonyl-*trans*-(trimethylphosphane)[methoxy(methyl)carbene]chromium(0) and Boron Trihalides[1]

By *Ernst Otto Fischer* and *Konrad Richter*[*]

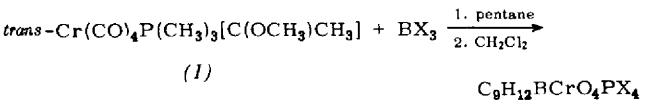
By reaction of pentacarbonyl[(methoxy)methyl(or phenyl)-carbene] complexes of chromium, molybdenum, and tungsten[2] with boron trihalides in alkanes at low temperature we were able in our laboratory to isolate the first stable representatives[3] of a class of compounds that contain as ligand a group $\equiv C-R$ ($R = CH_3$ or C_6H_5) triply bonded to the metal, *i.e.* a carbyne ligand. Since then two new possibilities for syntheses of carbyne complexes have been found: reaction of lithium (benzoyl)pentacarbonyltungstate(I) with dibromotriphenylphosphorane[4] and removal of water from pentacarbonyl(hydroxyorganylcarbene)tungsten(0) complexes with dicyclohexylcarbodiimide[5].

Independently of the route by which these compounds are formed, the course of the reaction involved in their formation involves three steps that are analogous in principle:

1. Removal of the OR′ group ($R' = CH_3$[3], Li[4], or H[5]) with the electron pair that produces the link to the previous carbene-carbon;
2. Elimination of a CO molecule from the complex;
3. Entry of a formally anionic group X^- (X = Cl, Br, I[3, 4], or $(CO)_5WCRO$[5]) in the position *trans* to the newly formed carbyne ligand.

The question arose as to how carbene complexes would react in which a ligand with a different, higher σ-donor/π-acceptor ratio in *trans*-position to the carbene ligand would at least hinder step 3.

On treatment of *trans*-$Cr(CO)_4P(CH_3)_3[C(OCH_3)CH_3]$[6] with BX_3 (X = Cl or Br) in pentane at a low temperature we obtained a reaction that occurred similarly to the formation of carbyne complexes but in which no evolution of CO could be observed; this afforded yellow, diamagnetic products for which, after careful purification by recrystallization from CH_2Cl_2, the molecular formula $C_9H_{12}BCrO_4PX_4$ was found by total analysis.



(1)

$C_9H_{12}BCrO_4PX_4$

(2), X = Cl
(3), X = Br

We were able to elucidate the structure of these compounds by IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy as well as on the basis of their chemical behavior.

The IR spectra of *(2)* and *(3)* (in CH_2Cl_2, LiF prism) in the ν_{CO} region show a very intense band (E_u) at 2045 and 2044 cm^{-1}, respectively, as well as very weak absorption (A_{1g}) at 2116 and 2115 cm^{-1}, respectively, and a shoulder (B_{1g}) at 2070 cm^{-1}. The number of bands and their intensity ratios indicate octahedral *trans*-disubstituted tetracarbonyl complexes. The shift of the very intense E_u-band with respect to the corresponding band of *(1)* amounts to approximately 150 cm^{-1} towards higher wavelengths.

The ^{1}H-NMR spectra of *(2)* and *(3)*, which are compared with that of *(1)* in Table 1, show that on the one hand the methoxy group is removed by the reaction whereas on the other the phosphane ligand in *trans*-position is retained in the complex. Positivization of the overall complex is proved by the shifts to lower field observed particularly for the protons of the methyl group bound to the former carbene-carbon but also for the phosphane protons.

Table 1. ^{1}H-NMR properties of the complexes *(1)*—*(3)* in CD_2Cl_2 at −40 °C (τ values relative to $CH_2Cl_2 = 4.57$; intensities and multiplicity s = singlet, d = doublet; coupling constants in Hz).

	OCH_3	CH_3	PCH_3
(1)	5.34 (1s)	7.09 (1s)	8.51 (3d) $^2J_{PH} = 7.5$
(2)	—	6.75 (1d) $^4J_{PH} = 4.5$	8.32 (3d) $^2J_{PH} = 9.5$
(3)	—	6.72 (1d) $^4J_{PH} = 4.5$	8.30 (3d) $^2J_{PH} = 9.5$

Table 2. ^{13}C-NMR data from complexes *(1)*—*(3)* in CD_2Cl_2 at −40 °C (ppm relative to TMS int. [*(1)*] or $CD_2Cl_2 = 54.26$ ppm [*(2)*, *(3)*]; coupling constants in Hz).

	CrC	CO	OCH_3	CCH_3	PCH_3
(1)	352.07 $^2J_{PC} = 12.2$	222.94 $^2J_{PC} = 12.2$	65.16	48.87	19.96 $J_{PC} = 24.4$
(2)	365.42 [a]	209.38 $^2J_{PC} = 17.9$	—	47.03	17.30 $J_{PC} = 29.8$
(3)	[b]	209.35 $^2J_{PC} = 17.1$	—	46.61	17.10 $J_{PC} = 26.9$

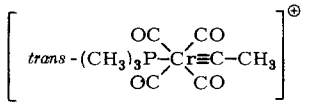
[a] *J* could not be determined; [b] resonance was not found.

The ^{13}C-NMR spectra of *(2)* and *(3)* contain four resonance signals (assignments in Table 2). The appearance of only one resonance for the CO-carbon atoms shows the equivalence of the CO groups, which agrees well with the IR-spectroscopic finding that the *trans*-disubstitution is retained in the reaction.

It is striking that the compounds *(2)* and *(3)* agree almost completely in their spectroscopic data. This justifies the conclusion that the portion of the compound containing the CO groups, the protons and the carbon atoms is independent of the halogen-containing portion, at least in solution, and possibly identical in the two compounds.

[*] Prof. Dr. E. O. Fischer and Dipl.-Chem. K. Richter
Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

On the basis of these arguments we ascribe the structure



to the new complexes. We assume that in pentane an "adduct" *trans*-$Cr(CO)_4P(CH_3)_3[C(OCH_3)CH_3]\cdot BX_3$ is first formed but that it cannot be studied because of its insolubility in apolar solvents and because of the by-products arising in the reaction. On dissolution in CH_2Cl_2 the "adduct" dissociates, whereupon even at $-20\,^{\circ}C$ the $BX_3OCH_3^-$ first formed presumably disproportionates in a rapid reaction with the excess of BX_3 to give BX_4^- and $B(OCH_3)_3$. That *(2)* and *(3)* have salt-like character can also be deduced from the electrolytic conductivity of their solutions in CH_2Cl_2: for very dilute solutions we observed linear dependence of the conductivity on concentration.

A final proof of structure was provided by reaction of *(2)* with anhydrous C_2H_5OH. As proved by IR, ^{1}H-NMR, and mass spectroscopic investigations as well as by total analysis, this leads to *trans*-$Cr(CO)_4P(CH_3)_3[C(OC_2H_5)CH_3]$ *(4)*, *i.e.* back to a carbene complex in which the OCH_3 group (of the initial complex *(1)*) is replaced by the OC_2H_5 group.

(4): IR (in hexane; ν_{CO}): 2008 vw (A_{1g}), 1936 w (B_{1g}), 1891 vs, br (E_u) cm^{-1}. ^{1}H-NMR (in [D_8]-toluene, 0 °C; τ-values, TMS int.): 5.28 q OCH_2, 7.18 s CCH_3, 8.85 t OCH_2CH_3, 9.00 d ($J = 7.5$ Hz) $P(CH_3)_3$. The mass spectrum shows the molecular ion ($m/e = 312$) and successive loss of 4 CO (284, 256, 228, 200); there follow removal of C_2H_5 (171), of COC_2H_5 (143) and of the whole carbene ligand (128).

Compounds of this new ionic type resemble uncharged carbyne complexes in many of their properties. They show clearly that when the *trans*-position in carbene complexes is blocked the reaction with BX_3 stops after removal of the OCH_3 group. Studies with π-$C_5H_5Mn(CO)_2C(OCH_3)C_6H_5$[7] and with π-$C_6H_3(CH_3)_3Cr(CO)_2C(OCH_3)C_6H_5$[8] show that this reaction principle can be generalized. At the same time they provide valuable indications on the mechanism of carbyne complex formation. Finally the reaction with nucleophiles opens up a new possibility for synthesis of carbene complexes, as is exemplified by the reaction of *(2)* with ethanol.

Experimental:

All operations must be carried out under N_2 and with dry (CaH_2, P_4O_{10}) solvents presaturated with N_2!

1. BCl_3 is passed into a solution of *(1)* (3 g) in pentane (75 ml) in a frit cooled to $-25\,^{\circ}C$ (or BBr_3 is added in slight excess from a pipette). When the originally orange-red solution is completely decolorized the pentane is sucked off and the yellowish-white precipitate is washed with pentane. The substance that slowly crystallizes at $-78\,^{\circ}C$ is recrystallized twice from CH_2Cl_2. Pouring off the mother-liquor, washing with pentane at $-78\,^{\circ}C$, and drying for several hours in a high vacuum affords beautiful pale yellow crystals. Further amounts of the product (as a yellow powder) can be obtained from the mother-liquors by addition of pentane. Yield: 72% of *(2)* or 60% of *(3)*.

2. C_2H_5OH (100 ml) is added to *(2)* (2 g) at $-30\,^{\circ}C$. On slow warming up to 0 °C, with stirring, *(2)* dissolves to an orange-red solution. After addition of some pentane, the solution is poured into a NaH_2PO_4/Na_2HPO_4 buffer solution. The orange-red pentane phase that separates contains mainly *(4)*, with a little $Cr(CO)_5P(CH_3)_3$. The aqueous phase is extracted a further three times with pentane, and the combined extracts are then dried over Na_2SO_4. Separation of $Cr(CO)_5P(CH_3)_3$ and decomposition products is achieved by chromatography at 0 °C on silica gel with pentane as eluant. Yield: 65% of *(4)*.

Received: November 18, 1974 [Z 156 IE]
German version: Angew. Chem. *87*, 359 (1975)

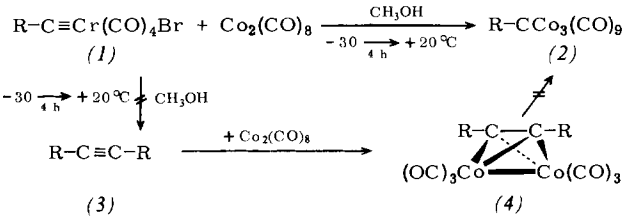
CAS Registry numbers:
(1), 51717-33-0; *(2)*, 54460-86-5; *(3)*, 54460-87-6; *(4)*, 54460-88-7; BCl_3, 10294-34-5; BBr_3, 10294-33-4; C_2H_5OH, 64-17-5

[1] Part 6 in the series: Transition Metal Carbyne Complexes.—Part 5: *E. O. Fischer, H. J. Kalder*, and *F. H. Köhler*, J. Organometal. Chem. *81*, C 23 (1974).
[2] *E. O. Fischer* and *A. Maasböl*, Chem. Ber. *100*, 2445 (1967).
[3] *E. O. Fischer, G. Kreis, C. G. Kreiter, J. Müller, G. Huttner*, and *H. Lorenz*, Angew. Chem. *85*, 618 (1973); Angew. Chem. internat. Edit. *12*, 564 (1973).
[4] *H. Fischer* and *E. O. Fischer*, J. Organometal. Chem. *69*, C 1 (1974).
[5] *E. O. Fischer, K. Weiss*, and *C. G. Kreiter*, Chem. Ber. *107*, 3554 (1974).
[6] *E. O. Fischer* and *H. Fischer*, Chem. Ber. *107*, 657 (1974).
[7] *E. O. Fischer* and *E. W. Meineke*, unpublished work.
[8] *E. O. Fischer* and *P. Stückler*, unpublished work.

Transfer of Carbyne Ligands from Chromium to Cobalt[1]

By *Ernst Otto Fischer* and *Albrecht Däweritz*[*]

We have succeeded in transferring carbyne ligands from one metal to another for the first time. *trans*-Bromomethyl- and -phenylcarbynetetracarbonylchromium complexes *(1a, b)*[2] react with octacarbonyldicobalt in methanol under very mild conditions (−30 to +20 °C, 4 h) to form the μ_3-methinylenneacarbonyltricobalt complexes *(2a, b)* which have been known for a long time[3–5]. The products were confirmed by ^{1}H-NMR spectroscopy [$(CD_3)_2CO$, TMS internal; *(2a)*, $\delta = 3.73$ ppm ([6]: 3.65)], IR spectroscopy (Table), mass spectrometry [M^+ *(2a)*, *m/e* 456; *(2b)*, *m/e* 518, fragmentation patterns identical to those reported in refs. [7, 8], 50 eV, boat source], and by complete elemental analysis.



(a), R = CH_3
(b), R = C_6H_5

It could be ruled out that μ_3-methinylenneacarbonyltricobalt complexes *(2)* are formed under the above conditions *via* dimerization of the carbyne ligands to alkynes *(3)* and formation of alkynehexacarbonyldicobalt complexes *(4)*. Alkyne would have immediately yielded the stable species *(4)*, which could not be detected. The absence of *(3)* and *(4)* also indicates that, in contrast to the course assumed for photolytic reactions of diethylmercury bisdiazoacetate with bromopentacarbonylmanganese[9] or alkenes[10], no free carbynes occur during the reaction.

IR spectroscopic data (ν_{CO}, cm^{-1}, *n*-hexane):

(2a):	2101 (w)	2050 (vs)	2037 (s)	2016 (w)
	2102.4	2052.0	2038.2	2018.0 [5]
(2b):	2101 (m)	2053 (vs)	2039 (s)	2020 (sh)
	2101.4	2054.2	2039.9	2020.9 [5]

[*] Prof. Dr. E. O. Fischer and Dipl.-Chem. A. Däweritz
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

Procedure:

All operations were performed in dry, oxygen-free solvents under N_2. *(1a)* (677 mg, 2.5 mmol) [*(1b)* (833 mg, 2.5 mmol)] and $Co_2(CO)_8$ (1.29 g, 3.75 mmol) are dissolved in cooled methanol at −30 °C and the temperature of the stirred reaction mixture allowed to rise to +20 °C within 4 h. The color of the mixture changes from ocher to brownish violet during the process and after evolution of gas has ceased the mixture is extracted several times with pentane at −95 °C. The solvent is removed from the extracts and the residue vacuum-sublimed on to a finger cooled with solid CO_2. *(2a)*, m.p. 183—185 °C (dec.) [183—185 °C (dec.)[11]], yield 130 mg (0.29 mmol) = 10.6% based on *(1a)*. *(2b)*, m.p. 104—105 °C [105—107 °C[12]], yield 92 mg (0.18 mmol) = 7.1% based on *(1b)*.

Received: January 22, 1975 [Z 191 IE]
German version: Angew. Chem. *87*, 360 (1975)

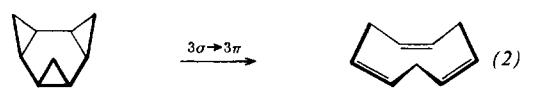
CAS Registry numbers:
(1a), 51005-78-8; *(1b)*, 50701-13-8; *(2a)*, 13682-04-7; *(2b)*, 20756-47-2; $Co_2(CO)_8$, 10210-68-1

[1] Transition Metal Carbyne Complexes, Part 8.—Part 7: *E. O. Fischer* and *U. Schubert*, J. Organometal. Chem., in press.
[2] *E. O. Fischer, G. Kreis, C. G. Kreiter, J. Müller, G. Huttner*, and *H. Lorenz*, Angew. Chem. *85*, 618 (1973); Angew. Chem. internat. Edit. *12*, 564 (1973); *G. Kreis*, Dissertation, Technische Universität München 1973.
[3] *R. Markby, I. Wender, R. A. Friedel, F. A. Cotton*, and *H. W. Sternberg*, J. Amer. Chem. Soc. *80*, 6529 (1958).
[4] *U. Krüerke* and *W. Hübel*, Chem. Ind. *1960*, 1264.
[5] *G. Bor, L. Markó*, and *B. Markó*, Chem. Ber. *95*, 333 (1962).
[6] *D. Seyferth, R. J. Spohn*, and *J. E. Hallgren*, J. Organometal. Chem. *28*, C 34 (1971).
[7] *M. J. Mays* and *R. N. F. Simpson*, J. Chem. Soc. *A 1968*, 1444.
[8] *B. H. Robinson* and *W. S. Tham*, J. Chem. Soc. *A 1968*, 1784.
[9] *W. A. Herrmann*, Angew. Chem. *86*, 895 (1974); Angew. Chem. internat. Edit. *13*, 812 (1974).
[10] *T. DoMinh, H. E. Gunning*, and *O. P. Strausz*, J. Amer. Chem. Soc. *89*, 6785 (1967); *O. P. Strausz, T. DoMinh*, and *J. Font*, *ibid. 90*, 1930 (1968); *O. P. Strausz, G. J. A. Kennepohl, F. X. Garneau, T. DoMinh, B. Kim, S. Valenty*, and *P. S. Skell*, *ibid. 96*, 5723 (1974).
[11] Gmelins Handbuch der Anorganischen Chemie, Ergänzungswerk zur 8. Aufl. Bd. 6, Kobalt-organische Verbindungen. Teil 2, p. 155, Tab. 29, Nr. 6. Verlag Chemie, Weinheim 1973.
[12] *D. Seyferth, J. E. Hallgren*, and *P. L. K. Hung*, J. Organometal. Chem. *50*, 265 (1973).

Chemistry of *cis*-Triazatris-σ-homobenzene. 3σ→3π Isomerization to the 1,4,7-Triaza-2,5,8-cyclononatriene System[**]

By *Horst Prinzbach, Reinhard Schwesinger, Manfred Breuninger, Bernd Gallenkamp*, and *Dieter Hunkler*[*]

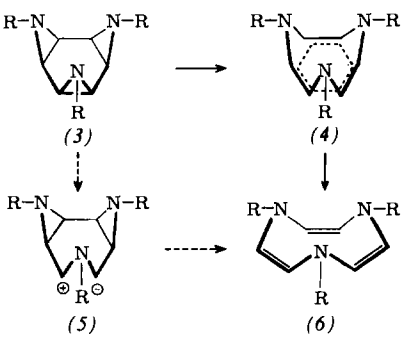
Thermal isomerization reactions of type *cis*-tris-σ-homobenzene *(1)* → 1,4,7-cyclononatriene *(2)* are presently attracting interest (i) preparatively as providing an entry to nine-membered rings, and (ii) theoretically as sterically and energetically predestinated 6-electron concerted processes[1, 2].



[*] Prof. Dr. H. Prinzbach, Dipl.-Chem. R. Schwesinger, Dipl.-Chem. M. Breuninger, Dipl.-Chem. B. Gallenkamp, and Dr. D. Hunkler
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Dr. *H. Fritz* for performing the the ^{13}C measurements, and Prof. Dr. *H. Achenbach* for the MS.

Thermolysis of *cis*-triazatris-σ-homobenzenes *(3b)—(3e)* has now rendered the first derivatives *(6b)—(6e)* of the 1,4,7-triaza-2,5,8-cyclononatriene system (1*H*-4,7-dihydro-1,4,7-triazonine) accessible. The *N,N',N''*-trisubstituted starting materials can be prepared conventionally from the triimine *(3a)*[3]: *(3b)* (methanesulfonic anhydride, pyridine; colorless crystals, yield 60%, m.p. 235 °C, ^1H-NMR (D_6-DMSO): τ = 6.78, ^{13}C-NMR: δ = 30.5 ppm)[4]; *(3c)* (*p*-toluenesulfonic anhydride, triethylamine; colorless needles, yield 70%, m.p. 186 °C, ^1H-NMR ($CDCl_3$): τ = 6.83, ^{13}C-NMR: δ = 31.1 ppm); *(3d)* (methyl chloroformate, Levatit MP 62 ion exchanger; colorless platelets, yield 65%, m.p. 95 °C (clouding above 80 °C), ^1H-NMR (CH_2Cl_2): τ = 7.17, ^{13}C-NMR (C_6D_6): δ = 30.06 ppm); *(3e)* (methyl methanesulfonate, Na_2CO_3, methanol; colorless crystals, yield 80%, m.p. 95 °C (dec.), ^1H-NMR (CCl_4): τ = 8.6, ^{13}C-NMR: δ = 33.5 ppm); *(3f)* (only produced in solution, $NOBF_4$, pyridine/$CHCl_3$, −20 °C; ^1H-NMR: τ = 6.45). The question of the arrangement of the *N*-substituents which is topical in connection with the crystal structure of *(3a)*[6] has been decided in favor of the all-*exo* configuration by ^1H- and ^{13}C-NMR spectra and pK_a measurements[7a].



	(a)	(b)	(c)	(d)	(e)	(f)
R	H	SO_2CH_3	$SO_2C_6H_4CH_3$	CO_2CH_3	CH_3	NO

Depending upon the kind of *N*-substitution, thermal isomerization of *(3b)—(3e)*[7b] to the π-analogs *(6b)—(6e)* requires a widely varying activation energy characterized by the approximately determined half-lives ($t_{1/2}$ *(3b)*: 160 °C (dimethyl sulfone), *ca.* 25 min; *(3c)*: 160 °C (dimethyl sulfone), *ca.* 12 min; *(3d)*: 60 °C ($CHCl_3$), *ca.* 57 min; *(3e)*: 60 °C (CCl_4), *ca.* 50 min, ($CHCl_3$), *ca.* 75 min, (water), *ca.* 900 min); the reaction proceeds uniformly. The gradation from *(3b)* to *(3d)* is parallel to the effect of these substituents on the benzene imine/azepine equilibrium[8]. While the trimethyl compound cannot be fitted into this series, the observed pronounced solvent effect, due to intermolecular hydrogen bonding, underlines the significance of the n-electron pair on nitrogen for the strength of the aziridine C—C bond, which has also been theoretically justified[9]. We consider intramolecular hydrogen bonds to be responsible for the enhanced thermal stability of the triimine *(3a)* relative to that of *(3e)*. In dimethyl sulfone *(3a)* is stable up to *ca.* 120 °C and decomposes with polymerization at 140 °C (N_2, 10 min) without any triene *(6a)* being observed by ^1H-NMR spectroscopy.

An argument opposing an ylide-type intermediate *(5)* or favoring a concerted process *(4)*, which, however, cannot be very convincing[10], comes from the absence of adduct formation when, *e.g.*, *(3d)* is thermolyzed in the presence of an excess of dimethyl acetylenedicarboxylate. The specificity of 3σ→3π isomerization in the case of the urethane *(3d)* is informative, inasmuch as the potential competing reaction involving C—N cleavage and forming oxazoline does not become operative. So far the only exception in the series

(3) is the trinitroso compound *(3f)*, in which cleavage to *(6f)* has no chance compared to the elimination of N_2O (giving over 50% of benzene) which occurs above $-10°C$.

The triazanonatrienes bearing electron-withdrawing substituents *(6b)* (colorless crystals, m.p. 210°C (dec.), ^{1}H-NMR (CD_3CN): $\tau = 4.05$, ^{13}C-NMR: $\delta = 119.4$ ppm), *(6c)* (colorless crystals, m.p. 150°C (dec.), ^{1}H-NMR ($CDCl_3$): $\tau = 4.40$, ^{13}C-NMR: $\delta = 119.0$ ppm), and *(6d)* (colorless oil, ^{1}H-NMR ($CDCl_3$): $\tau = 4.16$, ^{13}C-NMR: $\delta = 119.5$ ppm) are fairly stable thermally and on air exposure. Trimethyl derivative *(6e)* (colorless oil, m.p. *ca.* 0—10°C, ^{1}H-NMR ($CDCl_3$): $\tau = 5.29$, ^{13}C-NMR: $\delta = 123.3$ ppm), on the other hand, displays the typical pronounced sensitivity of enamines towards oxygen; it forms a deep red solid complex with trinitrobenzene[11]. Evidence for a preferential crown conformation having a mobility comparable with that of trioxanonatriene[12] and considerably enhanced relative to the hydrocarbon *(2)*[13] comes from the ^{1}H- and ^{13}C-data, and especially from the temperature measurements performed on *(6e)* which, unlike *(6d)*, displays no substituent-dependent variation with temperature.

Received: December 30, 1974 [Z 166a IE]
German version: Angew. Chem. *87*, 349 (1975)

CAS Registry numbers:
(3a), 52851-26-0; *(3b)*, 54724-90-2; *(3c)*, 54724-91-3; *(3d)*, 54724-92-4; *(3e)*, 54724-93-5; *(3f)*, 54724-94-6; *(6b)*, 54751-69-8; *(6c)*, 54724-87-7; *(6d)*, 54724-88-8; *(6e)*, 54724-89-9; *(8)*, 54724-95-7

[1] *H. Prinzbach* and *D. Stusche*, Angew. Chem. *82*, 836 (1970); Angew. Chem. internat. Edit. *9*, 799 (1970).

[2] *H. Prinzbach, H. Fritz, H. Hagemann, D. Hunkler, S. Kagabu*, and *G. Philippossian*, Chem. Ber. *107*, 1971 (1974); *S. Kagabu* and *H. Prinzbach*, Angew. Chem. *87*, 248 (1975); Angew. Chem. internat. Edit. *14*, 252 (1975), and further references cited therein.

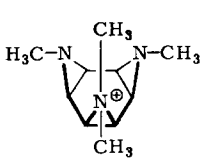
[3] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *85*, 1107 (1973); Angew. Chem. internat. Edit. *12*, 989 (1973).

[4] Only the NMR data relevant to structural proof and the discussion in ref. [5] are given. The structures of the new compounds are also confirmed by IR, UV, MS, and elemental analysis.

[5] *H. Prinzbach, M. Breuninger, B. Gallenkamp, R. Schwesinger*, and *D. Hunkler*, Angew. Chem. *87*, 350 (1975); Angew. Chem. internat. Edit. *14*, 348 (1975).

[6] *W. Littke* and *U. Drück*, to be published.

[7a] *(3e)* can be methylated to the aziridinium salt *(7)* with "magic methyl" (CH_3OSO_2F, benzene); at 80°C *(7)* undergoes rapid and complicated decomposition (*inter alia* to *N*-methylpyrrole), cf. the enhancement of stability of *(3e)* by H bonding in water. The steric compression due to the inner methyl group is probably responsible for the unexpected thermal lability of *(7)*.



$OSO_2F^{\ominus}$ *(7)*

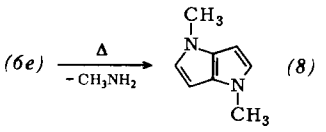
[7b] *Note added in proof* (March 24, 1975): The additionally synthesized derivatives *(3)* with $R = SO_2CF_3$ (yield 65%, m.p. 165°C) and $R = COC_6H_5$ (yield 63%, m.p. 199°C) with half-lives of *ca.* 120 min at 160°C (dimethyl sulfone) and *ca.* 90 min at 60°C ($CHCl_3$) fit as expected into the stability sequence *(3b)—(3e)*.

[8] *H. Günther, J. B. Pawliczek, B. D. Tunggal, H. Prinzbach*, and *R. H. Levin*, Chem. Ber. *106*, 984 (1973); *W.-D. Stohrer, ibid. 106*, 970 (1973), and references cited therein.

[9] *W.-D. Stohrer* and *R. Hoffmann*, Angew. Chem. *84*, 820 (1972); Angew. Chem. internat. Edit. *11*, 825 (1972).

[10] Cf. corresponding findings with monoheterotrishomobenzenes: *H. Prinzbach* and *D. Stusche*, Helv. Chim. Acta *54*, 755 (1971); see also *A. de Meijere, D. Kaufmann*, and *O. Schallner*, Tetrahedron Lett. *1973*, 553.

[11] So far the trimethyl compound *(6e)* is the only member to exhibit the mechanistically obscure reaction occurring on warming in solution (benzene, 150°C), but not in the gas phase, and affording a 40% yield of the dimethyl derivative *(8)* of the unknown dihydropyrrolo[3,2-*b*]pyrrole (colorless volatile crystals, m.p. 110°C). Its UV and NMR data indicate a relationship to naphthalene (UV: $\lambda_{max} = 260$ nm ($\varepsilon = 17450$), ^{1}H-NMR (CCl_4): $\tau = 6.4$ ($2CH_3$), 4.3 (2H), 3.65 (2H), $J_{AB} = 2.6$ Hz); *R. Schwesinger*, Dissertation, Universität Freiburg 1975.



(6e) $\xrightarrow[-CH_3NH_2]{\Delta}$ *(8)*

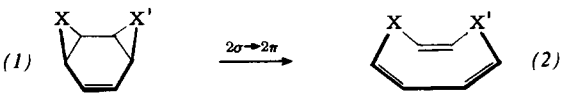
[12] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. internat. Edit. *11*, 942 (1972); *E. Vogel, H.-J. Altenbach*, and *C. D. Sommerfeld, ibid. 84*, 986 (1972); *11*, 939 (1972).

[13] *K. G. Untch* and *R. J. Kurland*, J. Mol. Spectrosc. *14*, 156 (1964).

cis-Diazabis-σ-homobenzene. Synthesis and $2\sigma \rightarrow 2\pi$ Isomerization to 1,4-Diaza-2,5,7-cyclooctatriene Derivatives[**]

By *Horst Prinzbach, Manfred Breuninger, Bernd Gallenkamp, Reinhard Schwesinger*, and *Dieter Hunkler*[*]

While the hydrocarbon *(1a)* (*cis*-"bis-σ-homobenzene"), which is expected to be thermally labile, is still unknown, the mono- and bis-hetero analogs *(1b)*[1]—*(1d)*[2] have been isolated in recent years. Their $2\sigma \rightarrow 2\pi$ isomerization opens a simple route to the heterocyclooctatrienes *(2b)—(2d)*.



(1) $\xrightarrow{2\sigma \rightarrow 2\pi}$ *(2)*

(a), X = X' = CH_2
(b), X = CH_2, X' = O
(c), X = CH_2, X' = N-Tos
(d), X = X' = O
(e), X = X' = NR

A synthetic route to the hitherto unknown diaza systems *(1e)* and *(2e)* was seen in the pathway entailing *N*-nitrosation of *cis*-"benzene triimines"[3] and N_2O elimination. Since *N*-nitrosoaziridines generally decompose between -20 and $0°C$[4], the prospects for identification or isolation of the *cis*-diazabis-σ-homobenzenes were favorable. However, it could not be ruled out that N_2O elimination and valence isomerization proceed synchronously—symmetry-allowed as a nonlinear cheletropic process—and lead directly [cf. *(7)*] to the diazacyclooctatrienes.

Basically in analogy to the *N,N',N''*-trisubstituted derivatives[3] we have prepared from *(3)* the bissulfonamide *(4a)*, the bisurethane *(4b)*, and the dimethyl derivative *(4c)* and separated them by crystallization or by chromatography, involving considerable losses in some cases, from the mono- or trisubstituted by-products (Table 1).

At $-40°C$ *(4a)* reacts fast ($CHCl_3$, pyridine) with nitrosyl tetrafluoroborate to form nitrosoaziridine *(5a)*; the progress of the reaction can be followed by observing the paramagnetic shift of the H^A signal ($\tau = 6.7$). On warming of the deep yellow solution to $-10°C$, evolution of N_2O is rapidly initiated;

[*] Prof. Dr. H. Prinzbach, Dipl.-Chem. M. Breuninger, Dipl.-Chem. B. Gallenkamp, Dipl.-Chem. R. Schwesinger, and Dr. D. Hunkler
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Dr. *H. Fritz* for the ^{13}C measurements, and to Prof. Dr. *H. Achenbach* for the MS.

Table 1. *N,N'*-Disubstituted products of types *(4)*, *(6)*, and *(8)* [5].

(4a): 2 equiv. *p*-toluenesulfonic anhydride, triethylamine, CH_2Cl_2, 0 °C, colorless needles, > 130 °C dec., yield 60 %, ^{1}H-NMR ($CDCl_3$): $\tau = 7.8$ (H^A), 6.5—6.9 (H^BH^C)

(4b): 2 equiv. methyl chloroformate, Levatit MP 62, $CHCl_3$, 0 °C, colorless needles, m.p. 123—124 °C (dec.), yield 60 %, ^{1}H-NMR ($CDCl_3$): $\tau = 7.7$ (H^A), 6.75—7.2 (H^BH^C), ^{13}C-NMR ($CDCl_3$): $\delta = 32.8$ ppm (C^B), 30.1 (C^C), 24.7 (C^A)

(4c): 2 equiv. methyl methanesulfonate, Na_2CO_3, methanol, 20 °C, colorless deliquescent needles, m.p. 51 °C, yield 45%, ^{1}H-NMR ($CDCl_3$): $\tau = 7.9$ (H^A), 8.3 (H^BH^C)

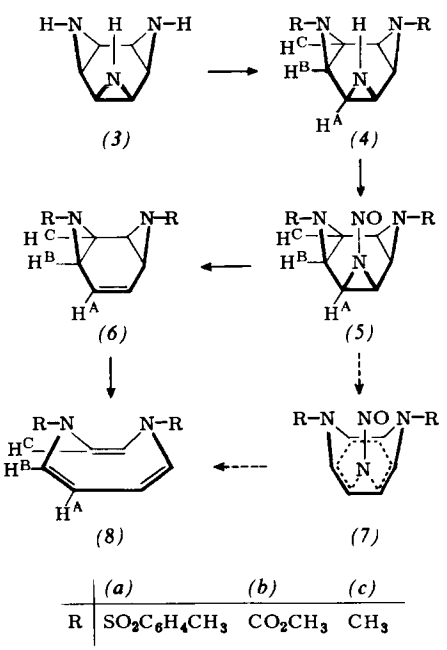
(6a): colorless needles, > 120 °C isomerization to *(8a)*, yield 70%, ^{1}H-NMR ($CDCl_3$): $\tau = 6.4$—6.8 (H^BH^C), 3.7 (H^A), ^{13}C-NMR ($CDCl_3$): $\delta = 127.7$ ppm (C^A), 33.3, 32.5 (C^BC^C); MS: *m/e* 416 (M^+)

(6c): ^{1}H-NMR ($CDCl_3$, −30 °C): $\tau = 8.1$ (H^C), 7.94 (H^B), 3.69 (H^A), 7.51 ($2CH_3$)

(8a): colorless crystals (CCl_4), m.p. 169 °C, ^{1}H-NMR ($CDCl_3$): $\tau = 4.53$ (H^A), 3.69 (H^C), 3.62 (H^B), ^{13}C-NMR ($CDCl_3$): $\delta = 122.0$ ppm (C^B), 116.5 (C^A), 109.0 (C^C)

(8b): colorless crystals (isopropanol), m.p. 81—82 °C, ^{1}H-NMR ($CDCl_3$): $\tau = 4.38$ (H^A), 3.99 (H^C), 3.77 (H^B), ^{13}C-NMR ($CDCl_3$): $\delta = 126.5$ ppm (C^B), 118.6 (C^A), 112.4 (C^C)

(8c): colorless oil, ^{1}H-NMR ($CDCl_3$): $\tau = 4.37$ (H^A), 4.12 (H^C), 3.50 (H^B), 6.02 ($2CH_3$), MS: *m/e* 136 (M^+)



R	(a) $SO_2C_6H_4CH_3$	(b) CO_2CH_3	(c) CH_3

the product (70 %) isolated as colorless crystals (CH_2Cl_2) is confirmed as *cis*-"benzene diimine" *(6a)* by its spectroscopic data, and especially by NMR comparison with *(2c)* and *(2d)*. At 75 °C (in solution) *(6a)* undergoes fast uniform isomerization to 1,4-diaza-2,5,7-cyclooctatriene (1,4-dihydro-1,4-diazocine) *(8a)*. The nitroso derivative *(5b)* ($\tau(H^A) = 6.8$) prepared analogously from *(4b)* in $CHCl_3$ solution likewise decomposes above *ca.* −10 °C with the—not unexpected—difference that *(6b)* is not detectable under these conditions and the triene *(8b)* appears immediately and quantitatively. Compound *(5c)*, which is more labile than *(5a)* and *(5b)* and is prepared at −60 °C ($CHCl_3$, 1,4-diazabicyclo[2.2.2]octane) already eliminates N_2O between −35 and −30 °C; under these conditions *(6c)* is stable and identifiable by NMR spectroscopy. It has a half-life of *ca.* 2 min at 20 °C ($CHCl_3$), under which conditions it is converted uniformly into *(8c)* (Table 1).

Judging from these first three examples *(6a)*—*(6c)* the *cis*-"benzene diimine" system fits well into the pattern set by the "benzene imines" and *cis*-"benzene triimines" and by 1,4-dioxocin[2] and 1,4-dithiocin[6] with respect to its readiness to undergo $2\sigma \rightarrow 2\pi$ valence isomerization and its spectroscopic properties.

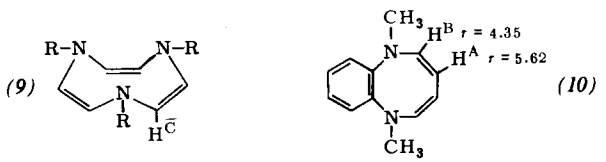
The following comparisons reveal an interesting aspect in connection with the potential "aromaticity" of 1,4-dihydrodiazocine *(8)*[7], and in general of the 1,4-dihetero[8]annulenes:

1) The chemical shifts of the proton pairs H^A, H^B, H^C in the derivatives *(8a)*—*(8c)* differ only slightly (Table 1). In the triazonine skeleton *(9)*[3]—as the nearest olefin model—the same substituents cause a $\Delta\delta$ value of over 1 ppm. $\tau(H^C)$ is slightly smaller for *(8b)* than for *(9b)*, but 1.17 ppm smaller for *(8c)* than for *(9c)*.

2) ^{1}H- and ^{13}C-N—CH_3 signals in *(8c)* are paramagnetically shifted by 0.9 and 8.2 ppm, respectively, as compared with the corresponding signals in *(9c)*.

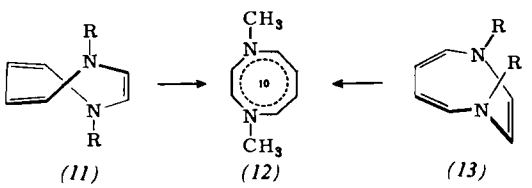
3) The $\tau(H^A)$ and $\tau(H^B)$ values in dimethylbenzodiazocine *(10)*[8] are *ca.* 1.3 and 0.8 ppm larger than in *(8c)*.

4) The ^{13}C-signals of the ring carbon atoms in *(8c)* ($\delta = 117.1$ ppm (C^B), 102.5 (C^A), 91.8 (C^C)) show substantial diamagnetic shifts with respect to those of the ring carbon atoms in *(9c)* and *(8a)*, *(8b)* (Table 1).



R	Tos *(9a)*	CO_2CH_3 *(9b)*	CH_3 *(9c)*
$\tau(H^C)$	4.40	4.16	5.29

The still tentative interpretation—decisive information is expected from the parent compound *(8)*, R = H, and its dianion[7]—states that in contrast to the situation in *(8a)* and *(8b)* or in 1,4-dioxocin[2] and 1,4-dithiocin[6] effective cyclic 10-electron delocalization induces a diamagnetic ring current *(12)* with flattening of the twist conformation *(11)*



preferred over *(13)* for *(8a)* and *(8b)*. Thus striking analogies become apparent between the 1,4-dihetero[8]annulenes and the extensively studied hetero[9]annulenes[9].

Received: December 30, 1974 [Z 166b IE]
German version: Angew. Chem. 87, 350 (1975)

CAS Registry numbers:
(3), 52851-26-0; *(4a)*, 54724-76-4; *(4b)*, 54724-77-5; *(4c)*, 54724-78-6; *(5a)*, 54724-79-7; *(5b)*, 54724-80-0; *(5c)*, 54724-81-1; *(6a)*, 54724-82-2; *(6c)*, 54724-83-3; *(8a)*, 54724-84-4; *(8b)*, 54724-85-5; *(8c)*, 54724-86-6; *(9a)*, 54724-87-7; *(9b)*, 54724-88-8; *(9c)*, 54724-89-9

[1] *D. Stusche*, *M. Breuninger*, and *H. Prinzbach*, Helv. Chim. Acta *55*, 2359 (1972).
[2] *E. Vogel*, *H.-J. Altenbach*, and *D. Cremer*, Angew. Chem. *84*, 983 (1972); Angew. Chem. internat. Edit. *11*, 935 (1972).
[3] *H. Prinzbach*, *R. Schwesinger*, *M. Breuninger*, *B. Gallenkamp*, and *D. Hunkler*, Angew. Chem. *87*, 349 (1975); Angew. Chem. internat. Edit. *14*, 347 (1975), and references cited therein.
[4] *W. Rundel* and *E. Müller*, Chem. Ber. *96*, 2528 (1963); *R. D. Clark* and *G. K. Helmkamp*, J. Org. Chem. *29*, 1316 (1964).
[5] Only the NMR data relevant to structural proof are given. The structures of the new compounds are also confirmed by IR, UV, MS, and elemental analyses.

[6] *H. J. Eggelte* and *F. Bickelhaupt*, Angew. Chem. *86*, 381 (1974); Angew. Chem. internat. Edit. *13*, 345 (1974).
[7] Attempts to prepare the parent compounds *(6)*, R = H, and *(8)*, R = H, from *(3)* and *(8b)*, respectively, are in progress.
[8] *H.-J. Shue* and *F. W. Fowler*, Tetrahedron Lett. *1971*, 2437.
[9] *A. G. Anastassiou*, Top. Nonbenzenoid Aromat. Chem. *1*, 1 (1973); *A. V. Kemp-Jones* and *S. Masamune*, *ibid. 1*, 121 (1973); cf. influence of the N-substituent on the diatropic character of aza[13]annulenes: *A. G. Anastassiou*, *R. L. Elliot*, and *E. Reichmanis*, J. Amer. Chem. Soc. *96*, 7823 (1974).

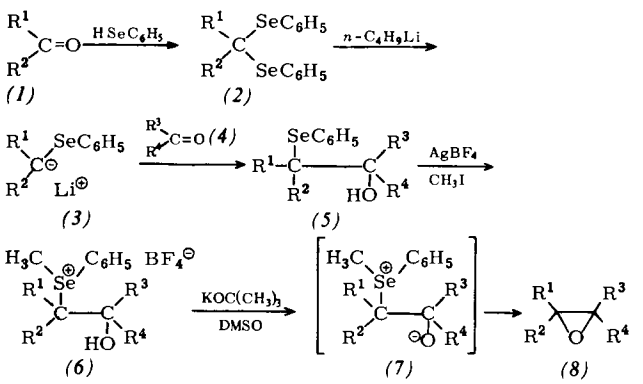
New Synthetic Route to Di- and Trisubstituted Epoxides[1]

By *Willy Dumont* and *Alain Krief*[*]

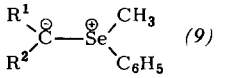
This communication reports the application of the C—Se bond cleavage to the connective synthesis of epoxides *(8)* starting from the carbonyl compounds *(1)* and *(4)*.

We[2] and *Seebach*[5] recently synthesized some β-hydroxyalkyl phenyl selenides *(5)* by reacting the selenoacetals *(2)* with *n*-butyllithium and trapping the resulting carbanions *(3)*[3-4] with carbonyl compounds *(4)*.

We have now found that β-hydroxyalkylselenonium salts *(6)* can be readily formed when β-hydroxyalkylphenyl selenides *(5)*, $R^1 = H$, $R^2 = H$, alkyl, are treated with methyl iodide in the presence of silver tetrafluoroborate[6]: subsequent treatment of the crude salts *(6)* with base (potassium *tert*-butoxide in DMSO) produces the desired epoxide *(8)* and methyl phenyl selenide *via* the betaine *(7)* (Table 1).



This betaine *(7)* is identical with that produced by addition of the ylide *(9)* to the carbonyl compound *(4)*[7].



(9)

The proposed synthon permits the synthesis of, *e.g.*, the epoxides *(8d)* and *(8g)* from the highly enolizable deoxybenzoin [35%, 28% overall yield based on *(4)*]; these epoxides are not accessible by standard procedures[7-9].

Unfortunately, we were unable to synthesize β-hydroxyalkylselenonium salts *(6)*, R^1, R^2 = alkyl. For instance, reaction of *(5j)* instead of *(6j)* yields 3-methyl-3-phenyl-2-butanone (80%). Tetrasubstituted epoxides are also not yet accessible by this route.

β-Hydroxyselenonium salts (6) and epoxides (8):

Methyl iodide (2.4 mmol) is added under N_2 at 20°C to a mixture of $AgBF_4$ (2.2 mmol) and *(5)* (2 mmol) in dry ether (5 ml). [*(5)*[2] was purified by TLC (silica gel; ether/petroleum ether 1:9).] After 2 h, the mixture is shaken with CH_2Cl_2 (50 ml) and silver iodide is filtered off. The CH_2Cl_2 is evaporated *in vacuo* and the salt *(6)* washed with ether (3 × 10 ml) and used without further purification.

(6) is dissolved in DMSO (10 ml) and $KOC(CH_3)_3$ is added (10% excess). After 2 h at 20°C, the mixture is extracted with ether (3 × 50 ml). The ethereal fractions are dried and evaporated and the epoxide *(8)* purified by TLC (silica gel, ether/petroleum ether 5:95).

Received: December 30, 1974 [Z 165 IE]
German version: Angew. Chem. *87*, 347 (1975)

CAS Registry numbers:
(1a), 50-00-0; *(1e)*, 75-07-0; *(1h)*, 123-38-6; *(1i)*, 123-72-8; *(1j)*, 67-64-1; *(4a)*, 100-52-7; *(4b)*, 98-86-2; *(4c)*, 98-53-3; *(4d)*, 451-40-1; *(4f)*, 119-61-9; *(4h)*, 2043-61-0; *(5a)*, 51558-95-3; *(5b)*, 53188-76-4; *(5c)*, 54724-66-2; *(5d)*, 54724-67-3; *(5e)*, 54724-68-4; *(5f)*, 54724-69-5; *(5g)*, 54724-70-8; *(5h)*, 53188-75-3; *(5j)*, 53188-71-9: *(6a)*, 54764-40-8; *(6b)*, 54764-42-0; *(6c)*, 54764-44-2; *(6d)*, 54764-46-4; *(6e)*, 54764-48-6; *(6f)*, 54764-50-0; *(6g)*, 54764-52-2; *(6h)*, 54764-54-4; *(6i)*, 54764-56-6; *(8a)*, 96-09-3; *(8b)*, 2085-88-3; *(8c)*, 54724-71-9; *(8d)*, 41979-17-3; *cis-(8e)*, 16127-54-1; *trans-(8e)*, 7443-58-5; *(8f)*, 4741-91-7; *cis-(8g)*, 54724-72-0; *trans-(8g)*, 54724-73-1; *cis-(8h)*, 54724-74-2; *trans-(8h)*, 54724-75-3; *cis-(8c)*, 1439-06-1; *trans-(8i)*, 1689-70-9

Table 1. Compounds *(5)*, *(6)*, and *(8)*. Yields refer to pure products. Spectroscopic data (IR, NMR, MS) are in accord with the proposed structures.

	R^1	R^2	R^3	R^4	Yield [%] *(5)* [a]	*(6)*	*(8)* [b]
a	H	H	C_6H_5	H	66 [c]	97	72
b	H	H	C_6H_5	CH_3	71 [d]	98	73
c	H	H	$-(CH_2)_2-CH(tC_4H_9)-(CH_2)_2-$		45 (55)	66	67
d	H	H	C_6H_5	$CH_2C_6H_5$	82	93	46
e	H	CH_3	C_6H_5	CH_3	57 (73) [e]	98	63 [f]
f	H	CH_3	C_6H_5	C_6H_5	41 (79)	83	46
g	H	CH_3	C_6H_5	$CH_2C_6H_5$	69 (75)	73	51 [f]
h	H	C_2H_5	n-C_6H_{13}	H	50	80	70 [f]
i	H	n-C_3H_7	n-C_3H_7	H		97	70 [f]
j	CH_3	CH_3	C_6H_5	CH_3	67 (81)	—	—

[a] Based on reacted *(4)*.
[b] Based on *(6)*.
[c] Diphenylmethanol also isolated (32%).
[d] Diphenylmethylmethanol also isolated (17%).
[e] Diphenylmethylmethanol also isolated (14%).
[f] Stereoisomeric mixture.

[*] Dr. W. Dumont and Prof. Dr. A. Krief [**]
Departement de Chimie, Facultés de Namur
61, rue de Bruxelles, B-5000 Namur (Belgium)
[**] On leave from C.N.R.S. (France).

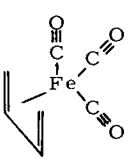
[1] Reported in part at the Ist IUPAC Symposium on Organic Synthesis (F.I.C.O.S.) held at Louvain-la-Neuve (Belgium), August 1974.

[2] *W. Dumont, P. Bayet*, and *A. Krief*, Angew. Chem. *86*, 857 (1974); Angew. Chem. internat. Edit. *13*, 804 (1974).
[3] Phenylselenoalkyllithium cannot be produced by the reaction of *n*-butyllithium and alkyl phenyl selenides [2].
[4] Phenylselenoalkyllithium derivatives are powerful intermediates for synthesis of allylic alcohols [2, 5], olefins, unsaturated carbonyl compounds, and nitriles (unpublished results from our laboratory).
[5] *D. Seebach* and *A. K. Beck*, Angew. Chem. *86*, 859 (1974); Angew. Chem. internat. Edit. *13*, 806 (1974), and paper cited therein.
[6] Dimethyl sulfate (neat; 100 °C) is also effective in the case of *(5)*, R^1, $R^2 = H$.
[7] a) *W. Dumont, P. Bayet*, and *A. Krief*, Angew. Chem. *86*, 308 (1974); Angew. Chem. internat. Edit. *13*, 274 (1974); b) unpublished results from our laboratory.
[8] *E. J. Corey* and *M. Chaykovsky*, J. Amer. Chem. Soc. *87*, 1353 (1965).
[9] a) *J. R. Shanklin, C. R. Johnson, J. Ollinger*, and *R. M. Coates*, J. Amer. Chem. Soc. *95*, 3429 (1973); b) for an extension of this method by cleavage of thioselenoacetals see refs. [1, 5].

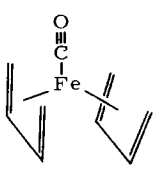
Bis(1,3-butadiene)monocarbonylmanganese—A Paramagnetic Butadiene Complex[**]

By *Max Herberhold* and *Abbas Razavi*[*]

Irradiation of pentacarbonyliron in the presence of 1,3-butadiene in solution affords two substitution products containing bidentate *cis*-butadiene chelate ligands: $Fe(CO)_3C_4H_6$ *(1)*[1] and $Fe(CO)(C_4H_6)_2$ *(2)*[1, 2]. The molecular structures of *(1)*[3] and *(2)*[4] have been determined by X-ray methods[5]. We have now photolyzed tetracarbonylnitrosylmanganese, which is isoelectronic with $Fe(CO)_5$, in the presence of 1,3-butadiene in order to establish the existence of the complexes $Mn(CO)_2(NO)C_4H_6$ *(3)* and $[Mn(NO)(C_4H_6)_2]$ analogous to *(1)* and *(2)*, respectively. Surprisingly, we found *(3)* to be accompanied not by the expected bis(1,3-butadiene)mononitrosylmanganese, which would possess a noble gas configuration, but by a paramagnetic complex of composition $Mn(CO)(C_4H_6)_2$ *(4)*.



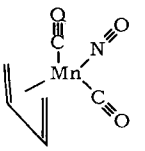
(1)



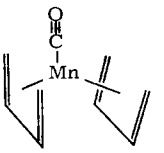
(2)

Irradiation of a THF solution of $Mn(CO)_4NO$ and excess 1,3-butadiene at −30 °C affords a green solution containing (at least) three new complexes. On chromatography of the reaction products, a yellow and a blue-green zone (I and II, respectively) can be eluted with benzene, and then an olive-green zone (III) with THF.

Zone I (yellow) essentially contains $Mn(CO)_2(NO)C_4H_6$ *(3)*. The diamagnetic complex is readily soluble in all organic solvents and volatile in a high vacuum at room temperature; on removal of solvent it is obtained as a yellow oil which solidifies at about 15 °C. The IR spectrum contains two C≡O stretching vibrations of approximately equal intensity at 2045 and 1994 cm^{-1} and an N≡O stretching band at 1751 cm^{-1} (in *n*-pentane). In the ^{1}H-NMR spectrum the characteristic pattern of the *cis*-butadiene ligand is observed with its three symmetrical groups of signals ($\tau = 5.08$ (2H), 8.53 (2H), and 9.95 (2H); in $[D_6]$benzene); the signal at $\tau = 5.08$ is due to the two protons on C^2 and C^3. Very similar ^{1}H-NMR spectra have been reported for the butadiene-iron complexes *(1)*[2, 8], *(2)*[2, 9], and $Fe(PF_3)(C_4H_6)_2$[10], as well as for a series of other butadiene-metal compounds[11]. In the mass spectrum[12] of *(3)* the molecular ion (*m/e* 195, $I_{rel.}$ 8.7%) is accompanied by the fragments $Mn(CO)(NO)C_4H_6^+$ (167, 15.0%), $Mn(NO)C_4H_6^+$ (139, 17.7%), $Mn(C_4H_6)^+$ (109, 14.7%), and Mn^+ (55, 100%); all ligand eliminations can be identified from metastable transitions.



(3)



(4)

Zone II (blue-green) affords $Mn(CO)(C_4H_6)_2$ *(4)*, which crystallizes as long needles from *n*-pentane (dec. pt. ≈150 °C). Their composition is confirmed by elemental analysis and by the mass spectrum[12], which reveals stepwise loss of the CO group and the two diene ligands: $Mn(CO)(C_4H_6)_2^+$ (*m/e* 191, $I_{rel.}$ 2.2%), $Mn(C_4H_6)_2^+$, (163, 27.4%), $Mn(C_4H_6)^+$ (109, 17.7%), Mn^+ (55, 100%). Here too, all the fragmentation steps are indicated by metastable transitions. The IR spectrum exhibits only one strong C≡O stretching absorption (1968 cm^{-1}, *n*-pentane). The complex *(4)* is paramagnetic, corresponding to one unpaired electron[13]. The ESR spectrum[14] in *n*-pentane solution shows an interaction of the single electron with the nuclear spin of the manganese ($I = 5/2$); the *g* factor is 2.018 (half-width 20 G). Splitting of the 6 absorptions by interaction with the nuclear spins of the butadiene protons is not observed. Just one signal (half-width 65 G) appears in the solid state; its asymmetric shape indicates slight differences in the *g* factors along the preferred directions of the molecular axes. To our knowledge paramagnetic complexes with *cis*-butadiene chelate ligands have not previously been reported. Complex *(4)* has a molecular structure[15] of symmetry C_{2v} corresponding to the iron complex *(2)*[4]; the CO ligand coincides with the C_2 axis.

The zone eluted with THF (zone III, green) comprises complexes containing $[Mn(NO)_3]$ groups. The IR spectrum indicates the presence of the adduct $[Mn(NO)_3(THF)]$ (ν(N≡O) 1778 (w), 1666 (vs) cm^{-1})[16] which decomposes on removal of the solvent. Butadiene is incapable of diplacing coordinated THF in THF solution to form $Mn(NO)_3C_4H_6$. In contrast, addition of triphenylphosphane to the green solution yields the known $Mn(NO)_3(PPh_3)$ (ν(N≡O) 1776, 1686/1679 cm^{-1})[16].

Irradiation of $Mn_2(CO)_{10}$ in the presence of 1,3-butadiene in solution affords a small yield of a dinuclear complex $Mn_2(CO)_8C_4H_6$[17] which contains both an Mn—Mn bond and a *trans*-butadiene bridging ligand[18]. Derivatives with two butadiene ligands per metal atom are not formed in detectable amounts.

Procedure[19]:

A solution of $Mn_2(CO)_{10}$ (0.390 g, 1 mmol) in THF (300 ml) is "photonitrosylated"[16] for about 15 min; $Mn(CO)_4NO$ is then condensed from the dark red solution with the solvent THF and thus separated from unchanged $Mn_2(CO)_{10}$ and from $[Mn(NO)_3(THF)]$. Two THF solutions of $Mn(CO)_4NO$ prepared in this way are united and about 20—25 ml of 1,3-butadiene condensed in at −30 °C. After 3 hours' irradiation (high pressure mercury arc, Hanovia L-450 W) at −30 °C the homogeneous green solution is dried and the residue

[*] Doz. Dr. M. Herberhold and Dr. A. Razavi
Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

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

chromatographed in benzene over silica gel. The first zone contains *(3)* (20 mg, 2.6%), the second *(4)* (15—30 mg, 2—4%). Elution with THF affords a third fraction from which $Mn(NO)_3(PPh_3)$ (82 mg, 15%) is obtained after addition of triphenylphosphane. The low yields of *(3)* and *(4)* based on $Mn_2(CO)_{10}$ are partly due to the low efficiency of the photonitrosylation method[16] employed in the preparation of $Mn(CO)_4NO$ which affords a very pure product in a short time.

Received: October 23, 1974 [Z 171a IE]
German version: Angew. Chem. 87, 351 (1975)

CAS Registry numbers:
(3), 54688-86-7; *(4)*, 54688-87-8; $Mn(CO)_4NO$, 16104-17-9

[1] *E. Koerner von Gustorf, Z. Pfajfer,* and *F.-W. Grevels,* Z. Naturforsch. *26b*, 66 (1971).
[2] *E. Koerner von Gustorf, J. Buchkremer, Z. Pfajfer,* and *F.-W. Grevels,* Angew. Chem. *83*, 249 (1971); Angew. Chem. internat. Edit. *10*, 260 (1971).
[3] *O. S. Mills* and *G. Robinson,* Acta Crystallogr. *16*, 758 (1963).
[4] *D. A. Whiting,* Cryst. Struct. Commun. *1*, 379 (1972).
[5] Carbonyliron complexes with monodentate ($Fe(CO)_4C_4H_6$ [6]) or bridging ($[Fe(CO)_4]_2C_4H_6$ [6, 7]) butadiene ligands are also known; they were prepared starting from $Fe_2(CO)_9$ [6].
[6] *H. D. Murdoch* and *E. Weiss,* Helv. Chim. Acta *45*, 1156 (1962).
[7] Cf. *K. A. Klanderman,* Diss. Abstr. *25*, 6253 (1965).
[8] *M. L. H. Green, L. Pratt,* and *G. Wilkinson,* J. Chem. Soc. *1959*, 3753; *R. Burton, L. Pratt,* and *G. Wilkinson, ibid. 1961*, 594; *H. G. Preston, Jr.* and *J. C. Davis, Jr.,* J. Amer. Chem. Soc. *88*, 1585 (1966).
[9] *A. Carbonaro* and *A. Greco,* J. Organometal. Chem. *25*, 477 (1970).
[10] *E. Koerner von Gustorf, O. Jaenicke,* and *O. E. Polansky,* Angew. Chem. *84*, 547 (1972); Angew. Chem. internat. Edit. *11*, 532 (1972); *D. L. Williams-Smith, L. R. Wolf,* and *P. S. Skell,* J. Amer. Chem. Soc. *94*, 4042 (1972).
[11] Cf. *E. O. Fischer* and *H. Werner:* Metal π-Complexes, Vol. 1, Complexes with Di- and Oligo-olefinic Ligands. Elsevier, Amsterdam 1966, pp. 161—163.
[12] Atlas CH4, ion source TO4, direct inlet, 50 eV; investigations by Dipl.-Chem. *W. Kalbfus.*
[13] Preliminary measurement of the magnetic moment by the ^{1}H-NMR method gave $\mu_{eff} = 1.79\ \mu_B$ (25 °C).
[14] Varian E3; measurements by Dipl.-Chem. *R. Weissgerber.*
[15] *G. Huttner, D. Neugebauer,* and *A. Razavi,* Angew. Chem. *87*, 353 (1975); Angew. Chem. internat. Edit. *14*, 352 (1975).
[16] *M. Herberhold* and *A. Razavi,* J. Organometal. Chem. *67*, 81 (1974).
[17] *M. L. Ziegler, H. Haas,* and *R. K. Sheline,* Chem. Ber. *98*, 2454 (1965).
[18] *H. E. Sasse* and *M. L. Ziegler,* Z. Anorg. Allg. Chem. *392*, 167 (1972).
[19] *Note added in proof* (March 20, 1975): Complex *(4)* was also obtained in low yield by co-condensation of Mn atoms with 1,3-butadiene at −196 °C and subsequent treatment of the product with CO (*P. S. Skell* and *M. P. Silvon,* unpublished results).

Crystal and Molecular Structure of Bis(1,3-butadiene)-monocarbonylmanganese[**]

By *Gottfried Huttner, Dietmar Neugebauer,* and *Abbas Razavi*[*]

The X-ray structure determination of bis(1,3-butadiene)-monocarbonylmanganese *(1)* first prepared by *Herberhold et al.*[1] should establish whether the electronic configuration of *(1)*, which deviates from the noble gas rule, has any detectable effect on the structure of the molecule[2], and whether the interaction between the unpaired electrons of different molecules induces specific changes in the lattice.

[*] Doz. Dr. G. Huttner, D. Neugebauer, and Dr. A. Razavi
Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstrasse (Germany)

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

Crystal data: $(C_4H_6)_2MnCO$ *(1)*, relative molecular mass 191.13, tetragonal; $a = b = 780 \pm 1$, $c = 721 \pm 1$ pm; $\alpha = \beta = \gamma = 90°$; $V = (439 \pm 2) \times 10^6$ pm^3; $Z = 2$; $d_{X\text{-ray}} = 1.446 \pm 0.006$, $d_{exp} = 1.44 \pm 0.01$ g cm^{-3}; space group $P\bar{4}2_1m$[3]. Figure 1 shows the structure of *(1)*, Figure 2 depicts its crystal structure, and Table 1 lists its positional parameters.

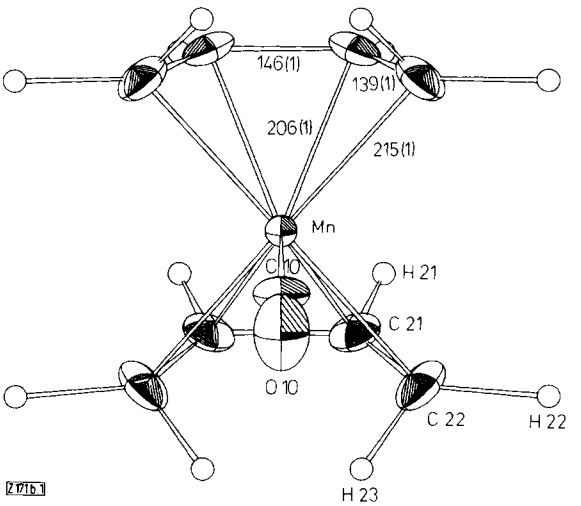


Fig. 1. Molecular structure of $(C_4H_6)_2MnCO$ *(1)*; bond lengths given in pm.

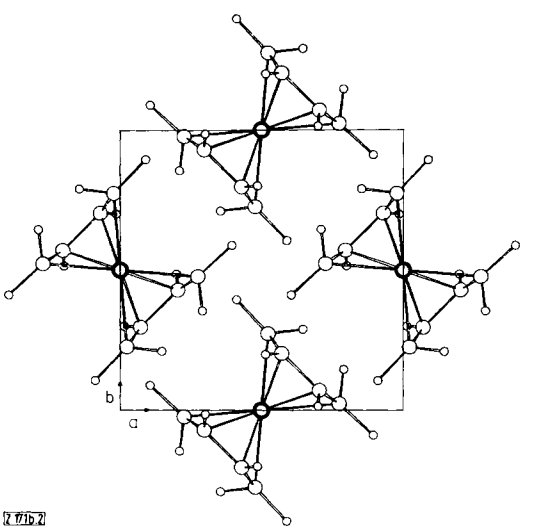


Fig. 2. Crystal lattice of $(C_4H_6)_2MnCO$ *(1)*.

Table 1. Atomic parameters of $(C_4H_6)_2MnCO$ *(1)* (standard deviations in units of the last decimal place given in parentheses).

Atom	x/a	y/b	z/c
Mn	0.0	0.5	0.27648 (19)
C(10)	0.0	0.5	0.5313 (17)
O(10)	0.0	0.5	0.6876 (21)
C(21)	0.2033 (9)	0.4289 (12)	0.1114 (14)
C(22)	0.2741 (9)	0.4769 (16)	0.2800 (17)
H(21)	0.200 (20)	0.485 (18)	−0.001 (17)
H(22)	0.290 (18)	0.354 (20)	0.329 (30)
H(23)	0.394 (18)	0.589 (18)	0.306 (29)

Structural analysis ($R_1 = 0.077$) shows that *(1)* crystallizes in the same space group as four other bis(butadiene)metal complexes: $(C_4H_6)_2Fe(CO)$ *(2)*[4], $(C_4H_6)_2FePF_3$ *(3)*[5], $(C_4H_6)_2RhCl$ *(4)*[6], and $(C_4H_6)_2IrCl$ *(5)*[7]. The isomorphism of the crystal structure of the diamagnetic compounds *(2)*—

(5) with the lattice structure of the paramagnetic complex *(1)* (Fig. 2) clearly demonstrates that the intermolecular interactions between the unpaired electrons in the lattice of *(1)* have no detectable effect upon the structure of the solid. The molecular structure of *(1)* likewise displays no fundamental deviations from those of the diamagnetic compounds *(2)*—*(5)*.

Like the analogs *(2)*—*(5)*, compound *(1)* possesses crystallographic C_{2v} symmetry. For this reason the butadiene ligands are strictly planar. Their "opening" points in the direction of the terminal CO group and the angle between their planes is 11.8°; their terminal carbon atoms form the base of an almost square pyramid whose apex is occupied by the carbonyl group (Mn—C_{CO}: 184±1 pm, C—O: 113±2 pm). Within the limits of error the manganese atom lies in the plane described by the terminal carbon atoms (±1 pm).

While the bond lengths in free butadiene correspond approximately to the values expected for C—C single and C=C double bonds[8], complexed butadiene ligands show compensation of bond lengths, as can be detected in *(1)* (Fig. 1) and likewise in its structural analogs *(2)*—*(5)*. Another characteristic feature of complexed butadiene is the closing of the C=C—C angle from 122.9±0.5°[8] in the free ligand to 118±1° in *(1)*, as has been found in all bis(butadiene)metal complexes so far investigated[9]. The difference in the distance between the metal and the central (Mn—C(21): 206±1 pm) and the terminal carbon atoms (Mn—C(22): 215±1 pm) is in full accord with analogous findings for other butadiene-metal complexes.

Compound *(1)* is the first bis(1,3-butadiene)metal complex whose hydrogen atoms have been located by X-ray analysis. Although the method does not give very accurate positional parameters for the protons (±17 pm) they show beyond any doubt that the *cis* H atoms of the terminal CH_2 groups (H(22) in Fig. 1) lie above the plane of the butadiene ligands on the side opposite to the metal (deviation: +72 pm). The *trans* H atoms (H(23) in Fig. 1), on the other hand, are situated in the ligand plane, while the hydrogen atoms H(21) bonded to the central carbon atoms occupy positions below this plane (deviation: −24 pm). Similar deviations observed for mono(1,3-butadiene)metal complexes were interpreted in terms of a rehybridization of the carbon atoms of the butadiene ligand[10].

Our results show that the presence of an unpaired electron in *(1)* affects neither the molecular structure of the complex nor its lattice structure.

Received: December 17, 1974 [Z 171b IE]
German version: Angew. Chem. 87, 353 (1975)

CAS Registry numbers:
(1), 54688-87-8

[1] *M. Herberhold* and *A. Razavi*, Angew. Chem. *87*, 351 (1975); Angew. Chem. internat. Edit. *14*, 351 (1975).
[2] Regarding the connection between noble gas electron configuration and structure, see, *e.g.*, *G. Huttner* and *S. Lange*, Acta Crystallogr. *B28*, 2049 (1972).
[3] 425 independent non-zero reflections were collected on a Stoe two-circle diffractometer in the layers *hkL* ($0 \leq L \leq 7$) (Mo-Kα radiation, graphite monochromator, λ = 71.069 pm).
[4] *D. A. Whiting*, Cryst. Struct. Commun. *1*, 379 (1972); *R. E. Davis*, *G. L. Cupper*, and *H. D. Simpson*, Abstr. Amer. Crystallogr. Ass. Summer Meeting *1970*, 80.
[5] *C. Krüger* and *Y. H. Tsay*, Eur. Cryst. Meeting *1973*; we are indebted to Dr. *C. Krüger* for supplying the structural data.
[6] *A. Immirzi* and *G. Allegra*, Acta Crystallogr. *B25*, 120 (1969).
[7] *C. van Soest*, *A. van der Ent*, and *E. C. Royers*, Cryst. Struct. Commun. *3*, 527 (1973).
[8] *D. J. Marais*, *N. Sheppard*, and *B. P. Stoicheff*, Tetrahedron *17*, 163 (1962); *A. A. Almenningen*, *O. Bastiansen*, and *M. Traetteberg*, Acta Chem. Scand. *12*, 1221 (1958).
[9] *M. R. Churchill*, J. Organometal. Chem. *4*, 258 (1965).
[10] *R. Eiss*, Inorg. Chem. *9*, 1650 (1970); *I. W. Bassi* and *R. Scordamaglia*, J. Organometal. Chem. *37*, 353 (1972).

Structure and Absolute Configuration of an Optically Active Square Pyramidal Molybdenum Complex[1]

By *S. J. La Placa*, *Ivan Bernal*, *Henri Brunner*, and *W. A. Herrmann*[*]

Dedicated to Professor Helmut Behrens on the occasion of his 60th birthday

The X-ray structure analysis of $(+)_{579}$-$[C_5H_5Mo(CO)_2NN']^+PF_6^-$ *(1)* (NN' = Schiff base derived from 2-pyridinecarbaldehyde and S-(−)-α-phenylethylamine) represents the first determination of the absolute configuration of an organometallic compound in which the transition metal atom constitutes the asymmetric center.

The orthorhombic single crystals of *(1)*[2, 3], obtained from acetone/methylene chloride/ethanol (20 : 3 : 1), crystallize in the polar space group $P2_12_12_1$ with cell constants $a = 12.245(5)$, $b = 9.237(4)$, $c = 20.693(7)$ Å; $V = 2340.53$ Å^3; $d_{exp} = 1.62$, $d_{calc.} = 1.61(2)$ g·cm^{-3}. The unit cell contains 4 molecules. 9730 *hkl* and *hkl̄* data were obtained with a computer-controlled diffractometer using monochromatized MoKα radiation (λ = 0.71069 Å) to $2\theta \leq 72°$. To solve and refine the structure, the reduced and averaged set with $2\theta \leq 41.6°$ (2359 reflections) was used. At this stage of the refinement, the residuals $R(F)$ and $R_w(F)$ are 7.3 and 9.0%, respectively.

The absolute configuration of *(1)* was determined by comparing 46 pairs of reflections of the type *hkl* and *hkl̄*, taking advantage of the anomalous scattering of Mo and P for MoKα radiation (Fig. 1).

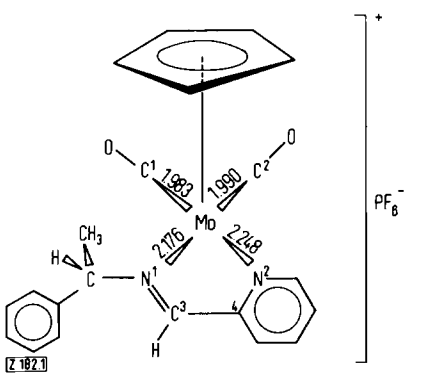


Fig. 1. Structure and absolute configuration of $(+)_{579}$-$[C_5H_5Mo(CO)_2NN']^+PF_6^-$ *(1)*.

Table 1. Bond angles [°] in the complex cation of *(1)*.

C1MoN1	N1MoN2	N2MoC2	C2MoC1
120.9	72.4	130.4	73.9
MoN1C3	N1C3C4	C3C4N2	C4N2Mo
118.7	118.0	115.4	115.2

In the approximately square pyramidal cation, the center of the π-bonded cyclopentadienyl ring occupies the apex of the pyramid. The 5 Mo—C distances are 2.265—2.369 Å. The

[*] Mr. S. J. La Placa [**] and Prof. Dr. I. Bernal [***]
Chemistry Department, Brookhaven National Laboratory
Upton, Long Island, N. Y. 11973 (USA)
Prof. Dr. H. Brunner and Dr. W. A. Herrmann
Fachbereich Chemie der Universität
84 Regensburg 2, Universitätsstrasse 31 (Germany)
[**] New address: IBM Research Laboratories, Yorktown, N. Y. 10598 (USA).
[***] New address: Department of Chemistry, University of Houston, Houston, Texas 77004 (USA).

atoms C1, C2, N1 and N2 are nearly coplanar, about 0.5 Å below the Mo atom. The most important distances and bond angles are given in Figure 1 and Table 1.

The X-ray structure analysis confirms the *S* configuration of the α-phenylethyl group. Before the configuration at the Mo atom can be specified with the *R,S*-system[4], rules for the treatment of π-bonded ligands must be developed.

Received: January 9, 1975 [Z 182 IE]
German version: Angew. Chem. *87*, 379 (1975)

CAS Registry numbers:
(1), 54750-18-4

[1] *S. J. La Placa* and *I. Bernal* thank the U. S. Atomic Energy Commission for support of this research while they were at Brookhaven National Laboratory. Part 30 of the series "Optically Active Transition Metal Complexes". This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 29: *H. Brunner* and *M. Langer*, J. Organometal. Chem. *87*, 223 (1975).

[2] *H. Brunner* and *W. A. Herrmann*, Chem. Ber. *105*, 3600 (1972).

[3] *H. Brunner* and *W. A. Herrmann*, Chem. Ber. *106*, 632 (1973).

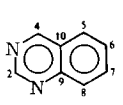
[4] *R. S. Cahn*, *C. Ingold*, and *V. Prelog*, Angew. Chem. *78*, 413 (1966); Angew. Chem. internat. Edit. *5*, 385 (1966).

Covalent Hydration—New Results Using ^{13}C-NMR Spectroscopy[1]

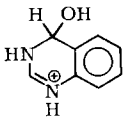
By *Ulrich Ewers*, *Harald Günther*, and *Lothar Jaenicke*[*]

The structure of covalent hydrates that are formed by addition of water to CN double bonds in nitrogen heterocycles[2] has been elucidated so far mainly with the help of UV spectroscopy[2, 3]. We now show that more precise and reliable information is obtained from ^{13}C-NMR spectroscopy because of the sensitivity of chemical shifts to hybridization changes and substituent effects.

According to previous results[4] quinazoline (1,3-diazanaphthalene) exists in $CDCl_3$ as neutral species *(1)* and in 2 N H_2SO_4 as protonated hydrate *(2)*. Hydrate formation is recognized ^{13}C-NMR spectroscopically by the strong shielding

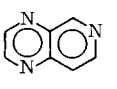


(1)

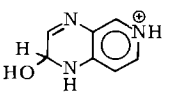


(2)

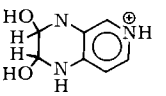
experienced by C-4 (Table 1), whose resonance shifts to 72.4 ppm, *i.e.* into the region typical for "carbinol" carbons. In addition, protonation at N-1 documents itself through upfield shifts for C-2 and C-9. Protonation alone does not change δ(4) significantly, since for the anhydrous cation *(1$^{\oplus}$)* (CF_3COOH) we find a value of 159.2 ppm.



(3)



(4)



(5)

Pyrido[3,4-*b*]pyrazine (1,4,6-triazanaphthalene) *(3)* was formulated in 1 N H_2SO_4 initially as protonated monohydrate *(4)*[5] and later as dihydrate *(5)*[5]. In the ^{13}C-NMR spectrum (Fig. 1) we find *two* resonances at 73.7 and 74.5 ppm. Therefore, *(5)* must be present, whose structure is also compatible with the other δ(^{13}C)-values. With the exception of C-9 all carbon resonances are strongly shielded as a result of protonation at N-6 and NH-substitution at C-9 and C-10. Since only five C(sp^2) resonances are observed, a mixture of two monohydrates can be ruled out.

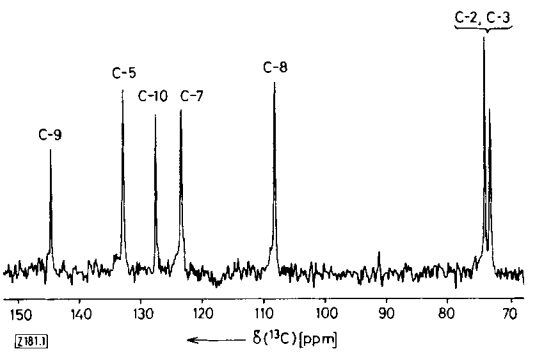


Fig. 1. ^{13}C-NMR spectrum of 1,4,6-triazanaphthalene in 1 N H_2SO_4; δ-values refer to TMS as standard (cf. footnote in Table 1).

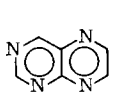
New results were obtained through ^{13}C-NMR spectroscopy for pteridine (1,3,5,8-tetra-azanaphthalene) *(6)*. Owing to slow hydration in aqueous solution, freshly prepared solutions of *(6)* at first show δ(^{13}C)-values that are also observed in $CDCl_3$[7] (Table 1). However, after equilibration (12 h) a spectrum is obtained that shows, besides the signals due to *(6)*, *three* CHOH-resonances at 73.7, 73.9, and 75.1 ppm. We assume that, already at pH 6.8 in addition to the monohydrate *(7)*[2] the dihydrate *(8)* is formed in almost equal amount. This interpretation would also best explain the new signals

Table 1. δ(^{13}C)-values (in ppm, relative to TMS) in heteroaromatics and their hydrates [a].

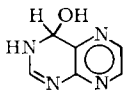
		C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
(1)	$CDCl_3$	156.1	—	161.1	128.1	128.8	135.1	129.3	151.3	126.0
(2)	2 N H_2SO_4	148.1	—	72.4	118.3	129.2	129.2	131.7	*130.4*	*121.4*
(3)	$CDCl_3$	*150.2*	*148.4*	—	155.8	—	147.8	122.8	146.3	139.0
(5)	1 N H_2SO_4	74.5	73.7	—	*133.5*	—	*124.0*	108.8	*145.2*	*128.2*
(6)	$CDCl_3$	160.0	—	164.6	—	148.8	153.4	—	153.4	135.9
(6)	H_2O	158.7	—	164.2	—	149.9	154.7	—	154.7	134.9
			CHOH					C(sp^2)		
(7)+(8)	H_2O	73.7,	73.9,	75.1	158.4,	154.4,	151.8,	149.5,	145.7,	142.1, 137.8, 124.9

[a] Assignments based on additivity relations and ^{13}C,^{1}H coupling constants; preliminary assignments are in italics. Following recent results [8] the older assignments for δ(2) and δ(4) in *(1)* [9] and *(6)* [7] must be reversed. Measurements were made at 22.63 MHz with a Bruker HX-90 spectrometer. External dioxane served as reference in all cases. Conversion of the δ-values to the δ_{TMS}-scale was based on δ_{TMS}(dioxane) = 67.4 ppm.

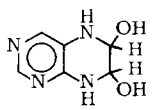
[*] Prof. Dr. H. Günther and Dipl.-Chem. U. Ewers
Institut für Organische Chemie der Universität
5 Köln, Zülpicher Strasse 47
Prof. Dr. L. Jaenicke
Institut für Biochemie der Universität
5 Köln, An der Bottmühle 2 (Germany)



(6)



(7)



(8)

found for sp^2 carbons (Table 1). For a trihydrate only 3 additional resonances are expected, whereas a mixture of three different monohydrates should yield 15 signals. Products of ring opening reactions cannot explain the spectrum, since they contain only sp^2 carbons and, in particular, should display a characteristic carbonyl resonance; *(8)* has so far been obtained in protonated form at pH 2[6].

The results for *(3)* and *(6)* each show that one heteroaromatic ring is preserved during hydrate formation. This finding is consistent with the fact that pyridine and pyrimidine do not form hydrates. The existence of a pteridine dihydrate under physiological conditions as substrate of xanthine oxidase could explain the formation of leukopterine as a degradation product of pteridine cofactors[10].

Received: January 9, 1975 [Z 181 IE]
German version: Angew. Chem. 87, 356 (1975)

CAS Registry numbers:
(1), 253-82-7; *(2)*, 54698-98-5; *(3)*, 254-86-4; *(5)*, 54698-99-6; *(6)*, 91-18-9; *(7)*, 14130-90-6; *(8)*, 14130-91-7

[1] Applications of ^{13}C-Resonance Spectroscopy, Part 19. This work has been supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 18 see: *U. Ewers, H. Günther*, and *L. Jaenicke*, Chem. Ber. *107*, 3275 (1974).

[2] *A. Albert* and *W. L. F. Amarego*, Advan. Heterocycl. Chem. *4*, 1 (1965).

[3] *D. D. Perrin*, Advan. Heterocycl. Chem. *4*, 43 (1965).

[4] *M. J. Cho* and *I. H. Pitman*, J. Amer. Chem. Soc. *96*, 1843 (1974); and lit. cited therein.

[5] *T. J. Batterham*, J. Chem. Soc. *C 1966*, 999.

[6] *A. Albert, T. J. Batterham*, and *J. McCormack*, J. Chem. Soc. *B 1966*, 1105.

[7] *U. Ewers, H. Günther*, and *L. Jaenicke*, Chem. Ber. *106*, 3951 (1973).

[8] *U. Ewers, H. Günther*, and *L. Jaenicke*, Chem. Ber. in preparation.

[9] *R. J. Pugmire, M. J. Robins, D. M. Grant*, and *R. K. Robins*, J. Amer. Chem. Soc. *91*, 6381 (1969).

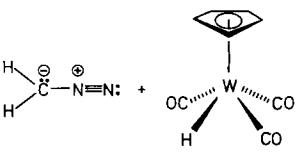
[10] *H. Rembold, H. Metzger*, and *W. Gutensohn*, Biochim. Biophys. Acta *230*, 117 (1971).

Metal-Stabilized *C*-Protonated Diazomethane: A Methanediazonium Complex[1]

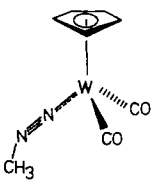
By *Wolfgang A. Herrmann*[*]

On reaction with simple aliphatic diazo compounds transition metal hydrides are generally converted into the corresponding alkyl derivatives, which can be explained as formal carbene insertion into the polar metal-hydrogen bond[2, 3]. In the course of investigations designed to elucidate the diazo method leading to carbene complexes of transition metals[4], diazomethane has now been stabilized as an intact, subsequently protonated molecule by coordination to a metal.

Addition of an excess of diazomethane *(1)* at −85 °C to a THF solution of cyclopentadienyltricarbonyltungsten hydride *(2)* followed by a gradual raising of the temperature to +25 °C affords a dark red neutral compound *(3)* which can be isolated by column chromatography. Compound *(3)* is extremely air-sensitive in solution, and slowly decomposes with evolution of gas when heated to above its melting range of 36—39 °C in a sealed tube.



(1) (2)



(3)

Complete elemental analysis and spectroscopic data show the new complex to possess a diazomethane ligand which has been protonated at the originally sp^2-hybridized carbon atom, and is bound to the metal *via* the terminal nitrogen atom, as a characteristic structural component. While the stretching vibrations of the two metal carbonyl groups are observed in the IR spectrum (benzene) at 1968 vs and 1886 cm^{-1} vs, the bands at 1635 s and 1595 cm^{-1} m are to be assigned to the stretching vibrations of the complexed azo function[5, 6]. The ^1H-NMR spectrum (60 MHz; $CDCl_3$; external TMS) establishes the presence of the cyclopentadienyl ring ($\tau = 4.17$ ppm, singlet) as well as the newly formed methyl group ($\tau = 6.37$ ppm, singlet); absorption no longer occurs in the high-field hydride region. The proposed structure is further supported by the mass spectrum of *(3)* which shows, in addition to the intense molecular peak (*m/e* 350 for ^{186}W), successive elimination of CH_3, N_2, and the two CO groups (70 eV; direct inlet at 10 °C; ion source 30—40 °C).

The above reaction which entails a lowering of the coordination number of the central metal is the first example of CO substitution effected by diazomethane, even though it is associated with a 1,4-hydrogen shift[7]. The ligand CH_3N_2 which corresponds to the highly unstable methanediazonium ion assumes the function of a neutral three-electron donor in the complex.

Procedure:

All operations are carried out with rigorous exclusion of oxygen and moisture (N_2 atmosphere).—A precooled (−35 °C) approximately 0.25 M ethanol-free solution of *(1)* (10 mmol) in diethyl ether[8] is added dropwise to a magnetically stirred solution of *(2)*[2] (1.67 g, 5 mmol) in THF (100 ml) at −85 °C in a thermostated darkened Schlenk flask (programmed cryostat LAUDA K 120 W). After 1 h at −85 °C the mixture is warmed to room temperature over 12 h and stirring continued to complete the reaction (12 h). Chromatography of the concentrated crude product at +10 °C over silica gel 60 (Merck 7734; $l = 80$, $\varnothing = 1.8$ cm) with benzene permits elution of a rapidly migrating yellow zone whose residue affords the methyl derivative $C_5H_5W(CO)_3CH_3$[2] (26 mg, 1.5 %) on high vacuum sublimation at 55 °C. A second red zone is concentrated and rechromatographed under the same conditions. The complex *(3)* initially obtained as a red oil yields fine crystals on reprecipitation (diethyl ether/*n*-pentane; 0 °C) and is analytically pure after recrystallization from diethyl ether/*n*-pentane (1:2) at −100 °C and several hours' drying in high vacuum (0 °C). Yield 1.08 g (62 %).

Received: January 24, 1975 [Z 192 IE]
German version: Angew. Chem. 87, 358 (1975)

CAS Registry numbers:
(1), 334-88-3; *(2)*, 12128-26-6; *(3)*, 54774-68-9

[*] Dr. W. A. Herrmann
Chemisches Institut der Universität
84 Regensburg 1, Universitätsstrasse 31 (Germany)

[1] Complex Chemistry of Reactive Organic Compounds, Part 7.—Part 6: *W. A. Herrmann*, J. Organometal. Chem. *84*, C 25 (1975).

[2] *E. O. Fischer, W. Hafner*, and *H. O. Stahl*, Z. Anorg. Allg. Chem. *282*, 47 (1955).

[3] *M. F. Lappert* and *J. S. Poland*, Advan. Organometal. Chem. *9*, 397 (1970); literature cited therein.
[4] *W. A. Herrmann*, Angew. Chem. *86*, 556 (1974); Angew. Chem. internat. Edit. *13*, 599 (1974); Chem. Ber. *108*, 486 (1975).
[5] *R. B. King* and *M. B. Bisnette*, J. Amer. Chem. Soc. *86*, 5694 (1964); Inorg. Chem. *5*, 300 (1966).
[6] *M. F. Lappert* and *J. S. Poland*, Chem. Commun. *1969*, 1061.
[7] The behavior of higher diazoalkanes towards *(2)* clearly shows the initial reaction step to be CO substitution. The transient diazo complexes $C_5H_5W(CO)_2(H)(N_2{=}CRR')$ can undergo either intramolecular or intermolecular stabilization with participation of the hydride ligand (*W. A. Herrmann* and *H. Biersack*, to be published).
[8] *T. J. DeBoer* and *H. J. Backer*, Rec. Trav. Chim. Pays-Bas *73*, 229 (1954).

Selective Oxidation of the Methyl Group of *p*-Cresols by Base-Catalyzed Oxygenation

By *Akira Nishinaga*, *Toshio Itahara*, and *Teruo Matsuura*[*]

Oxidation of simple alkylarenes to arenecarboxylic acids by base-catalyzed oxygenation in diphenyl sulfoxide[1] or hexamethylphosphoramide (HMPA)[2] is well known. In contrast, little work has been done on side-chain oxidation of alkylphenols because the benzene ring is normally attacked under the reaction conditions. Thus oxygenation of alkylphenols in HMPA/potassium *tert*-butoxide affords 4-hydroxy-5,6-epoxy-2-cyclohexenone derivatives quantitatively[3]. We have now found that if a large excess of potassium *tert*-butoxide is used in dimethylformamide (DMF) the methyl group of substituted *p*-cresols *(1)* is exclusively oxygenated, affording the corresponding *p*-hydroxybenzaldehydes *(2)* in excellent yield (Table 1).

No oxidation of the *o*-methyl group was observed for 2,4,6-trimethylphenol *(1b)*, 2,4-xylenol *(1c)*, and *o*-cresol. *m*-Cresols did not react. The reactivity of the *p*-methyl group depends upon the *o*-substituent and decreases in the order $C(CH_3)_3 > OCH_3 > CH_3 > H > Br$ (Table 1). The use of an excess of base is essential for this selective oxidation; oxidation of the benzene ring increases with decreasing amount of butoxide. The failure of 3,5-di-*tert*-butyl-1-methyl-4-oxo-2,5-cyclohexadienyl hydroperoxide *(3)* [formed from the *p*-cresol *(1a)* by oxygenation in aqueous alkaline solution] to give the *p*-hydroxybenzaldehyde *(2a)* on treatment with potassium *tert*-butoxide in DMF[3] indicates that the reaction does not proceed *via* a hydroperoxide.

General procedure:

Oxygen is passed through a solution of a substituted *p*-cresol *(1)* (2 mmol) in DMF (20 ml) containing potassium *tert*-butoxide (20 mmol) at room temperature. After acidification of the reaction mixture and extraction with ether the aldehydes *(2)* are isolated by TLC and identified by comparison with authentic material (IR and NMR).

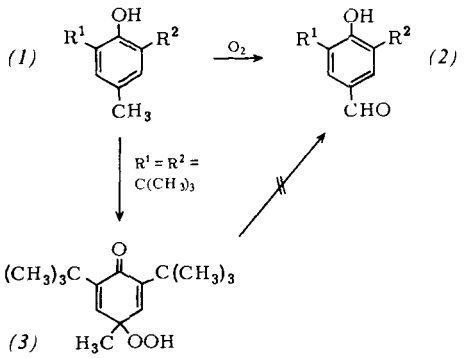


Table 1. Formation of *p*-hydroxybenzaldehydes *(2)* by base-catalyzed oxygenation of *p*-cresols *(1)* at room temperature with potassium *tert*-butoxide as base.

	R^1	R^2	Solvent [a]	Reaction time [h]	Conversion [%]	Yield [%]
a	$C(CH_3)_3$	$C(CH_3)_3$	DMF	12	100	90 [b]
			DEF	15	100	90 [b]
			DMAc	15	100	83 [b]
			DMSO	15	100	10 [b, c]
			HMPA	15	100	6 [b, c]
			tBuOH	15	100	trace
			$DMSO\text{-}HNEt_2$ (15:1)	24	100	35 [b, c]
			$DMSO\text{-}HNEt_2$ (2:1)	24	100	40 [b, c]
			$DMSO\text{-}NEt_3$ (15:2)	24	100	35 [b, c]
			$HMPA\text{-}HNEt_2$ (15:2)	24	100	17 [b, c]
b	CH_3	CH_3	DMF	48	60	70 [b]
c	CH_3	H	DMF	48	20	93 [d]
d	CH_3O	H	DMF	48	55	43 [d]
e	Br	Br	DMF	48	10	92 [d]
f	H	H	DMF	48	15	90 [e]

[a] DMF = dimethylformamide, DEF = diethylformamide, DMAc = *N*,*N*-dimethylacetamide, DMSO = dimethyl sulfoxide, Bu = butyl, Et = ethyl. Values in parentheses: v/v.
[b] Yield of isolated aldehyde.
[c] Accompanying 4-hydroxy-5,6-epoxy-2-cyclohexenone derivatives.
[d] Yield determined by TLC analysis (Shimazu Co. Ltd. TLC scanner CS-900).
[e] Yield determined by NMR spectroscopy.

Received: January 27, 1975 [Z 190 IE]
German version: Angew. Chem. *87*, 386 (1975)

CAS Registry numbers:
(1a), 128-37-0; *(1b)*, 527-60-6; *(1e)*, 105-67-9; *(1d)*, 93-51-6; *(1e)*, 2432-14-6; *(1f)*, 106-44-5

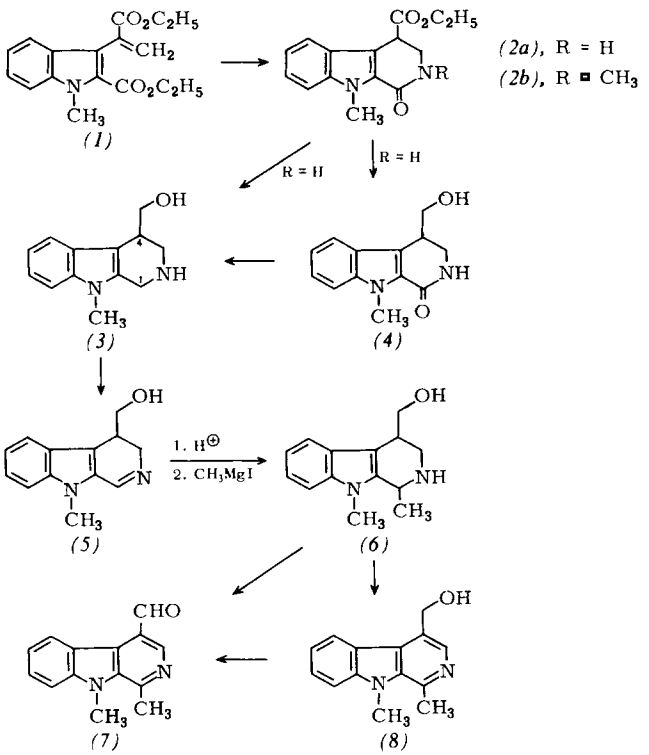
[*] Dr. A. Nishinaga, T. Itahara, and T. Matsuura
Department of Synthetic Chemistry, Faculty of Engineering
Kyoto University, Kyoto (Japan)

[1] *T. J. Wallace*, *A. Schriesheim*, and *N. Jacobson*, J. Org. Chem. *29*, 2907 (1964).
[2] *J. E. Hofmann*, *A. Schriesheim*, and *D. D. Rosenfeld*, J. Amer. Chem. Soc. *87*, 2523 (1965).
[3] *A. Nishinaga*, *T. Itahara*, and *T. Matsuura*, Chem. Lett. *1974*, 667.

Facile Entry to 1,4-Disubstituted β-Carboline Derivatives. Total Synthesis of N^a-Methylbrevicollin[1][**]

By *Wolfgang Müller*, *Reinhard Preuss*, and *Ekkehard Winterfeldt*[*]

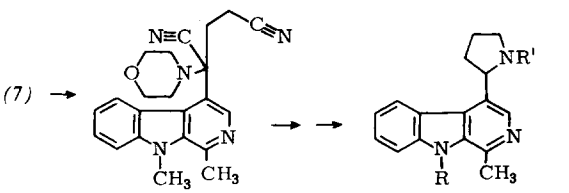
In principle the proton-catalyzed condensation of α-substituted indole compounds with ketones is a known process[2]. We have now found that indole synthesis from methylphenylhydrazine and ethyl pyruvate immediately yields the product *(1)*, and have also established the intermediate occurrence of ethyl *N*-methylindole-2-carboxylate in the reaction. Thus even this acceptor-substituted indole derivative reacts with the carbonyl group of the pyruvate. However, *N*-methylindole-2-carbaldehyde and 2-acetyl-*N*-methylindole do not undergo this condensation. Compound *(1)* proves to be a highly useful and versatile starting material[***] for the synthesis of 1,4-disubstituted β-carboline derivatives such as *(7)*—*(10)*[3].



Compound *(1)* reacts with ammonia or methylamine to form the lactams *(2a)* and *(2b)*, respectively. Reduction of *(2a)* with $LiAlH_4$ proceeds with high selectivity and affords the lactam alcohol *(4)* at room temperature whereas the cyclic amine *(3)* is obtained under reflux. The latter compound is well suited to the introduction of alkyl groups on C^1. The dihydropyridine *(5)*, readily obtainable by lead tetraacetate oxidation, reacts smoothly as the hydrogen chloride with Grignard compounds to give, for example, *(6)*, which directly affords the aldehyde *(7)* on oxidation of small portions with MnO_2. When working on a larger scale it is convenient to first prepare *(8)* with lead tetraacetate and then to obtain the aldehyde *(7)* by treatment of *(8)* with MnO_2.

This aldehyde is an interesting intermediate for the introduction of substituents on C^4. As an example we shall describe the conversion of *(7)* into N^a-methylbrevicollin *(10b)* by a method resembling that used by *Leete*[4] for the synthesis of pyrrolidine derivatives.

Reaction of *(7)* with morpholine and cyanide ion and subsequent Michael addition to acrylonitrile affords the morpholinodinitrile *(9)*. Acid hydrolysis to the keto nitrile followed by reductive cyclization gives *(10a)*, which is converted into N^a-methylbrevicollin *(10b)* by reductive methylation (formaldehyde and cyanotrihydridoborate). This base is found to be identical to the methylation product of brevicollin *(10c)* in all its spectroscopic data and on thin-layer chromatography[5].



Procedure:

(1): Glacial acetic acid (720 ml) and H_2SO_4 (80 ml) are mixed together and 1,1-methylphenylhydrazine (60 g, 0.453 mol) is added dropwise under N_2 to the warm mixture, the temperature being maintained under 50 °C. Ethyl pyruvate (114 g, 0.99 mol) is then added dropwise, the temperature being kept below 70 °C. After completion of reaction the mixture is poured onto five times its volume of ice water and extracted several times with ether. The ethereal phase is washed three times with water, neutralized with Na_2CO_3 solution, and dried over Na_2SO_4. The solvent is drawn off and the residue distilled at 150—170 °C/0.02 torr. The yellowish oily distillate is stirred with ether whereupon crystallization sets in. Yield after recrystallization from ether/5% methanol: 96.2 g (71%), m.p. 72 °C.

(7): Compound *(8)* is refluxed for 3 h in $CHCl_3$ with a tenfold weight of activated MnO_2 (according to *Attenburrow*). Yellow oblong crystals, yield 85%, m.p. 171 °C.

(10b): Compound *(10a)* (33 mg) in CH_3OH (10 ml) containing CH_2O (200 mg) is reduced at room temperature with an excess of $NaBH_3CN$ (40 mg). The reaction is complete within a few minutes. Yield 26.2 mg (82%), m.p. 162 °C (racemate).

Received: February 27, 1975 [Z 203 IE]
German version: Angew. Chem. 87, 385 (1975)

CAS Registry numbers:
(1), 54932-45-5; *(7)*, 54932-46-6; *(8)*, 54932-47-7; *(10a)*, 54932-48-8; *(10b)*, 54932-49-9; 1,1-methylphenylhydrazine, 618-40-6; ethyl pyruvate, 617-35-6

[*] W. Müller, Dr. R. Preuss, and Prof. Dr. E. Winterfeldt [+]
Organisch-Chemisches Institut der Technischen Universität
3 Hannover, Schneiderberg 1 B (Germany)

[+] To whom correspondence should be addressed.

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

[***] All the compounds mentioned were characterized by spectroscopy and gave correct elemental analyses.

[1] Reactions of Indole Derivatives, Part 29.—Part 28: *K. Krohn* and *E. Winterfeldt*, Chem. Ber., in press.

[2] *R. J. Sundberg*: The Chemistry of Indoles. Academic Press, New York 1970, p. 47.

[3] Compounds of this type were isolated several years ago from *Carex brevicollis* (Cyperaceae) (*P. A. Vember*, *I. V. Terent'eva*, and *G. V. Lazurevskii*, Khim. Prir. Soedin. *3*, 249 (1967); Chem. Abstr. *67*, 108816 (1967). For a survey with a description of pharmacological activity, see *M. Baumgarth*, Chem.-Ztg. *97*, 217 (1973).

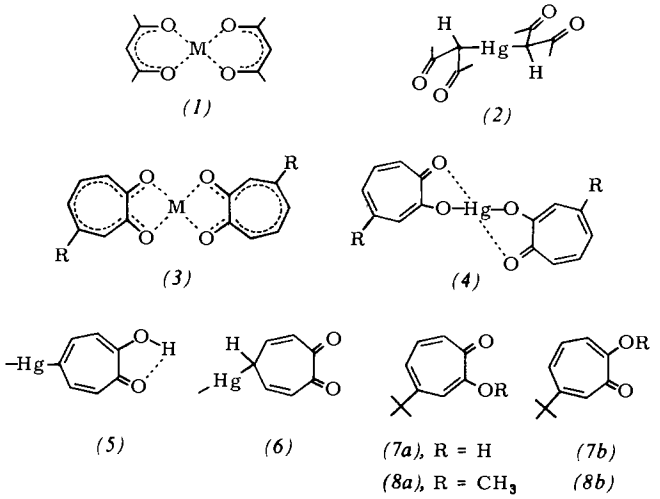
[4] *E. Leete*, *M. R. Chedekel*, and *G. B. Bodem*, J. Org. Chem. *37*, 4465 (1972).

[5] We are indebted to Prof. Dr. *Terent'eva*, Institute for Chemistry of the Academy of Sciences of the Moldavian SSR, for a sample of the alkaloid.

Structure of Mercury(II) Tropolonate[1]

By *Klaus Dietrich* and *Hans Musso*[*]

Nearly all light and heavy metals add acetylacetone and other β-diketones, such as dipivaloylmethane, symmetrically as bidentate ligands *via* the two oxygen atoms, as in *(1)*[2]. Only few exceptions are known[3]; in particular, Hg bonds almost linearly to two β-diketones at carbon giving structure *(2)*[4, 5]. Vinylogous alternatives are offered by tropolone[6]. X-ray structure analysis of several metal complexes (Al, Fe)[7, 8] and comparison of their vibrational spectra[9] likewise demonstrate symmetrical chelate formation *via* the oxygen atoms, as in formula *(3)* (R = H).



(1) *(2)* *(3)* *(4)* *(5)* *(6)* *(7a)*, R = H *(7b)* *(8a)*, R = CH_3 *(8b)*

The sparingly soluble mercury tropolonate ($Hg(tr)_2$) has already been prepared by *Muetterties et al.*[10] but not characterized in detail. Several possibilities exist for its structure: a symmetrical chelate *(3)*; an unsymmetrical chelate or open enolate *(4)*; and the formulas with Hg—C bonds *(5)* and *(6)* analogous to *(2)*. This question has now been settled in favor of structure *(4)* ($R = C(CH_3)_3$) for the more readily soluble derivatives of *tert*-butyl-tropolone (tBtr) *(7a)* ⇌ *(7b)* with Cu, Pd, Zn, Cd, and Hg.

(7) was obtained according to the conventional tropolone synthesis[11] by hydrolysis of the [2+2]-adduct of dichloroketene to *tert*-butylcyclopentadiene, and purified by way of the copper complex. Treatment with diazomethane affords the isomeric methyl ethers *(8a)* and *(8b)* which were separated by gas chromatography and assigned on the basis of their ^{1}H-NMR spectra recorded in the presence of $Eu(dpm)_3$[12].

The ^{1}H-NMR spectrum of $Hg(tBtr)_2$ is in full accord with those of the complexes with Pd and Zn (Table 1). It contains signals for four protons on the tropolone ring and none for OH or Hg—CH protons, thus ruling out structures *(5)* and *(6)*, as previously suspected[10]. The IR spectra of the tropolonates and *tert*-butyltropolonates of Cu, Pd, Zn, and Cd concur in indicating strongly coupled C=O and C=C frequencies of the ligands; those of sparingly soluble $Hg(tr)_2$ and readily soluble $Hg(tBtr)_2$ are similar but show significant deviations to higher and lower wave numbers relative to those of the other metals in the range of vibrations having large C=O components assigned according to *Junge*[9] (Table 2). Thus it is seen that mercury(II) is coordinated to tropolone *via* oxygen atoms, but that a structure *(4)* must result having two roughly linear short Hg—O bonds and two longer ones, as in the case of mercury acetate[13].

Table 1 ^{1}H-NMR signals of the *tert*-butyltropolone derivatives ($CDCl_3$), δ in ppm (integrated number of protons).

	s OR	d [a] 2-H (1)	m [a] 4-H, 5-H, 6-H	s $C(CH_3)_3$ (9)	M.p. [°C]
(7a) ⇌ *(7b)*	8.84 (1)	7.56	7.12—7.32	1.36	33—34
(8a)	3.92 (3)	7.38	6.98—7.15, 6.71	1.30	63—64
(8b)	3.98 (3)	m 6.97—7.22 (4, max. 7.03, 7.16)		1.37	71—73
$Pd(tBtr)_2$	—	7.55	7.15—7.35	1.33	271 (dec.)
$Zn(tBtr)_2$	—	7.81	6.94—7.37	1.27	346—347
$Hg(tBtr)_2$	—	7.78	6.98—7.40	1.31	180—181

[a] $J_{H^2H^4}$ *ca.* 1.5—3.0 Hz, $J_{H^4H^5}$ and $J_{H^5H^6}$ *ca.* 11 Hz.

Table 2. IR frequencies (KBr) in cm^{-1} (estimated intensities 1—10) [a].

$Zn(tr)_2$	$Hg(tr)_2$	Δ^{Hg}_{Zn}	$Zn(tBtr)_2$	$Hg(tBtr)_2$	Δ^{Hg}_{Zn}	assignment [9]
1592 (8)	1591 (9)	− 1	1583 (9)	1583 (8)	0	νC=C
1572 (5)	sh 1576 (3)	+ 4	1570 (9)	1565 (8)	− 5	
			1555 (6)	sh 1559 (7)	+ 4	
1507 (9)	1496 (9)	−11	1500 (9)	1497 (9)	− 3	νC=C
1470 (5)	1470 (4)	0	1461 (8)	1445(10)	−16	+C=O
sh 1438 (8)						
1427 (9)	1420(10)	− 7	1421(10)	1416(10)	− 5	
1410(10)	1403 (9)	− 7	1409(10)	1397 (9)	−12	
1383 (6)				sh 1390 (9)		
			1370 (8)	1367 (6)	− 3	
1348 (9)	1358 (6)	+10	1353(10)	1346(10)	− 7	νC=O
1332(10)	1322 (8)	−10	1326 (8)	1322 (9)	− 4	
			1269 (4)	1267 (3)	− 2	
1250 (7)	1252 (5)	+ 2	1245 (9)	1235(10)	−10	
1221 (9)	1232 (8)	+11				
	1216 (9)					
			sh 1199 (2)	1199 (2)	0	

[a] The IR spectra of $M(tr)_2$, M = Cu, Zn, Cd, and $M(tBtr)_2$, M = Cu, Pd, Zn, Cd, are so similar that only those of the Zn and Hg complexes are given.

[*] Prof. Dr. H. Musso and Dr. K. Dietrich
Institut für Organische Chemie der Universität
75 Karlsruhe 1, Richard-Willstätter-Allee (Germany)

Preparative details and correct analyses of all the new compounds will be found in ref. [12].

Received: December 3, 1974;
supplemented: January 22, 1975 [Z 184 IE]
German version: Angew. Chem. 87, 384 (1975)

CAS Registry numbers:
(7a), 25469-14-1; *(8a)*, 54750-95-7; *(8b)*, 54750-96-8;
$Zn(tr)_2$, 15393-05-2; $Hg(tr)_2$, 15393-06-3; $Cu(tr)_2$, 15663-10-2;
$Cd(tr)_2$, 42947-15-9; $Pd(tBtr)_2$, 54751-08-5; $Zn(tBtr)_2$, 54751-09-6;
$Hg(tBtr)_2$, 54751-10-9; $Cu(tBtr)_2$, 54751-11-0; $Cd(tBtr)_2$, 54774-71-9

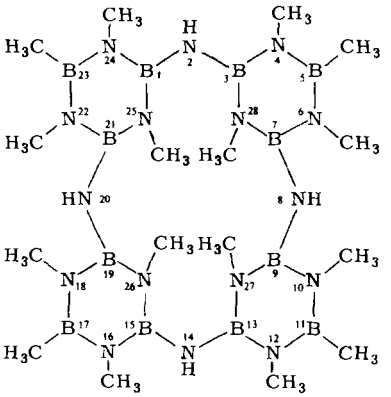
[1] Organic Metal Complexes, Part 12. This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.—Part 11: *R. Allmann, K. Dietrich*, and *H. Musso*, J. Organometal. Chem., in press.
[2] *B. Bock, K. Flatau, H. Junge, M. Kuhr*, and *H. Musso*, Angew. Chem. *83*, 239 (1971); Angew. Chem. internat. Edit. *10*, 225 (1971); *E. C. Lingafelter* and *R. L. Brown*, J. Amer. Chem. Soc. *88*, 2951 (1966).
[3] *D. Gibson*, Coord. Chem. Rev. *4*, 225 (1969).
[4] *R. Allmann, K. Flatau*, and *H. Musso*, Chem. Ber. *105*, 3067 (1972).
[5] *R. Allmann* and *H. Musso*, Chem. Ber. *106*, 3001 (1973).
[6] *F. Pietra*, Chem. Rev. *73*, 293 (1973).
[7] *E. L. Muetterties* and *L. J. Guggenberger*, J. Amer. Chem. Soc. *94*, 8046 (1972).
[8] *R. J. Irving, M. L. Post*, and *D. C. Povey*, J. C. S. Dalton *1973*, 697.
[9] *H. Junge*, Spectrochim. Acta *24 A*, 1957 (1968); *L. G. Hulett* and *D. A. Thornton, ibid, 27 A*, 2089 (1971).
[10] *E. L. Muetterties, H. Roesky*, and *C. M. Wright*, J. Amer. Chem. Soc. *88*, 4856 (1966).
[11] *H. G. Stevens, D. A. Reich, D. R. Brandt, K. R. Fountain*, and *E. G. Gaughan*, J. Amer. Chem. Soc. *87*, 5257 (1965).
[12] *K. Dietrich*, Dissertation, Universität Karlsruhe 1974.
[13] *R. Allmann*, Z. Kristallogr. *138*, 366 (1973).

A Pentacyclic Derivative of Cyclododecaborazane[**]

By *Anton Meller* and *Hans-Jürgen Füllgrabe*[*]

Of the cyclic systems having an alternant arrangement of tricoordinate boron and nitrogen[1], *s*-diazaboretidines[2], *s*-triazaborines (borazines)[3], and *s*-tetraazatetraborocines[4] have so far been described. Moreover, starting from the borazine ring, polycyclic compounds having biphenyl- and naphthalene-type structure are also known, as are condensed borazine derivatives linked *via* tricoordinate nitrogen[1].

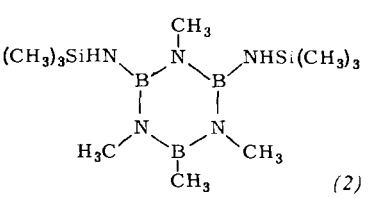
We have now succeeded in the first preparation of a $(BN)_{12}$ ring system by reaction of 1,2,3,5-tetramethyl-4,6-dichloroborazine with hexamethyldisilazane. The major product formed in *ca.* 60% yield is a colorless crystalline compound having m.p. (dec.) 350 °C, and which sublimes at 250 °C/10^{-5} torr and is gradually hydrolyzed by water. Its mass spectrum (250 °C, 70 eV) indicates a relative molecular mass of 598. The *m/e* values (most intense peaks of the individual groups of signals) are M, 598, 100%; $M-CH_3$, 583, 9%; $M-2CH_3$, 568, 14%; $M-3CH_3$, 553, 6%; $M-4CH_3$, 538, 6%; doubly charged ions 299, 15%; 291.5, 2%; 284, 4%; 276.5, 2%; 269, 4%. No fragments of the B—N skeleton occur at measurable intensities above *m/e* 80, fragmentation in this range being limited to elimination of methyl groups. Elemental analysis and the high-resolution mass spectrum confirm the empirical formula $C_{16}H_{52}B_{12}N_{16}$. The ^{1}H-NMR spectrum (20% solution in CH_2Cl_2, TMS internal standard) contains four singlets (relative intensity, assignment) at $\delta = -2.86$ (6, NCH_3), -2.58 (3, NCH_3), -2.32 (1, NH), and -0.48 ppm (3, BCH_3). The ^{11}B-NMR spectrum (30% solution in CH_2Cl_2, $F_3B{\cdot}OEt_2$ as external standard) exhibits broad resonance at $\delta = -30.5$ (± 0.5) ppm, no splitting being recognizable on account of the large half-width (500 Hz) of the signal. These findings are in accord with the cyclotetrakis(aminoborazine) derivative *(1)*[***].



(1)

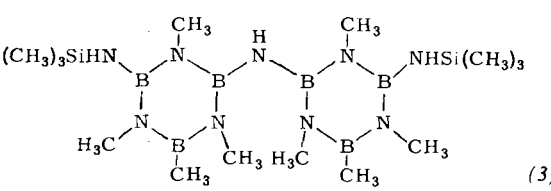
The vibrational spectrum of *(1)* contains a large number of lines. Some of the bands can be assigned with the aid of the spectra of methylborazines[5]. The stronger bands in the spectrum include: 3410 m (νNH), 2950 s, 2900 s, 2825 m (νCH), 1443 vs + 1398 vs ($\delta_s NCH_3$ and $\nu_{as}BN$, coupled), 1300 m ($\delta_s BCH_3$), 1270 m ($\nu_{as}BN$), 1255 sh (?), 1200 w, 1182 m (νBN), 1132 s (ρNCH_3), 1103 s (?), 925 w (?), 892 sh, 880 w (ρBCH_3), 705 m + 693 s (γBN), 665 w (?) cm^{-1}. Apart from that at 1103 cm^{-1} all these bands coincide with Raman lines. Thus the structure of *(1)* is probably not planar, most likely due to the strong steric hindrance of the four "endocyclic" NCH_3 groups. It has not yet been established whether the sterically imposed arrangement leads to the extreme situation in which the borazine rings are located on the sides and the bridge NH groups on the edges of a square prism. Such a structure would preclude π-bonding contributions between the bridge N atoms and borazine B atoms. According to the ^{11}B-NMR spectrum these contributions can only be slight. An X-ray structure analysis is in progress.

A low-yield by-product of the synthesis of *(1)* is 1,2,3,5-tetramethyl-4,6-bis(trimethylsilylamino)borazine *(2)*, b.p. 120 °C/10^{-3} torr.



(2)

Furthermore, bis(1,3,4,5-tetramethyl-6-trimethylsilylamino-2-borazinyl)amine *(3)* can also be isolated in about 25% yield, b.p. 150 °C/10^{-3} torr (bath temperature on molecular distillation).



(3)

[*] Prof. Dr. A. Meller and H. J. Füllgrabe
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstrasse 4 (Germany)

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

[***] Systematic name: 4,5,6,10,11,12,16,17,18,22,23,24,25,26,27,28-hexadecamethyl-1,3,5,7,9,11,13,15,17,19,21,23-dodecabora-2,4,6,8,10,12,14,16,18,20,22,24,25,26,27,28-hexadecaazapentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosane.

Procedure:

Hexamethyldisilazane (25 g) is added dropwise to a stirred solution of 1,2,3,5-tetramethyl-4,6-dichloroborazine[6] (12.8 g) in dry toluene with exclusion of moisture. After refluxing for 3 h and removal of toluene by distillation the residue is refluxed with a further portion (100 ml) of hexamethyldisilazane for another 2.5 h. The colorless residue obtained on distillation of the hexamethyldisilazane is subjected to molecular distillation (10^{-3} torr) and yields a small amount of *(2)* at 120 °C bath temperature and *(3)* at 150 °C. On heating to more that 500 °C in an air bath compound *(1)* sublimes over.

Received: January 16, 1975 [Z 183 IE]
German version: Angew. Chem. *87*, 382 (1975)

CAS Registry numbers:
(1), 54750-92-4; *(2)*, 54750-93-5; *(3)*, 54750-94-6;
1,2,3,5-tetramethyl-4,6-dichloroborazine, 7387-21-5;
hexamethyldisilazane, 999-97-3

[1] Cf. *H. Steinberg* and *R. J. Brotherton*: Organoboron Chemistry, Vol. 2. Wiley-Interscience, New York 1966.
[2] *M. F. Lappert* and *M. K. Majumdar*, Proc. Chem. Soc. London *1963*, 88.
[3] *A. Stock* and *E. Pohland*, Chem. Ber. *59*, 2215 (1926).
[4] *H. S. Turner* and *R. J. Warne*, Proc. Chem. Soc. London *1962*, 69.
[5] *A. Meller* and *M. Wechsberg*, Monatsh. Chem. *98*, 513 (1967).
[6] *R. J. Wagner* and *J. C. Bradford*, Inorg. Chem. *1*, 93 (1962); *R. H. Toeniskoetter* and *F. R. Hall*, *ibid.* *2*, 29 (1963).

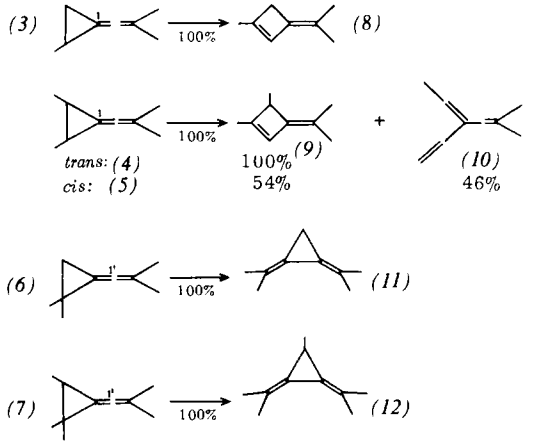
Isomerizations of Alkenylidenecyclopropanes Catalyzed by Lewis Acids

By *Lutz Fitjer*[*]

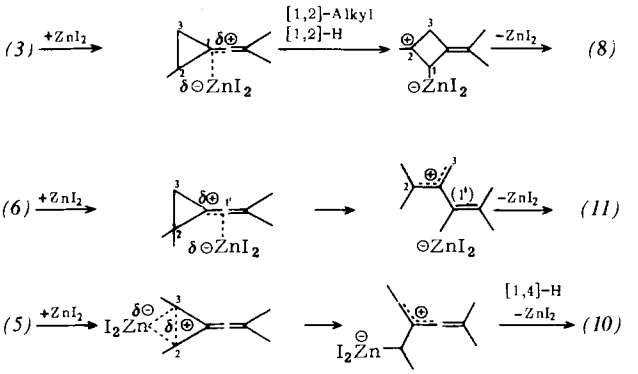
Cyclopropyl and cyclopropylmethyl cations are usually generated in the presence of a nucleophile which is incorporated into the final product[1]. However, they should also be accessible in the form of the complexes *(1)* and *(2)* in the absence of nucleophiles by reaction of suitably substituted methylenecyclopropanes with Lewis acids and thus permit pure isomerizations during cyclopropyl-allyl or cyclopropylmethyl-cyclobutyl rearrangements. This is indeed the case.

Treatment of 2-methyl(2-methyl-1-propenylidene)cyclopropane *(3)*[2] and *trans*-2,3-dimethyl(2-methyl-1-propenylidene)-cyclopropane *(4)*[2] with boiling ethereal zinc iodide solution[5] affords 3-isopropylidene-1-methyl-1-cyclobutene *(8)*[6] and 3-isopropylidene-1,4-dimethyl-1-cyclobutene *(9)*[3], respectively, each as the sole reaction product. In contrast, 2,2-dimethyl(2-methyl-1-propenylidene)cyclopropane *(6)*[2] and 2,2,3-trimethyl(2-methyl-1-propenylidene)cyclopropane *(7)*[2] underwent quantitative isomerization to diisopropylidenecyclopropane *(11)*[7] and 1,2-diisopropylidene-3-methylcyclopropane *(12)*[8]. *cis*-2,3-Dimethyl(2-methyl-1-propenylidene)-cyclopropane *(5)*[2] gave a mixture of *(9)* and 3-ethylidene-5-methyl-1,4-hexadiene *(10)*[3].

As shown for the case of *(3)*, the isomerizations of *(3)*—*(5)* can only be explained in terms of complex formation *via* C^1 and subsequent [1,2]-alkyl and [1,2]-hydride shifts[9]. In contrast, the isomerizations of *(6)* and *(7)* must be preceded by complex formation *via* $C^{1'}$. In this case cyclopropyl-allyl rearrangement and *trans*-1,3-elimination lead to formation of *(11)* and *(12)*, respectively. Formation of *(10)* is presumably attributable to direct opening of the C^2—C^3 bond of *(5)* with subsequent allenylmethyl-butadienyl rearrangement and [1,4]-hydride shift[10].



Remarkably, it is always the carbon atom displaying the lowest degree of substitution (C^3) which undergoes alkyl shift and 1,3-elimination in all the cited isomerizations. This leads to clear-cut reaction courses in all cases.



The above examples demonstrate that cyclopropyl, cyclopropylmethyl (or 1-cyclopropylvinyl), and possibly also allenylmethyl cations are accessible by complex formation of suitably substituted alkenylidenecyclopropanes with Lewis acids, the nature of the cations formed being crucially dependent upon the substitution pattern of the cyclopropane ring.

Received: January 15, 1975 [Z 187 IE]
German version: Angew. Chem. *87*, 381 (1975)

CAS Registry numbers:
(3), 54724-63-9; *(4)*, 37817-46-2; *(5)*, 37817-36-0; *(6)*, 28438-32-6;
(7), 14803-30-6; *(8)*, 10412-56-3; *(9)*, 54677-56-4; *(10)*, 54677-57-5;
(11), 3761-85-1; *(12)*, 13303-32-7; ZnI_2, 10139-47-6

[*] Dr. L. Fitjer
Organisch-Chemisches Institut der Universität
34 Göttingen, Tammannstrasse 2 (Germany)

[1] *C. D. Gutsche* and *D. Redmore*, Advan. Alicyclic Chem. Suppl. 1, p. 1 (1968).
[2] *(3)* [3], *(4)* [4a], *(5)* [4a], *(6)* [4b, 4c], and *(7)* [4c, 4d] were prepared according to *Crandall* [4d] by reaction of 1-bromo-3-methyl-1,2-butadiene with potassium *tert*-butoxide in an excess of the corresponding alkenes.
[3] The new compounds *(3)*, *(9)*, and *(10)* gave correct analytical values; IR, UV, MS data accord with the structures given. The configuration of *(10)* was not determined. ^{1}H-NMR data (100 MHz, CCl_4, TMS int.): *(3)*: δ = 0.93 (m, 1 H), 1.16 (d, CH_3, J = 6 Hz), 1.47 (m, 2 H), 1.68 (s, 2 CH_3); *(9)*: δ = 1.07 (d, CH_3, J = 7 Hz), 1.55 (br. s, 2 CH_3), 1.77 (br. s, CH_3), 2.88 (br. q, 1 H, J = 7 Hz), 5.95 (q, =CH—, J = 1.5 Hz); *(10)*: δ = 1.47 (d, CH_3, J = 1.5 Hz), 1.59 (d, CH_3, J = 7.5 Hz), 1.81 (d, CH_3, J = 2.0 Hz), 4.80 (br. d, 1 H, J = 10 Hz), 4.89 (br. d, 1 H, J = 17 Hz), 5.50 (br. q, 1 H, J = 7.5 Hz), 5.53 (br. s, 1 H), 6.20 (dd, 1 H, J = 10 and 17 Hz).
[4] a) *H. D. Hartzler*, J. Amer. Chem. Soc. *83*, 4997 (1961); b) *ibid.* *83*, 4990 (1961); c) *G. Leandri* and *C. Santelli-Rouvier*, Bull. Soc. Chim.

Fr. 1970, 1515; d) D. R. Paulson, J. K. Crandall, and C. A. Bunell, J. Org. Chem. 35, 3708 (1970).
[5] Isomerization was performed by refluxing solutions of (3)—(7) (5 mmol) in 2.0 M (12.5 ml) ethereal zinc iodide solution for 2—4 h. The isomerizations can also be carried out on a preparative scale: 10 ml of 3.5 M ethereal zinc iodide solution isomerized up to 70 mmol (6).
[6] (8) was hitherto only accessible by quaternization of 1-aminomethyl-3-isopropylidenecyclobutane and subsequent Hofmann degradation (J. K. Williams and W. H. Sharkey, J. Amer. Chem. Soc. 81, 4269 (1959)).
[7] (11) can also be prepared by reaction of 1,1-dibromo-2-methyl-1-propene with methyllithium in the presence of 3-methyl-1,2-butadiene (R. F. Bleiholder and H. Shechter, J. Amer. Chem. Soc. 86, 5032 (1964)).
[8] (12) is also obtained alongside isomeric dialkylidenecyclopropanes on thermal isomerization of (7) [4d].
[9] Compare the results obtained on solvolysis of substituted 1-cyclopropylvinyl cations (D. R. Kelsey and R. G. Bergmann, J.C.S. Chem. Comm. 1973, 589).
[10] Alternatively, consecutive [1,3]- and [1,2]-hydride shifts are also conceivable; specific deuteration of (5) should clarify this matter.

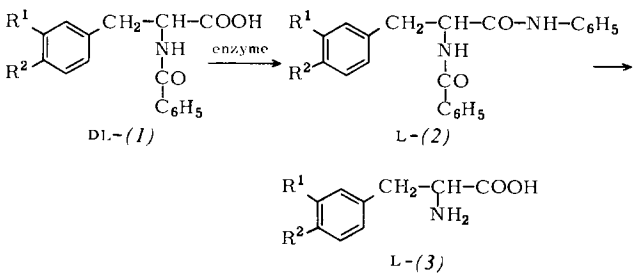
Facile Synthesis of L-3-(3,4-Dihydroxyphenyl)alanine (L-Dopa) and Related Compounds

By *E.-O. Renth*[*]

Dedicated to Professor Karl Zeile on the occasion of his 70th birthday

Use of L-dopa *(3b)* in the treatment of Parkinson's disease prompted us to search for a simple and inexpensive synthesis of this compound. The synthesized L-dopa must be free from the D-enantiomer, which leads to clinical side effects.

Our process consists in enzyme-induced (*e.g.* by papain) asymmetric synthesis. Substituted DL-*N*-benzoylphenylalanine derivatives are transformed into the optically active L-amino acid anilides *(2)*, which are then hydrolyzed to give the L-amino acids *(3)*.



	R^1	R^2	L-(2) Yield [%]	L-(2) $[\alpha]_D^{20}$ [°] in CH_3OH	L-(3) Yield [%]	L-(3) $[\alpha]_D^{20}$ [°] in 1 N HCl
a	OCH_3	OH	100	+40.0 *c* = 1	68	− 5.83 *c* = 1
b	OH	OH			69	−12.15 *c* = 4
c	OH	OCH_3	95	+41.8 *c* = 0.5	61	− 8.5 *c* = 2

L-N-Benzoyl-3-(4-hydroxy-3-methoxyphenyl)alanylanilide (2a)

DL-*N*-Benzoyl-3-(4-hydroxy-3-methoxyphenyl)alanine *(1a)* (31.5 g, 0.1 mol) is dissolved with warming in 0.05 N sodium hydroxide solution (200 ml). After addition of 2 M sodium acetate solution (150 ml) the mixture is filtered. 0.05 N citrate buffer (pH 5.0, 300 ml), cysteinium chloride (2 g), and distilled aniline (18 ml) are then added successively to the filtrate. A solution of about 3 g of papain in 0.05 N citrate buffer (300 ml) is then added and the pH adjusted to 5.80 by addition of glacial acetic acid or 1 N sodium hydroxide solution. After a short time the L-anilide *(2a)* begins to precipitate; after 48 h it is filtered off under suction, washed with water (300 ml), and dried; m.p. 208—209 °C.

L-3-(3,4-Dihydroxyphenyl)alanine (L-dopa) (3b)

L-*N*-Benzoyl-3-(3-hydroxy-4-methoxyphenyl)alanylanilide *(2c)* (9.75 g, 25 mmol) is refluxed for 7 h with 48% hydrobromic acid (50 ml). After cooling, benzoic acid is filtered off and rinsed with a small volume of cold 48% hydrobromic acid, and the slightly yellow solution evaporated down *in vacuo*. The residue is dissolved in methanol (50 ml) and propylene oxide (5 ml) is added. The temperature is maintained at 50 °C until the pH value of 6.0 has been attained, and the mixture is then cooled and the product *(3b)* is filtered off under suction and recrystallized from water.

L-N-Benzoyl-3-(4-hydroxy-3-methoxyphenyl)alanine (3a) and -3-(3-hydroxy-4-methoxyphenyl)alanine (3c)

The L-anilide *(2a)* or *(2c)* is refluxed for 16 h in the tenfold amount of 2 N HCl. The reaction mixture is then cooled and repeatedly extracted with ether. The aqueous phase is filtered over charcoal and vacuum distilled. The residue is dissolved in a fivefold amount of ethanol. Propylene oxide is added and the temperature maintained at 50 °C for 1 h until the pH value 6.0 is attained. The solution is allowed to stand for *ca.* 12 h in a refrigerator, filtered under suction, and *(3a)* or *(3c)* recrystallized from water; the monohydrate is obtained.

Received: February 6, 1975 [Z 199 IE]
German version: Angew. Chem. 87, 379 (1975)

CAS Registry numbers:
(1a), 2901-78-2; *(2a)*, 38152-95-3; *(2c)*, 50713-71-8; *(3a)*, 300-48-1; *(3b)*, 59-92-7; *(3c)*, 35296-56-1

[*] Dr. E.-O. Renth
C. H. Boehringer Sohn, Abteilung Pharmachemie
6507 Ingelheim (Germany)

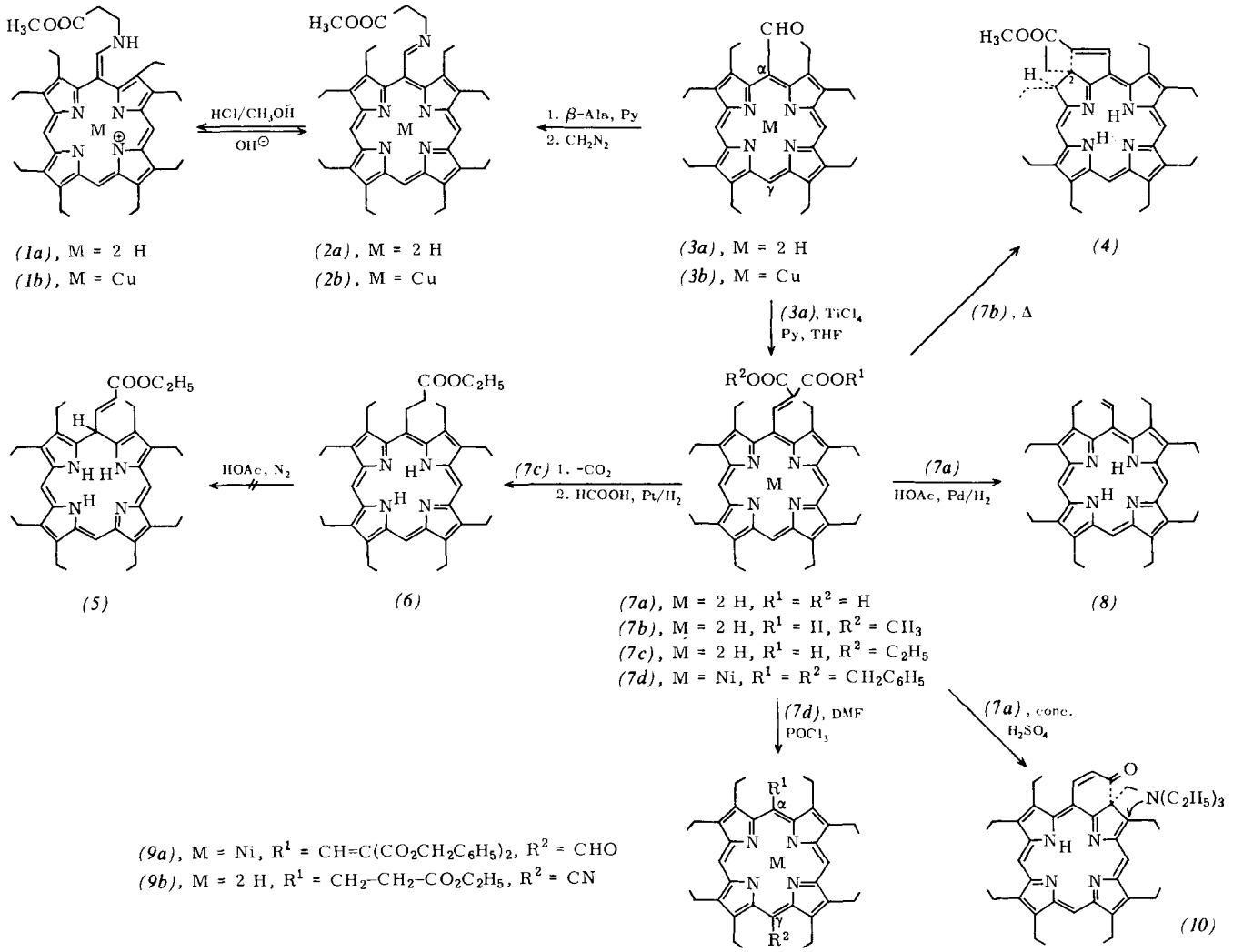
Preparation and Reactivity of Sterically Crowded Porphyrins[**]

By *Ludger Witte* and *Jürgen-Hinrich Fuhrhop*[*]

Recent biochemical concepts on the activation of oxygen by heme enzymes[1, 2] and the photolysis of water by chlorophyll dimers[3] should be amenable to checking with synthetic metalloporphyrins *in vitro*. Simple analogs of these important redox catalysts would be of interest from the preparative standpoint both for the oxygenation of olefins as well as for the hydroxylation of non-activated hydrocarbons. For the synthesis of rigid ligand fields about the central iron atom in heme analogs or of dimers having porphyrin planes at a well-defined distance, we require porphyrins containing the same side chains, which are capable of being coupled with each other, at oppositely lying methine bridges (α,γ). From these it should be possible, *e.g.*, to prepare sterically fixed ansa porphyrins having rigid axial ligands through the central ion. To our knowledge, porphyrins with highly substituted methine bridges were previously only accessible by lengthy total synthesis[4]. We now wish to report on their prepara-

[*] Dipl.-Chem. L. Witte and Doz. Dr. J.-H. Fuhrhop
Gesellschaft für Molekularbiologische Forschung mbH
3301 Stöckheim bei Braunschweig, Mascheroder Weg 1
and
Institut für Organische Chemie A der Technischen Universität
Braunschweig (Germany)

[**] This work was supported by the Bundesministerium für Forschung und Technologie as part of the technology program, by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.



tion from unsubstituted porphyrins and on a few of the most important reactions.

The formylporphyrins, *e.g. (3)*, which are accessible in yields of 75% from porphyrins by Vilsmeier formylation[5], each yielded the acrylic acid derivatives *(7a)—(7d)* in yields of over 70%[6] in a variant of the Knoevenagel condensation with titanium tetrachloride as catalyst. On heating in toluene *(7)* rearranges into *(4)* in analogy to the purpurin reaction described by *Woodward*[4]. *(7)* was converted into the propionate *(6)*, which, however, did not form any phlorin *(5)* on heating in a nitrogen atmosphere. Likewise *(7a)—(7c)*, *(6)*, and the nitrile *(9b)* cannot be transformed into phlorins by thioacetic acid[4]. The presence of an electron-attracting group in a β-pyrrolic position [*e.g.* position 2 in *(4)*] is evidently a prerequisite for this reaction discovered by *Woodward*[7]. On the other hand, a reversible conversion of the Schiff base *(2)* into the phlorinoid compound *(1)* [*(1b)*: $\lambda_{max} = 720$ nm ($\varepsilon = 9500$)] could be accomplished by protonation. It would seem therefore that the formation of phlorins is determined to a lesser extent by steric factors than by electronic factors, a fact which is not so evident from experimental findings in the field of chlorophyll synthesis[4].

In hydrogenation experiments in acetic acid *(7)* was doubly decarboxylated and converted into the vinylporphyrin *(8)* in 60% yield. Treatment of *(7)* with concentrated sulfuric acid leads to the novel, presumably cross-conjugated verdin *(10)*. With reducing agents, *e.g.* triethylamine, long-lived radicals are formed.

Our main interest centered on the preparation of α,β-disubstituted porphyrins. Compound *(7)* can in fact be converted into the desired porphyrin *(9a)* in yields of *ca.* 50% by reaction with dimethylformamide and $POCl_3$. α,β-Substituted porphyrins are formed in a similar fashion. The formylporphyrin *(3b)* cannot be further formylated in this way.

Octaethyl-α-(2,2-dicarboxyvinyl)porphyrin (7a)

$TiCl_4$ (11 ml) in CCl_4 (25 ml) was added dropwise at 0°C to anhydrous tetrahydrofuran (200 ml); a flocculent yellow precipitate was formed. A solution of *(3a)* (100 mg) in tetrahydrofuran (25 ml) and malonic acid (5g) was then added to the mixture. This was followed by dropwise addition of a solution of anhydrous pyridine (16 ml) in tetrahydrofuran (30 ml) within 3—4 h at 0°C. More rapid addition of bases leads to precipitation of tarry products. After a further 10 hours' stirring at room temperature water was added and work-up carried out in the usual manner[8]. Yield of *(7a)* 78 mg (68%).

Received: January 14, 1975 [Z 186a IE]
German version: Angew. Chem. 87, 387 (1975)

CAS Registry numbers:
(3a), 10250-36-9; *(7a)*, 54699-00-2

[1] *V. Ullrich*, Angew. Chem. *84*, 689 (1972); Angew. Chem. internat. Edit. *11*, 701 (1972).
[2] *J.-H. Fuhrhop*, Struct. Bond. *18*, 1 (1974).
[3] *F. K. Fong*, J. Theor. Biol. *46*, 407 (1974).

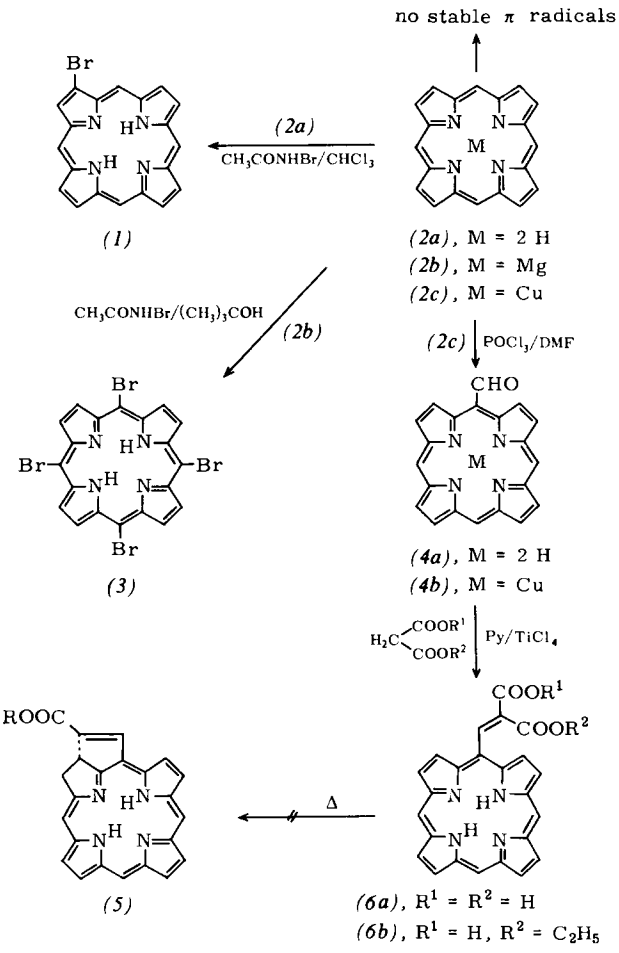
[4] *R. B. Woodward*, Angew. Chem. *72*, 651 (1960); Ind. Chim. Belge *1962*, 1293.
[5] *H. H. Inhoffen, J.-H. Fuhrhop, H. Voigt*, and *H. Brockmann jr.*, Liebigs Ann. Chem. *695*, 133 (1966).
[6] *W. Lehnert*, Tetrahedron *28*, 663 (1972). It seems to us remarkable that no other addition reaction (*e.g.* base-catalyzed condensation, Wittig reaction, addition of allyllithium and alkylmagnesium compounds) has led to some sort of product in mentionable (> 5 %) yields.
[7] *T. T. Howarth, A. H. Jackson*, and *G. W. Kenner*, J. C. S. Perkin I *1974*, 502.
[8] For work-up procedure see *e.g.* in [6] and [5].

Reactivity of Unsubstituted Porphin[**]

By *Rüdiger Schlözer* and *Jürgen-Hinrich Fuhrhop*[*]

The unsubstituted porphin *(2a)* and its metal complexes, *e.g. (2b)* and *(2c)*, offer the chance of investigating the relative reactivity of the methine bridges and β-pyrrole carbon atoms without interference from substituent effects.

Both of the previous publications on the reactions of porphin *(2a)* imply that bromination leads exclusively to the β-substituted product *(1)*[1], which we confirm, while nitration takes place at the methine bridges[2]. Surprisingly the magnesium complex *(2b)* reacts with *N*-bromoacetamide in *ca.* 40% yield to give the *meso*-tetrabromo derivative *(3)* without β-pyrrolic bromination being detectable. Such a sharp distinction between the relative reactivities of the free porphyrin bases and their metal complexes has never been observed in the case of other porphyrins.



[*] Dipl.-Chem. R. Schlözer and Doz. Dr. J.-H. Fuhrhop
Gesellschaft für Molekularbiologische Forschung mbH
3301 Stöckheim bei Braunschweig, Mascheroder Weg 1 (Germany)

[**] This work was supported by the Bundesministerium für Forschung und Technologie, by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie.

Vilsmeier formylation of the copper complex *(2c)* likewise leads exclusively to substitution at one of the methine bridges, *i.e.* to the formylporphyrin *(4b)*. Demetalation and Knoevenagel condensation with malonic acid derivatives and titanium tetrachloride[3] led to the acrylic acid derivatives *(6)*. Neither *(6a)* nor *(6b)* formed even traces of a purpurin *(5)* on heating. Rather, these compounds are stable under the conditions of the purpurin reaction, while above 200 °C or on prolonged reaction (several days) undefined decomposition and regeneration of unsubstituted porphin *(2a)* took place. The octaethyl derivatives corresponding to *(6)*, on the other hand, rearrange into the purpurins. This contradictory behavior confirms that relaxation of steric stresses in highly substituted porphyrins might be the most important driving force behind their spontaneous rearrangement into chlorins such as *(5)*[3].

The metal complexes *(2b)* and *(2c)* as well as *(2)*, M = Zn, Ni, Co and Mn, give reversible one-electron oxidation and reduction steps in cyclic voltammograms. The equivalence potential lies, without exception, about 200 mV higher than that of the corresponding octaethylporphyrin-metal complex[4]. The difference $E^{ox}_{1/2} - E^{red}_{1/2}$ is 2.1 ± 0.2 V in the metal complexes of the two porphyrins. The manganese complex *(2)*, M = Mn (ΔE = 2.9 V) deviates from this norm like the octaethylporphyrin-manganese complex[4]. The metalloporphyrin radicals, which are usually very stable and whose formation is a basic step in photosynthesis[5], could not however be detected in redox reactions of the named metal complexes of *(2)*. On the contrary, these radicals—unhindered by steric interactions of substituents—polymerized on the surface of the electrodes to black powders, which were insoluble even in concentrated sulfuric acid.

Received: January 14, 1975 [Z 186b IE]
German version: Angew. Chem. *87*, 388 (1975)

CAS Registry numbers:
(2a), 101-60-0; *(2b)*, 13007-95-9; *(2c)*, 13007-96-0; *(2)*, M = Zn, 14052-02-9; *(2)*, M = Ni, 15200-33-6; *(2)*, M = Co, 32662-36-5; *(2)*, M = Mn, 32662-37-6; *(3)*, 54714-00-0; *(4b)*, 54713-77-8; *(6a)*, 54713-98-3; *(6b)*, 54713-99-4; $HO_2CCH_2CO_2H$, 141-82-2; $HO_2CCH_2CO_2C_2H_5$, 1071-46-1

[1] *E. Samuels, R. Shuttleworth*, and *T. S. Stevens*, J. Chem. Soc. *C 1968*, 145.
[2] *J. E. Drach* and *F. R. Longo*, J. Org. Chem. *39*, 3282 (1974).
[3] *L. Witte* and *J.-H. Fuhrhop*, Angew. Chem. *87*, 387 (1975); Angew. Chem. internat. Edit. *14*, 361 (1975).
[4] *J.-H. Fuhrhop, K. Kadish*, and *D. G. Davis*, J. Amer. Chem. Soc. *95*, 5140 (1973).
[5] *J.-H. Fuhrhop*, Angew. Chem. *86*, 363 (1974); Angew. Chem. internat. Edit. *13*, 321 (1974).

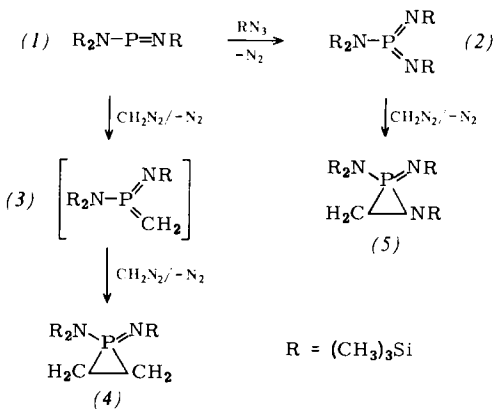
1,2-Cycloaddition Reactions of "Phosphazenes" Having an Unusual Coordination Number: λ⁵-Phosphirane and 1,2 λ⁵-Azaphosphiridine[**]

By *Edgar Niecke* and *Wilhelm Flick*[*]

As we were recently able to show for the first time, oxidation of bis(trimethylsilyl)aminotrimethylsilyliminophosphane *(1)*[1] with trimethylsilyl azide leads to a diiminophosphorane *(2)*, a previously unknown type of phosphorus compound having trigonal-planar coordination[2].

[*] Dr. E. Niecke and Dipl.-Chem. W. Flick
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstrasse 4 (Germany)

[**] Presented in part at the 2nd Symp. Inorg. Phosphorus Compounds at Prague, September 1974. This work was supported by the Deutsche Forschungsgemeinschaft.



During the corresponding reaction of *(1)* with diazomethane the ylide *(3)* eludes isolation, reacting instead with the diazoalkane to give the λ^5-phosphirane *(4)* *via* 1,2-cycloaddition[3]. Analogous bifunctional behavior is also observed with the diiminophosphorane *(2)* which reacts smoothly with diazomethane to form the 1,2λ^5-azaphosphiridine *(5)*, a novel phosphorus heterocycle.

The heterocycles *(4)* and *(5)* are colorless hydrolysis-sensitive liquids of varying stability[4].

The compositions and structures of the compounds were established by elemental analysis, cryoscopic molecular weight determination, mass [only for *(5)*], IR, and NMR (^{1}H, ^{29}Si, ^{31}P) spectra.

In the mass spectrum of *(5)*[5] (*m/e* (relative intensity), the molecular peak at 379 (12%) is accompanied by the following characteristic fragments: M−CH_3 364 (3%); M−CH_3, −CH_2 350 (1%); M−Si$(CH_3)_3$ 306 (1%); M−$CH_2NSi(CH_3)_3$ 278 (100%).

The IR spectrum (capillary film) shows ν(P=N) as a strong and broad absorption at 1305 *(4)* and 1338 cm^{-1} *(5)*, respectively, while the weak bands at 3060 and 3015 cm^{-1} are assignable to the CH ring stretching vibrations[6].

The ^{1}H-NMR spectrum (30% solution in CH_2Cl_2; TMS internal standard) displays the expected AA'BB'X *(4)* and ABX *(5)* multiplet structure for the methylene protons and singlets and doublets for the trimethylsilyl protons ($^4J_{HP}$).

(4): silylimino H:	δ = 0.03 ppm, $^4J_{HP}$ = 0.55 Hz
silylamino H:	δ = −0.29 ppm
methylene H:	δ = −1.35 ppm, $^2J_{HP}$ = 10.8 Hz
	δ = −1.55 ppm, $^2J_{HP}$ = 11.0 Hz [7]
(5): silylimino H:	δ = 0.0 ppm, $^4J_{HP}$ = 0.58 Hz
silylamino H:	$\delta_{(SiN<)}$ = −0.19 ppm, $^4J_{HP}$ = 0.52 Hz
	$\delta_{(Si_2N)}$ = −0.29 ppm
methylene H:	δ = −2.27 ppm, $^2J_{HP}$ = 11.75 Hz
	δ = −2.58 ppm, $^2J_{HP}$ = 10.8 and $^{gem}J_{HH}$ = 2.05 Hz

In accord with the proton spectrum, the ^{1}H-decoupled PFT ^{29}Si-NMR spectrum (70% solution in C_6F_6; TMS internal standard) reveals two [*(4)*] and three [*(5)*] differently bound silicon atoms. The magnitude of the ^{29}Si-^{31}P interaction lies in the range expected for *N*-trimethylsilyl-substituted iminophosphoranes[8].

(4): silylimino Si:	δ = 13.4 ppm, $^2J_{SiP}$ = 24.2 Hz
silylamino Si:	δ = −10.5 ppm
(5): silylimino Si:	δ = 14.1 ppm, $^2J_{SiP}$ = 26.9 Hz
silylamino Si:	$\delta_{(SiN<)}$ = −8.2 ppm, $^2J_{SiP}$ = 11.0 Hz
	$\delta_{(Si_2N)}$ = −7.6 ppm

In the ^{31}P-NMR spectrum (50% in C_6H_{12}; 85% H_3PO_4 as external standard) the resonance signal is observed as a pseudoquintet *(4)* and a triplet *(5)* respectively, ($J_{AX} \approx J_{BX}$) at relatively high field[9]: δ_{31P} = 66.9 and 60.1 ppm, respectively.

Procedure:

(4) and *(5)*: A solution of *(1)* (14 g, 0.05 mol) or *(2)* (18.5 g, 0.05 mol) in ether (50 ml) is added dropwise to a stirred and cooled (0 °C) ethereal solution of diazomethane which has been repeatedly dried[10] and saturated at 0 °C (250 ml) in a 500 ml two-necked flask fitted with a dropping funnel and a reflux condenser. The reaction solution is stirred at room temperature for 3—4 h. Ether and unreacted diazomethane are removed under reduced pressure and the residue fractionally distilled. The reaction affords 10 g (65%) of *(4)*, b.p. 67—68 °C/0.1 torr, and 17 g (90%) of *(5)*, b.p. 109 to 110 °C/0.2 torr, respectively.

Received: January 7, 1975 [Z 180 IE]
German version: Angew. Chem. 87, 355 (1975)

CAS Registry numbers:
(1), 50732-21-3; *(2)*, 52111-28-1; *(4)*, 54677-65-5; *(5)*, 54677-66-6; $(CH_3)_3SiN_3$, 4648-54-8; CH_2N_2, 334-88-3

[1] a) *E. Niecke* and *W. Flick*, Angew. Chem. *85*, 586 (1973); Angew. Chem. internat. Edit. *12*, 585 (1973); b) *O. J. Scherer* and *N. Kuhn*, Chem. Ber. *107*, 2123 (1974).

[2] *E. Niecke* and *W. Flick*, Angew. Chem. *86*, 128 (1974); Angew. Chem. internat. Edit. *13*, 134 (1974); *S. Pohl*, *E. Niecke*, and *B. Krebs*, *ibid.* *87*, 284 (1975) and *14*, 261 (1975), respectively; cf. [1b].

[3] Compounds of the phosphirane type have, to our knowledge, only been obtained with tricoordinate phosphorus: *R. I. Wagner*, *Le Vern*, *D. Freeman*, *G. Goldwhite*, and *D. G. Rowell*, J. Amer. Chem. Soc. *89*, 102 (1967); *S. Chan*, *H. Goldwhite*, *H. Keyzer*, *D. G. Rowell*, and *R. Tang*, Tetrahedron Lett. *1969*, 1097.

[4] While the phospirane already decomposes gradually with discoloration at room temperature, the azaphosphiridine can be kept almost indefinitely in the absence of moisture.

[5] Owing to the low thermal stability of the phosphirane no interpretable mass spectrum can be recorded. Molecular weight (cryoscopic in C_6H_{12}): 308 and 312 (306.62).

[6] The CH_2 stretching vibrations appearing at low wave numbers are obscured by the strong trimethylsilyl absorptions setting in at 3000 cm^{-1}.

[7] A complete spectral analysis has still to be performed.

[8] *W. Buchner* u. *W. Wolfsberger*, Z. Naturforsch. *29b*, 328 (1974); as well as our own yet unpublished results.

[9] *M. M. Crutchfield*, *C. H. Dungan*, *L. H. Letcher*, *V. Mark*, and *J. R. Van Wazer*, Top. Phosphorus Chem. *5*, 236 (1967); *G. Mavel*, Annu. Rep. NMR Spectrosc. *5B*, 95 (1973).

[10] The presence of moisture during the oxidation of iminophosphane leads *inter alia* to formation of R_2N—P(OCH_3,CH_3)=NR, which cannot be completely separated from the phosphirane by distillation.

Determination of Conformation of Conjugated Dienes by Means of Vibrational Frequencies

By *Bernhard Schrader* and *Achim Ansmann*[*]

The frequencies of the stretching vibrations of double bonds of conjugated dienes reflect, on account of the mechanical coupling of these oscillators, the spatial arrangement of the double bonds. In conjugated dienes with *s-trans* geometry the in-phase stretching vibration ν_s has a higher frequency than the out-of-phase vibration ν_a (cf. Table 1, 1,3-butadienes). In the case of the *s-cis* arrangement the converse is true (cf. Table 1, cyclopentadiene)[1].

Generally valid conclusions about the magnitude of the torsion angle β and the bond angle ε can be derived from values of ν_s and ν_a with the aid of calculations for a gerneralized model of a conjugated diene which are based on normal coordinate analyses of 1,3-butadiene[2], cyclopentadiene[3], 1,3-

[*] Prof. Dr. B. Schrader and Dr. A. Ansmann [**]
Abteilung für Theoretische Organische Chemie der Universität Dortmund
46 Dortmund-Hombruch, Postfach 500 (Germany)

[**] Present address: Henkel & Cie. GmbH, Düsseldorf.

Table 1. Observed frequencies [cm^{-1}] of ν_s and ν_a for a few conjugated dienes. β = torsion angle.

Diene	ν_s	ν_a	$\Delta\nu$	β
1,3-Butadiene	1630	1596	+34	180°
Cyclopentadiene	1500	1588	−88	0°
1,3-Cyclohexadiene	1578	1604	−26	18°
1,3-Cycloheptadiene	1613	1645	−32	0°
1,3-Cyclooctadiene	1629	1640	−11	≈ 60°

cyclohexadiene[3] and 1,3-cycloheptadiene[3] (results see Fig. 1):

1. On going from the *s-cis* to the *s-trans* conformation in the diene the frequencies of ν_s and ν_a cross, so that with strong twisting of the π-system the difference $\Delta\nu = \nu_s - \nu_a$ is small.

2. The mean value of the two frequencies for the stretching vibrations of the double bonds increases with increasing bond angle ε. This applies for each of the similarly substituted conjugated dienes on the π-system.

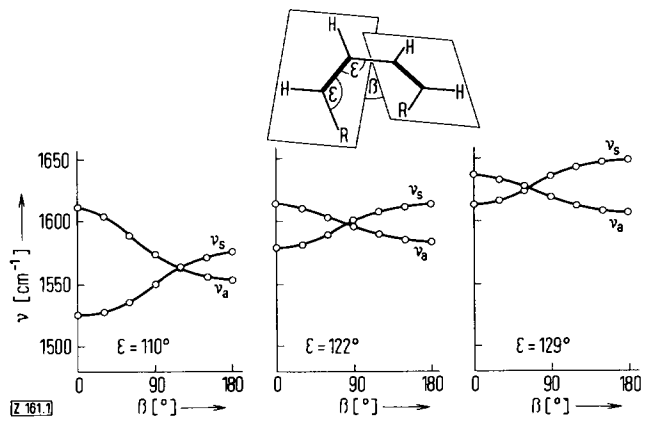


Fig. 1. Dependence of frequency values (ν_s and ν_a) on the torsion angle β and the bond angles ε (model calculation); a point mass of 14 atomic weight units (CH_2) was chosen for R.

A comparison of the observed frequencies of the 1,3-cycloheptadiene (see Table 1) with these results shows that a planar *s-cis* conformation ($\beta = 0°$), as in Fig. 2a, is present, the bond angle being greater than 120°. This result contradicts the ^{1}H-NMR findings of *Crews*[4], which suggest a twisted arrangement (cf. Fig. 2b). It is confirmed however by the complete analysis of the vibration spectra[3], the results of electron diffraction investigations[5] and the UV spectra[6, 7].

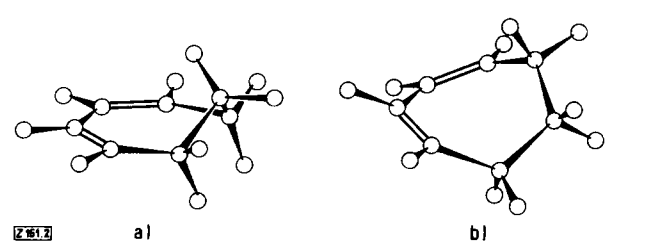


Fig. 2. a) Planar *s-cis* ($\beta = 0°$) and b) twisted arrangement ($\beta \approx 48°$) of the double bonds in 1,3-cycloheptadiene.

For 1,3-cyclooctadiene the frequencies of ν_s and ν_a and their small difference (cf. Table 1) show that the π system must be strongly twisted. This evidence is supported by other structural investigations[2, 7, 8]. Further, a more accurate investigation of the vibration spectra and their temperature dependence shows that 1,3-cyclooctadiene is present as an equilibrium mixture of two conformations which are twisted to different extents[3].

As these examples show, it is possible to determine the conformation of conjugated dienes by means of the vibration frequencies. Prerequisite however is a reliable assignment for ν_s and ν_a: the in-phase vibration ν_s usually exhibits a very strong Raman band and an IR band of moderate to very weak intensity. The out-of-phase vibration ν_a, on the other hand, is usually very weak in the Raman spectrum while in the IR spectrum it shows a band of moderate to weak intensity, which can be stronger than the band of ν_s. Occasionally, the accurate assignment of ν_a can be rendered difficult by appearance of overtones and combination bands in the region of 1500—1700 cm^{-1}.

Received: November 13, 1974 [Z 161 IE]
Supplemented: February 3, 1975
German version: Angew. Chem. 87, 345 (1975)

CAS Registry numbers:
1,3-butadiene, 106-99-0; cyclopentadiene, 542-92-7;
1,3-cyclohexadiene, 592-57-4; 1,3-cycloheptadiene, 4054-38-0;
1,3-cyclooctadiene, 1700-10-3

[1] *V. T. Aleksanyan* and *E. V. Sobolev*, Dokl. Akad. Nauk SSR *150*, 1062 (1963).
[2] *A. Ansmann*, Dissertation, Universität Dortmund 1974.
[3] *A. Ansmann* and *B. Schrader*, unpublished.
[4] *P. Crews*, Chem. Commun. *1971*, 583.
[5] *J. F. Chiang* and *S. H. Bauer*, J. Amer. Chem. Soc. *88*, 420 (1966); *K. Hagen* and *M. Traetteberg*, Acta Chem. Scand. *26*, 3643 (1972).
[6] *P. Pesch* and *S. L. Friess*, J. Amer. Chem. Soc. *72*, 5756 (1950); *K. Hafner* and *W. Rellensmann*, Chem. Ber. *95*, 2567 (1962).
[7] *E. A. Braude*, Chem. Ind. (London) *1954*, 1557.
[8] *E. Merkel*, Z. Elektrochem. *63*, 373 (1959); *C. Y. Chen*, *R. J. W. Le Fevre*, and *K. M. S. Sundermann*, J. Chem. Soc. *1965*, 553; *M. Traetteberg*, Acta Chem. Scand. *24*, 2285 (1970).

Insertion of a Carbon Atom into Olefinic Double Bonds: Synthesis of Fluorodienes and Fluoroalkenes[**]

By *Manfred Schlosser*, *Bojana Spahic*, *Claudio Tarchini*, and *Le Van Chau*[*]

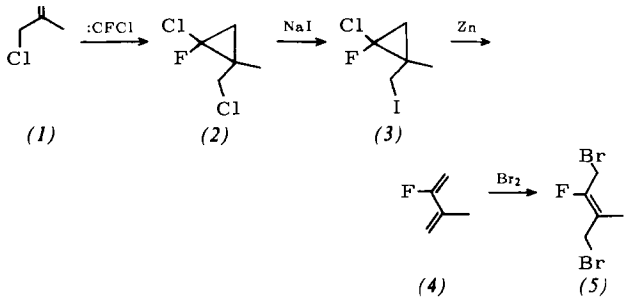
The chain-lengthening insertion of carbenoid carbon into CH-, CCl- or SiH bonds is well-known[1]. Analogous insertion reactions into CC single bonds occur only in very exceptional cases[2]. CC double bonds offer much better prospects provided that one pursues the circuitous route of a cycloaddition/elimination sequence. Thus it is possible to convert olefins into allenes by first preparing *gem*-dihalocyclopropanes which are subsequently subjected to reductive ring opening[1, 3]. The cyclopropane intermediates can, furthermore, be solvolyzed to allyl alcohol derivatives[4, 5] or converted into halodienes by base-induced ring-opening 1,4-dehydrohalogenation[6]. The latter type of rearrangement however requires drastic reaction conditions and does not proceed uniformly when—as is usual—various types of hydrogen atoms are available for cleavage. This disadvantage does not arise if halogen instead of hydrogen halide is detached in the 1,4-elimination step The approach will be examplified by means of a new method for the preparation of fluorodienes and fluoroalkenes.

2-Methylallyl chloride *(1)* can be converted into 1-chloro-2-chloromethyl-1-fluoro-2-methylcyclopropane with negligible hydrolysis by treatment with dichlorofluoromethane and 80% potassium hydroxide in a two-phase system. The macrocyclic polyether "dicyclohex-18-crown-6" (2,5,8,15,18,21-hexaoxatri-

[*] Prof. Dr. M. Schlosser, Dipl.-Chem. B. Spahić, Dipl.-Chem. C. Tarchini, and Dr. Le Van Chau
Institut de Chimie Organique de l'Université
CH-1005 Lausanne, Rue de la Barre 2 (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project No. 2.593.71 and 2.0530.73) and by Hoechst AG.

cyclo[20.4.0.0^{9,14}]hexacosane) is significantly superior[9] to the commonly used ammonium salts[7,8] as a phase transfer agent. After Finkelstein replacement of the chlorine in the side



chain by iodine [*(2)* → *(3)*][10] treatment with zinc effects 1,4-elimination and ring-opening. The ring-opening follows *Grobs*'s fragmentation scheme. The hitherto barely known[11] 3-fluoroisoprene (2-fluoro-3-methyl-1,3-butadiene) *(4)* is formed in almost quantitative yield. Addition of bromine leads to (*Z*)-1,4-dibromo-2-fluoro-3-methyl-2-butene *(5)*. It is expected to be a suitable building unit for planned fluoroterpene syntheses.

Further examples illustrate the scope of the reaction sequence described: 3-fluoro-4-methyl-1,3-pentadiene and 3-fluoro-2,4-dimethyl-1,3-pentadiene (overall yield 75 and 54%, resp.). All these fluorodienes polymerize at room temperature.

1-Chloro-2-chloromethyl-1-fluoro-2-methylcyclopropane (2)

To a cylinderical reaction vessel immersed in an ice-bath was transferred (*via* a side arm) 200 ml 80% potassium hydroxide, 27 g (0.3 ml) *(1)* and 50 g (about 30 ml) difluoromethane (all precooled) as well as 1.1 g (3 mmol) "dicyclohex-18-crown-6". A vibromixer was fitted to the reaction vessel such that its disk just touched the interphase. The middle part of its shaft was enclosed by a Liebig condenser mounted on top of the reaction vessel and sealed at the upper end by a tight fitting rubber sleeve (coolant: methanol, −30 °C). Reaction was complete after 30—60 min vibromixing. After extraction with ether (3 × 50 ml), washing of the ether phase with water (3 × 50 ml), and drying with $CaSO_4$, distillation afforded 33 g (70%) pure *(2)*[12]; b.p. 55—56 °C/torr.

1-Chloro-1-fluoro-2-iodomethyl-2-methyl-cyclopropane (3)

A solution of 15.6 g (0.1 mol) *(2)* and sodium iodide in acetone (100 ml) was allowed to boil under reflux for 24 h. The solvent was evaporated and the residue treated with water and taken up in ether (3 × 50 ml). Vigorous shaking with 20 ml saturated thiosulfate solution decolorized the solution which was then washed with water (2 × 50 ml), dried, and distilled. 21.2 g (85%) of *(3)* distilled over in the boiling range 86 to 88 °C/30 torr[12].

2-Fluoro-3-methyl-1,3-butadiene (4)

7.4 g (30 mmol) *(3)* was dissolved in 40 ml propanol, treated with 10 ml water, and poured onto 2.1 g (33 mmol) zinc powder (previously digested with 5% hydrochloric acid, filtered under suction, and washed). The mixture was stirred with a magnetic stirrer, slowly at first and later more rapidly. The reaction mixture became warm and released a volatile product that was carried over in a gentle stream of N_2 into an efficient cold trap kept at −78 °C. After about 20 min the reaction slackened off and had to be driven to completion by gentle heating (water bath, 60 °C). The condensate (yield 98%) was distilled under nitrogen (but no longer in the gas current) into a flask; b.p. 26 °C. According to gas chromatography *(4)* was completely pure. It was converted with an equivalent amount of maleic anhydride quantitatively in 24 h at 50 °C into a Diels-Alder adduct; m.p. 42—43 °C (ether).

(Z)-1,4-Dibromo-2-fluoro-3-methyl-2-butene (5)

A solution of 2.6 g (30 mmol) *(4)* in 10 ml dichloromethane, into which 4.8 g (30 mmol) of bromine had been pipetted at −78 °C, was allowed to reach a temperature of 25 °C within 1 h. On distillation 4.65 g (63%) of a colorless liquid was obtained; b.p. 64—65 °C/3 torr. According to gas chromatography the product consisted initially of 90% *(5)*, but underwent slow transformations by isomerization and possibly also by loss of HBr.

Received: December 5, 1974 [Z 162 IE]
German version: Angew. Chem. *87*, 346 (1975)

CAS Registry numbers:
(1), 563-47-3; *(2)*, 40841-57-4; *(3)*, 54699-04-6; *(4)*, 338-68-1; *(5)*, 54699-05-7; dichlorofluoromethane, 75-43-4; maleic anhydride, 108-31-6

[1] *W. Kirmse*: Carbene, Carbenoide und Carbenanaloge. Verlag Chemie, Weinheim 1969; Carbene Chemistry. 2nd edit. Academic Press, New York 1971.
[2] Apart from intramolecular insertions into β,γ neighboring C—C bonds (= 1,2 migration of an alkyl group, often accompanied by ring expansion), only a single case of carbene insertion into a C—C single bond has hitherto been observed: Photochemically generated methylene combines with bicyclobutane to give bicyclo[1.1.1]pentane in 1% yield (*K. B. Wiberg, G. M. Lampman, R. P. Ciula, D. S. Connor, P. Schertler*, and *J. Lavanish*, Tetrahedron *21*, 2749 (1965)).
[3] *W. v. E. Doering* and *P. LaFlamme*, Tetrahedron *2*, 75 (1958).
[4] *P. S. Skell* and *S. R. Sandler*, J. Amer. Chem. Soc. *80*, 2024 (1958).
[5] *Le Van Chau* and *M. Schlosser*, Synthesis *1974*, 115; and references cited therein.
[6] *P. Weyerstahl, D. Klamann, C. Finger, M. Fligge, F. Nerdel*, and *J. Buddrus*, Chem. Ber. *101*, 1303 (1968).
[7] *J. Donckx*, Synthesis *1973*, 441.
[8] *E. V. Dehmlow*, Angew. Chem. *86*, 187 (1974); Angew. Chem. internat. Edit. *13*, 170 (1974).
[9] Cf. also *R. A. Moss* and *F. G. Pilkiewicz*, J. Amer. Chem. Soc. *96*, 5632 (1974); *D. Landini, F. Montanari*, and *F. M. Pirisi*, J. C. S. Chem. Comm. *1974*, 879; *M. Makosza* and *M. Ludwikow*, Angew. Chem. *86*, 744 (1974); Angew. Chem. internat. Edit. *13*, 665 (1974).—Surprisingly, the Polish authors—and to some extent also the Italian authors—worked with *sodium* hydroxide as the base even though the 18-membered polyether used binds *potassium* ions much more selectively.
[10] It is simpler to convert the iodine compound *(3)* further *in situ*: it suffices to let zinc react with *(2)* in the presence of sodium iodide.
[11] *D. D. Coffman* and *L. F. Salisbury*, US-Pat. 2451612 (1948), Du Pont; Chem. Abstr. *49*, 2218e (1949).
[12] Present as *syn/anti* mixture.
All the substances described have been confirmed by elemental analysis and spectra.

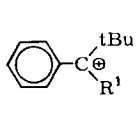
Conformation of Sterically Hindered Benzyl Radicals and Cations; Comparison of ESR Findings and Conclusions from Space-Filling Models[1]

By *Kurt Schreiner* and *Armin Berndt*[*]

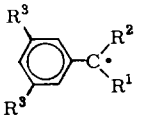
Dedicated to Professor K. Dimroth

In order to explain the unexpected rates of solvolysis of the *p*-nitrobenzoates of α,α-dialkylbenzyl alcohols it was assumed—with supporting evidence from considerations of Stuart-Briegleb models—that the planes of the aromatic ring and the sp^2 center in the benzyl cations *(1a)*—*(1d)* are "forced into an orthogonal arrangement" as a result of steric hindrance, "so that resonance is completely suppressed"[2]. Steric hindrance of resonance should also have considerable influence on the rate of formation of the α,α-dialkylbenzyl radicals *(2e)* and *(2f)* by azoalkane thermolysis[2].

[*] Prof. Dr. A. Berndt and Dr. K. Schreiner
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)



(1a-d)



(2a-i), R^3 = H
(3a-g), R^3 = tBu

Since ESR coupling constants provide a direct measure of the delocalization of the unpaired electron, *i.e.* of resonance, these assumptions can be checked ESR spectroscopically, in the case of the radicals *(2e)* and *(2f)* directly, and in the case of the cations *(1a)*—*(1d)* by means of the corresponding benzyl radicals, which according to space-filling models have the same conformation as the cations.

The planar conformation assigned to the α,α-dimethylbenzyl cation from space-filling model considerations[2] is confirmed by the ESR coupling constants of the α,α-dimethylbenzyl radical *(2h)*, which agree with those of the unsubstituted planar benzyl radical *(2i)*[3]. We have recently proved the orthogonal conformation for the α,α-di-*tert*-butylbenzyl radical *(2d)*[4]. To determine the conformation of the species sterically hindered between these two extremes we have now prepared the radicals *(3a)*—*(3c)* and *(3e)*—*(3g)* (cf. Table 1).

The *tert*-butyl substituents in the *meta* position lead to simplification of the ESR spectra—they have no influence on the conformation[5]. The short-lived radicals *(3a)*, *(3b)*, *(3e)*, and *(3g)* were obtained from the respective bromides with the aid of photochemically generated triethylsilyl radicals[6] at the temperatures given in Table 1; the longer-lived radicals *(3e)* and *(3f)*, which are stable for days and hours, respectively, were prepared by reductive cleavage of the oxalic diesters[4] of the respective benzyl alcohols. The ESR coupling constants of all the named radicals are listed in the Table.

ESR coupling constants of protons directly bound to a C atom of spin density ρ_i, and of protons of methyl groups bound to a C atom of spin density ρ_i are directly proportional to this spin density, *i.e.* practically to the residing probability of the unpaired electron[7, 8] (cf. a_p^H 6.0 G in planar *(2i)* and a_p^H 0.31 in orthogonal *(2d)*). A comparison of the coupling constants of the ring protons of the radicals *(3a)*—*(3c)* with those of the radical twisted through 90° therefore shows immediately that none of these radicals has an orthogonal conformation. It follows from the only slightly increased coupling constant of the methyl protons on C_α of radical *(3a)* of 17.8 G, as against 16.5 G in the case of planar *(2h)*, that *(3a)* can be only slightly twisted. *(3e)* must be almost planar, since $a_{CH_3}^H$ is almost exactly as large as in planar *(2h)*. Thus, steric hindrance of resonance can only play a subordinate role in the formation of *(3f)*, *(1a)*, *(1b)*, and *(3e)*.

The angles of twist listed in Table 1 for the radicals *(3a)* to *(3c)*, *(3e)* and *(3f)* can be estimated by comparison with those calculated for twisted benzyl radicals by the INDO method[9]. The discrepancy between the experimentally determined angles of twist and those deduced from space filling models, which in the meantime we have also been able to detect in sterically hindered allyl radicals[10], shows that the conformation of a molecule can be determined only insufficiently on the basis of its space-filling model.

Received: November 29, 1974 [Z 172 IE]
German version: Angew. Chem. *87*, 285 (1975)

CAS Registry numbers:
(2d), 52168-45-3; *(3a)*, 54764-36-2; *(3b)*, 54764-37-3; *(3c)*, 54699-01-3; *(3d)*, 54764-38-4; *(3e)*, 54699-02-4; *(3f)*, 54699-03-5

[1] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.
[2] *W. Duismann* and *Ch. Rüchardt*, Chem. Ber. *106*, 1083 (1973).
[3] *A. Hudson* and *H. A. Hussain*, J. Chem. Soc. *B 1969*, 793.
[4] *K. Schreiner* and *A. Berndt*, Angew. Chem. *86*, 131 (1974); Angew. Chem. internat. Edit. *13*, 144 (1974).
[5] *K. Schreiner*, *A. Berndt*, and *F. Bär*, Mol. Phys. *26*, 929 (1973).
[6] *A. Hudson* and *R. A. Jackson*, Chem. Commun. *1969*, 1323.
[7] *H. M. McConnell*, J. Chem. Phys. *24*, 632, 764 (1956).
[8] *A. D. McLachlan*, Mol. Phys. *1*, 233 (1958).
[9] *J. A. Pople* and *D. L. Beveridge*, J. Chem. Phys. *49*, 4725 (1968).
[10] *H. Regenstein*, *W. Ahrens*, and *A. Berndt*, Tetrahedron, in press.

Table 1. ESR coupling constants of benzyl radicals [G].

Radical	R^1	R^2	$a_{R^1}^H$	$a_{R^2}^H$	a_o^H	a_p^H	Angle of twist [°] [a]	T [°C]
(2i) [b]	H	H	16.5	16.5	5.2	6.0	0	−70
(2h) [b]	Me	Me	16.5	16.5	5.2	6.0	0	−70
(3g)	H	t-Bu	16.35	0.26	4.93	5.75	0—10	−55
(3e)	Me	i-Pr	16.2 [c]	4.9 [c, d]	4.9 [c]	4.9 [c]	0—10	−45
(3f)	i-Pr	i-Pr	2.30, 0.36 [e]	2.30, 0.36 [e]	4.56	4.87	25	+20
(3a)	Me	t-Bu	17.8	[d]	4.4 [f]	4.4 [f]	25	−45
(3b)	Et	t-Bu	8.0	0.23	4.40	5.03	25	−55 [g]
(3c)	i-Pr	t-Bu	4.30, 0.46 [e]	0.46	1.95	2.18	55	+20
(2d)	t-Bu	t-Bu	0.47	0.47	0.91	0.31	90	+20

[a] ±5°; [b] Ref. [3]; [c] ±0.9 G, line width 2—3.5 G; [d] fine structure of γ-protons not resolved; [e] γ-protons; [f] ±0.4 G, line width 1.6 G; [g] detectable up to +20°C.

Synthesis of Bis(dimethylamino)carbenetetracarbonyliron

By *Wolfgang Petz*[*]

The "halogen acceptor property" of enneacarbonyldiiron has been exploited in the preparation of numerous complexes whose ligands are incapable of existing in the free state. We have reacted tetramethylchloroformamidinium chloride *(1)* with $Fe_2(CO)_9$ and thus obtained the carbene complex *(2)*.

$$3\ Fe_2(CO)_9 + [C(NMe_2)_2Cl]Cl \longrightarrow \underset{(1)}{} \quad (CO)_4Fe{=}C(NMe_2)_2 \ (2) + 4\ Fe(CO)_5 + FeCl_2 + 3\ CO$$

Complexes having two nitrogen atoms on the carbene carbon have hitherto been synthesized by cleavage of electron-rich olefins by pentacarbonyliron[1] or by elimination of hydrogen from hydridocarbonylmetalates and C—H acidic heterocyclic cations[2, 3]. The present method enhances the synthetic accessibility of this class of compounds.

[*] Doz. Dr. W. Petz
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

Since the ^{1}H-NMR spectrum of *(2)* contains only one signal at $\tau = 7.31$, both at 20 °C in benzene and at −70 °C in [D_8]-toluene, the methyl groups can be regarded as equivalent. In contrast, the methyl groups of $(CO)_4FeC(NHMe)_2$ are located in different chemical environments[2]. The mass-spectrometric fragmentation pattern confirms the structure proposed for *(2)*.

Procedure:

A suspension of $Fe_2(CO)_9$ (8.40 g, 23 mmol) and *(1)* (3.95 g, 23 mmol) in benzene (*ca.* 80 ml) is stirred with rigorous exclusion of air for 20 h at room temperature. The mixture is filtered over a G 3 frit and freed from solvent in a high vacuum. The dark red oily residue is extracted with dry pentane (50 ml). On cooling of the extract to −60 °C pale yellow crystals are formed which melt to a yellow oil at 12 °C. Yield: 1.18 g (58 %) of *(2)*.

Received: January 27, 1975 [Z 175 IE]
German version: Angew. Chem. *87*, 288 (1975)

CAS Registry numbers:
(1), 13829-06-6; *(2)*, 54688-85-6; $Fe_2(CO)_9$, 15321-51-4

[1] *B. Cetinkaya, P. Dixneuf,* and *M. F. Lappert,* J. C. S. Dalton *1974*, 1827.
[2] *K. Öfele* and *C. G. Kreiter,* Chem. Ber. *105*, 529 (1972).
[3] *K. Öfele,* Angew. Chem. *81*, 936 (1969); Angew. Chem. internat. Edit. *8*, 916 (1969).

Chloro (di-*tert*-butylphosphino)germanediyl and -stannanediyl: Stable Germanium(II) and Tin(II) Organophosphorus Compounds[**]

By *Wolf-Walther du Mont* and *Herbert Schumann*[*]

Reactions of element(IV) tetrachlorides with organosilylphosphanes do not always proceed unequivocally as substitution reactions[1, 2]. Whereas reaction of di(*tert*-butyl)trimethylsilylphosphane *(1)* with silicon tetrachloride or germanium tetrachloride under certain reaction conditions leads to di(*tert*-butyl)trichlorosilylphosphane *(2a)* and -germylphosphane *(2b)*[3], reaction with tin tetrachloride proceeds exclusively *via* oxidative cleavage of the silicon-phosphorus bond.

$$ECl_4 + R_2PSi(CH_3)_3 \xrightarrow{E = Si,\ Ge} R_2PECl_3 + (CH_3)_3SiCl$$
(1) *(2)*

$$\xrightarrow{E = Sn} R_2PCl + ECl_2 + (CH_3)_3SiCl$$
(3)

R = $C(CH_3)_3$; *(2a)*, E = Si; *(2b)*, E = Ge

On the other hand, both substitution and redox reactions take place concurrently if the silylphosphane *(1)* is in excess on reaction with germanium or tin tetrachloride in benzene.

$$2\ R_2PSi(CH_3)_3 + ECl_4 \rightarrow (R_2P)_2ECl_2 + 2\ (CH_3)_3SiCl$$
(4)

$$\rightarrow R_2PECl + R_2PCl + 2\ (CH_3)_3SiCl$$
(5) *(3)*

R = $C(CH_3)_3$; *(4a)*, *(5a)*, E = Ge; *(4b)*, *(5b)*, E = Sn

A complete separation of the reaction products *(4)* and *(5)* has so far not been achieved. The reason for this could

$$R_2PSi(CH_3)_3 + (C_6H_5)_3P \cdot GeCl_2 \rightarrow R_2PGeCl + (CH_3)_3SiCl + (C_6H_5)_3P$$

$$R_2PSi(CH_3)_3 + SnCl_2 \rightarrow R_2PSnCl + (CH_3)_3SiCl$$

R = $C(CH_3)_3$

be that α-elimination reactions take place[4] in which di(*tert*-butyl)chlorophosphane *(3)* is also formed along with chloro(di-*tert*-butylphosphino)germanediyl *(5a)* or -stannanediyl *(5b)*, respectively, from dichlorobis(di-*tert*-butylphosphino)-germane *(4a)* or -stannane *(4b)*. The compounds of type *(4)* could however be identified NMR-spectroscopically (Table 1), and the novel compounds *(5)* could be synthesized by an alternative route and isolated in pure form. Thus chloro(di-*tert*-butylphosphino)germanediyl *(5a)* if formed in the reaction of di(*tert*-butyl)trimethylsilylphosphane *(1)* with triphenylphosphanedichlorogermanediyl, and chloro(di-*tert*-butylphosphino)stannanediyl *(5b)* in the reaction of *(1)* with tin dichloride, in each case in benzene.

Intensely yellow solutions are obtained from which *(5a)* and *(5b)*, respectively, separate out as yellow powders after *ca.* 30 minutes. The two compounds are thermally very stable (Table 2) and, as expected, sensitive to oxidation and only sparingly soluble in hydrocarbons and ethers. The data of the Mössbauer spectrum of *(5b)* (I.S. = 2.96 + 0.06 mm/s; Q.S. = 1.68 + 0.12 mm/s) prove the presence of tin(II), thus ruling out oligomeric or polymeric structures with tin-tin bonds. Preliminary chemical investigations on chloro(di-*tert*-butylphosphino)stannanediyl show that the di-*tert*-butylphosphino group can be readily transferred to other element halides, *e.g.* germanium tetrachloride, with reformation of tin dichloride.

$$R_2PSnCl + GeCl_4 \rightarrow R_2PGeCl_3 + SnCl_2$$

Table 1. NMR data of compounds *(4)*.

E	^{1}H-NMR (C_6H_6)	^{31}P-NMR (C_6D_6) proton decoupled
(4a), Ge	$\delta(CH_3)_3C$ = 1.5 ppm (d) $J(^1HCC^{31}P)$ = 12.8 Hz	$\delta P = -68.7$ ppm
(4b), Sn	$\delta(CH_3)_3C$ = 1.5 ppm (d) $J(^1HCC^{31}P)$ = 12.7 Hz	$\delta P = -84.5$ ppm $J(^{31}P^{117/119}Sn)$ = 1720/1800 Hz

Table 2. Properties of $[(CH_3)_3C]_2PECl$ *(5)*.

E [a]	M.p. [b] [°C]	νPECl [cm^{-1}] IR	Raman	νPC_2 [cm^{-1}] IR	Raman
(5a), Ge	120 (dec.)	318	326	598	575 603
(5b), Sn	175 (dec.)	279	288	570 600	572 596

[a] Composition confirmed by elemental analysis.
[b] Closed capillary (Cu block).

Received: December 11, 1974 [Z 179 IE]
German version: Angew. Chem. *87*, 354 (1975)

CAS Registry numbers:
(1), 42491-34-9; *(4a)*, 54677-63-3; *(4b)*, 54677-61-1; *(5a)*, 54724-60-6; *(5b)*, 54724-61-7; $(C_6H_5)_3PGeCl_2$, 54677-62-2; $SnCl_2$, 7772-99-8; $GeCl_4$, 10038-98-9; $SnCl_4$, 7646-78-8

[*] Prof. Dr. H. Schumann and Dr. W. W. du Mont
Institut für Anorganische und Analytische Chemie der Technischen Universität
1 Berlin 12, Strasse des 17. Juni 135 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and by the Senator für Wirtschaft des Landes Berlin. We thank Prof. Dr. *J. J. Zuckerman*, SUNY, Albany (USA) for recording the Mössbauer spectra.

[1] *G. Fritz* and *H. Schäfer*, Z. Anorg. Allg. Chem. *407*, 295 (1974).
[2] *J. E. Byrne* and *Ch. Russ*, J. Organometal. Chem. *38*, 319 (1972).
[3] Identity and purity of *(2a)* and *(2b)* confirmed by ^{1}H-NMR, ^{31}P-NMR, IR, and Raman spectra, and by elemental analysis and molecular weight determinations.
[4] Analogous α-elimination reactions on *(2b)* have been proved in the meantime: *W. W. du Mont* and *H. Schumann*, J. Organometal. Chem. *85*, C 45 (1975).

The Platinum-Promoted Cyclization of 4-Pentenylamine

By *Jürg Ambühl, P. S. Pregosin, L. M. Venanzi, Giovanni Ughetto,* and *Luigi Zambonelli*[*]

The thermodynamics and kinetics of reactions of the type:

$$[PtX_4]^{2\ominus} + CH_2{=}CH(CH_2)_nX' \rightleftharpoons [PtCl_3\{CH_2{=}CH(CH_2)_nX'\}]^{\ominus} + X^{\ominus} \quad (1)$$

X = Cl and Br; n = 1, 2, 3 and 4; X' = $NH_3^{\oplus}$, OH and $SO_3^{\ominus}$

have been discussed in a number of publications[1]. Later it was observed[2] that although the reaction of tetrachloroplatinate(II) *(1)* and 4-pentenylammonium *(2)* ions leads initially to the formation of olefin complex *(3)*, this is subsequently converted, in a slower, quantitative reaction into *(1)* with the total disappearance of *(2)*[3]:

$$\underset{(1)}{[PtCl_4]^{2\ominus}} + \underset{(2)}{CH_2{=}CH(CH_2)_3NH_3^{\oplus}} \rightleftharpoons \underset{(3)}{[PtCl_3\{CH_2{=}CH(CH_2)_3NH^3\}]} + Cl^{\ominus} \quad (2)$$

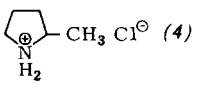
$$(3) + Cl^{\ominus} \rightarrow \underset{(1)}{[PtCl_4]^{2\ominus}} + \text{organic product(s)} \quad (3)$$

Reaction (3) leads to only one organic product *(4)*, which was characterized as follows:

1. A 10^{-2} M solution of *(3)* in D_2O containing DCl (*ca.* 0.1 mol/l) and NaCl (1.9 mol/l) was kept at 60 °C for 14 days[4]; the ^{1}H-NMR spectrum of this solution indicated that *(4)* was 2-methylpyrrolidinium chloride.

2. An aqueous solution, prepared and equilibrated as described above, was evaporated to dryness on a rotary evaporator and the residue extracted with chloroform. The ^{1}H-NMR spectrum of the extract, which was identical with that obtained in experiment 1, showed that *(4)* was the only organic product present. The ^{13}C-NMR spectrum of this solution confirmed that *(4)* is in fact 2-methylpyrrolidinium chloride.

3. The ^{1}H- and ^{13}C-NMR spectra of an HCl solution of 2-methylpyrrolidine, prepared by reduction of γ-valerolactam[5] provided conclusive structural identification.



(4)

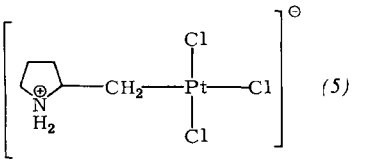
It was also found that:

1. A second, as yet unidentified, organic product accompanies *(4)* when complex *(1)* is reacted with an excess of *(2)*.

2. Addition of ligand *(2)* to a solution which has undergone reaction (3) starts a new cycle of reactions (2) and (3) with formation of additional amounts of compound *(4)*. Up to three such cycles have been carried out indicating that the formation of *(4)* from *(1)* and *(2)* can be considered as "catalytic".

3. Reaction (3) is accelerated by an increase in pH. At pH = 2 one cycle is completed in *ca.* six days.

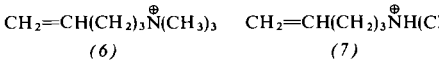
We assume that 2-methylpyrrolidinium chloride *(4)* is formed by intramolecular, nucleophilic attack by the NH_2-group, produced by deprotonation of *(3)*, at the coordinated double bond giving intermediate *(5)* which then undergoes acid cleavage of the Pt—C bond[6].



(5)

While $[PtCl_3(CH_2{=}CH(CH_2)_2NH_3)]$ does not undergo reaction (3) when kept at 60 °C for *ca.* 6 weeks, $[PtCl_3(CH_2{=}CH(CH_2)_4{\cdot}NH_3)]$ does undergo a very slow reaction under the same conditions.

Finally, it has been observed that the ion *(6)* gives the true equilibrium indicated by reaction (1), whereas the ion *(7)* appears to react as *(2)*. The product of this reaction is being characterized.



(6) *(7)*

It should be pointed out here that, in the light of the above results, the previously published[7] equilibrium constant for reaction (2) could be inaccurate.

Received: December 23, 1974 [Z 164 IE]
German version: Angew. Chem. *87*, 380 (1975)

CAS Registry numbers:
(1), 13965-91-8; *(2)*, 54677-52-0; *(3)*, 12144-82-0; *(4)*, 54677-53-1; *(5)*, 54688-81-2

[1] *R. M. Milburn* and *L. M. Venanzi*, Inorg. Chim. Acta *2*, 97 (1968), and references cited therein.

[2] *G. Dolcetti, L. M. Venanzi*, and *L. Zambonelli*, unpublished observations.

[3] Unless otherwise stated, these and all subsequent reactions were carried out at 60 °C in aqueous solutions containing $Cl^{\ominus}$ (2 mol/l) and $H^{\oplus}$ (0.1 mol/l). The reactions were followed spectrophotometrically [1].

[4] The electronic spectra of such solutions in H_2O indicate that complex *(3)* has reacted quantitatively to form $[PtCl_4]^{2\ominus}$ *(1)* after 2 weeks.

[5] *R. Bonnett, V. M. Clark, A. Giddey*, and *A. Todd*, J. Chem. Soc. *1959*, 2087.

[6] a) *A. Panunzi, A. De Renzi*, and *G. Paiaro*, J. Amer. Chem. Soc. *92*, 3488 (1970); b) The authors are indebted to Professor *R. F. Heck* for suggesting the possible similarity between reaction (3) and the work of *Panunzi et al.*

[7] *F. R. Hartley* and *L. M. Venanzi*, J. Chem. Soc. *A 1967*, 330.

[*] Prof. L. M. Venanzi, Dr. P. S. Pregosin, and J. Ambühl
Inorganic Chemistry Laboratory
Swiss Federal Institute of Technology
CH-8006 Zürich, Universitätstrasse 6 (Switzerland)
Prof. L. Zambonelli and Dr. G. Ughetto [**]
Laboratorio di Strutturistica Chimica "Giordano Giacomello"
C.N.R. Areadi Ricerca di Roma, Casella Postale 10, 00016 Roma (Italy)

[**] These authors gratefully acknowledge the assistance of Mr. *P. Mura*.

Oxidative Addition of Isocyanide Dichlorides to Metal Complexes[**]

By *Wolf Peter Fehlhammer, Andreas Mayr*, and *Bernhard Olgemöller*[*]

As a rule isocyanides experience increased stability when coordinated to a metal[1], as can be shown by the isolation of stable complexes of labile isocyanides (*e.g.* $[Cu(C{\equiv}N{-}NR_2)_4]ClO_4$[2]) or those that are incapable of free existence (*e.g.* π-$C_5H_5Mn(CO)_2CNH$[3]). This prompted us to search for methods which would permit "*in situ*" synthesis of the isocyanide on the protecting metal. The only previous method of this type having a broad spectrum of application consists in the alkylation (acylation, protonation) of cyano complexes.

We have now found that the reaction of isocyanide dichlorides *(1)* with metal complexes, in which the metal is present in a low valency state, also opens up a general route to isocyanide complexes [equations (1)—(6)].

[*] Dr. W. P. Fehlhammer, A. Mayr, and B. Olgemöller
Institut für Anorganische Chemie der Universität
8 München 2, Meiserstrasse 1 (Germany)

[**] Isonitrile Syntheses on the Metal, Part 1.

$$Pt(PPh_3)_4 \xrightarrow[C_6H_6,\ 20\,^\circ C,\ 1\ d]{Cl_2CNR\ (1)} Cl_2Pt(PPh_3)CNR + Cl_2Pt(PPh_3)_2 \quad (1)$$
$$R = C_6H_{11},\ C_6H_5,\ p\text{-}C_6H_4NO_2$$

$$ClRh(PPh_3)_3 + (1) \xrightarrow[-PPh_3]{THF,\ 20\,^\circ C,\ 1\ d} Cl_3Rh(PPh_3)_2CNR \quad (2)$$
$$R = C_6H_{11},\ C_6H_5$$

$$[Rh(CO)_2Cl]_2 + 2\ (1) \xrightarrow[-2\ CO]{THF,\ 20\,^\circ C,\ 1\ h} [Cl_3Rh(CO)CNR]_2 \quad (3)$$
$$(2),\ R = C_6H_{11}$$

$$Pd\text{-}Metal + (1) \xrightarrow{100\,^\circ C,\ 2\ d} [Cl_2PdCNR]_2 \quad (4)$$

$$Na_2Fe(CO)_4 + (1) \xrightarrow[-2\ NaCl]{THF} Fe(CO)_4CNR \quad (5)$$
$$R = C_6H_5$$

$$Na_2Cr(CO)_5 + (1) \xrightarrow[-2\ NaCl]{THF} Cr(CO)_5CNR\ (3) \quad (6)$$
$$(a),\ R = C_6H_{11};\ (b),\ R = C_6H_5;$$
$$(c),\ R = C(O)C_6H_5;$$
$$(d),\ R = SO_2\text{-}C_6H_5$$

The advantages of our method lie, on the one hand, in the mildness of the procedure, which is often very pronounced—*e.g.* reactions *(5)* and *(6)* proceed rapidly enough even at temperatures well below 0 °C—and, on the other hand, in the availability of numerous interesting isocyanide dichlorides to which there are no corresponding isocyanides[4]. Even relatively unstable isocyanide complexes such as *(2)* are obtainable in good yields. In this connection the possibility of *fixing novel functional isocyanides to the complex* warrants special interest [cf. *(3c)*, *(3d)*][5].

In reactions (1)—(6) the three fragments of the isocyanide dichloride (2 chlorine atoms, 1 isocyanide molecule) add formally to the central metal, if necessary *via* substitution of other ligands, with the oxidation number of the central metal being increased by two units. It is possible that an intermediate *(4)* is involved which is stabilized by migration of chlorine to the metal atom. The converse of this step, namely the insertion of methyl isocyanide into the metal—chlorine bond has been observed in the case of niobium and tantalum pentachlorides[6].

$$Cl\text{–}\overset{(n+2)+}{M}\text{–}\underset{Cl}{\overset{|}{C}}\text{=}N\text{–}R \quad (4)$$

The three-fragment oxidative addition of geminal dichlorides—apparently a general type of reaction—has also been used with success for the synthesis of thiocarbonyl complexes[7] (from thiophosgene) and carbene complexes (from 1,1-dichloro-2,3-diphenylcyclopropene[8] and chloroformiminium or chloroformamidinium chlorides[9]).

Trichlorobis(triphenylphosphane)(cyclohexyl isocyanide)rhodium(III):

Cyclohexyl isocyanide dichloride (0.2 ml, 1.3 mmol) is added dropwise under nitrogen to a solution of 240 mg (0.26 mmol) $ClRh(PPh_3)_3$ in tetrahydrofuran (20 ml). After 48 hours' stirring the reaction mixture is concentrated to half its volume. On allowing to cool to 0 °C, orange colored crystals (m.p. 220 °C, yield >70%) are formed. IR(KBr): 2217 s (νNC); 345 sh, 336 w-m, 311 w cm^{-1} ($\nu RhCl_3$).

(Benzoyl isocyanide)pentacarbonylchromium (3c):

Benzoyl isocyanide is added in slight excess (0.75 g, 5.7 mmol) to a THF solution of "$Na_2Cr(CO)_5$" (30 ml)[10]. After stirring for one hour at −10 °C the reaction mixture is evaporated to dryness and the residue extracted several times with petroleum ether. The combined extracts are cooled to −50 °C. Ocher-colored crystals separate out which can be sublimed in a high vacuum at 35 °C. Yellow needles, m.p. 85 °C, yield >20%. IR (cyclohexane): 2108 vs (νNC); 2008 w, 1975 s, 1945 vs ($\nu Cr(CO)_5$); 1712 w (νC=O).

Received: December 30, 1974 [Z 178 IE]
German version: Angew. Chem. 87, 290 (1975)

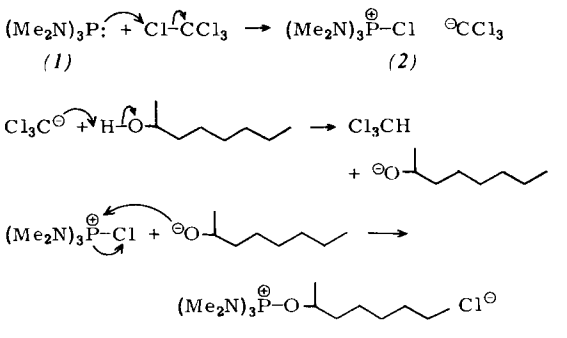
CAS Registry numbers:
$Cl_2CNC_6H_{11}$, 2666-80-0; $Cl_2CNC_6H_5$, 622-44-6;
$Cl_2CN(p\text{-}C_6H_4NO_2)$, 2666-74-2; $Cl_2CNC(O)C_6H_5$, 3911-55-5;
$Cl_2CNSO_2\text{—}C_6H_5$, 1886-60-8; $Pt(PPh_3)_4$, 14221-02-4;
$ClRh(PPh_3)_3$, 14694-95-2; $[Rh(CO)_2Cl]_2$, 14523-22-9;
Pd, 7440-05-3; $Na_2Fe(CO)_4$, 14878-31-0; $Na_2Cr(CO)_5$, 51233-19-3;
$Cl_2Pt(PPh_3)CNC_6H_{11}$, 54712-92-4; $Cl_2Pt(PPh_3)CNC_6H_5$, 54712-93-5;
$Cl_2Pt(PPh_3)CN\text{-}p\text{-}C_6H_4NO_2$, 54712-94-6;
$Cl_3Rh(PPh_3)_2CNC_6H_{11}$, 54688-88-9;
$Cl_3Rh(PPh_3)_2CNC_6H_5$, 54724-64-0; $[Cl_3Rh(CO)CNC_6H_{11}]_2$, 54844-31-4;
$Fe(CO)_4CNC_6H_5$, 17595-21-0; $Cr(CO)_5CNC_6H_{11}$, 19706-05-9;
$Cr(CO)_5CNC_6H_5$, 14782-94-6; $Cr(CO)_5CNC(O)C_6H_5$, 15365-59-0;
$Cr(CO)_5CNSO_2\text{—}C_6H_5$, 54688-89-0

[1] Cf. however: *K. Bartel* and *W. P. Fehlhammer*, Angew. Chem. *86*, 588 (1974); Angew. Chem. internat. Edit. *13*, 599 (1974).
[2] *W. P. Fehlhammer*, unpublished.
[3] *E. O. Fischer* and *R. J. J. Schneider*, J. Organometal. Chem. *12*, P 27 (1968).
[4] *E. Kühle*, *B. Anders*, and *G. Zumach*, Angew. Chem. *79*, 663 (1967); Angew. Chem. internat. Edit. *6*, 649 (1967).
[5] The scope of the method for the synthesis of such isocyanide complexes, which are not accessible *via* other routes, is presently under investigation.
[6] *B. Crociani* and *R. L. Richards*, J. C. S. Chem. Comm. *1973*, 127.
[7] *R. J. Angelici*, J. Amer. Chem. Soc. *95*, 7516 (1973); *M. Kubota* and *C. J. Curtis*, Inorg. Chem. *13*, 2277 (1974).
[8] *K. Öfele*, Angew. Chem. *81*, 936 (1969); Angew. Chem. internat. Edit. *8*, 916 (1969).
[9] *B. Cetinkaya*, *M. F. Lappert*, *G. M. McLaughlin*, and *K. Turner*, J. C. S. Chem. Comm. *1972*, 851; J. C. S. Dalton *1974*, 1591.
[10] Obtainable by irradiation (24 h) of a solution of $Cr(CO)_6$ (5 g) in THF (130 ml) over sodium amalgam (150 g, 1.2%). After *R. G. Hayter*, J. Amer. Chem. Soc. *88*, 4376 (1966).

Preparation of Aryl-Alkyl Ethers and Thioethers[**]

By *Ian M. Downie*, *Harry Heaney*, and *Graham Kemp*[*]

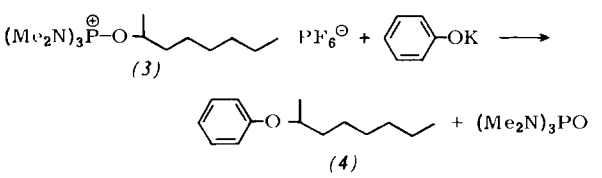
In connection with another study[1], we required a method for the preparation of aryl-alkyl ethers which was both stereospecific and did not lead to any rearrangement. In particular we wished to prepare chiral aryl-(1-methylheptyl)ethers, and aryl-neopentyl ethers which were free from other isomers. The previous isolation[2] of a stable tris(dimethylamino)-alkoxyphosphonium hexafluorophosphate suggested the use of this type of reagent. We now present our results in this area.



[*] I. M. Downie, Dr. H. Heaney, and G. Kemp
Organic Chemistry Laboratories, The University of Technology
Loughborough, Leicestershire, LE11 3TU (England)

[**] This work was supported by the Science Research Council.

Reaction of chiral 2-octanol with tris(dimethylamino)phosphane *(1)* and carbon tetrachloride leads, with complete inversion of configuration, to 2-chlorooctane[3]. We have now found that when this reaction is carried out at −20 °C a precipitate of trichloromethyltris(dimethylamino)phosphonium chloride is formed which can be removed and characterized as its stable perchlorate (5% yield). Addition of aqueous ammonium hexafluorophosphate to the filtrate gave the phosphonium salt *(3)* in 46% yield; a small amount of 2-chlorooctane was also formed, despite the low working temperature.



(3)

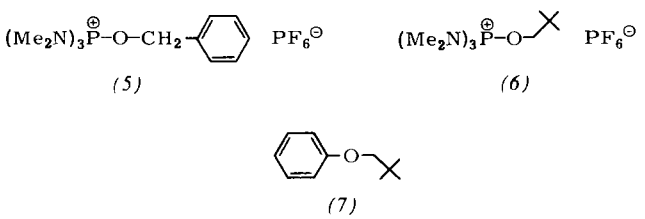
(4)

Reaction of the salt *(3)*, prepared from (*R*)-(−)-2-octanol, with potassium phenolate in dimethylformamide gave (*S*)-(+)-2-phenoxyoctane, (+)-*(4)* in 93% yield; $\alpha_D^{26} = +15.5°$ ($c = 5.0$, C_2H_5OH) [(*R*)-(−)-2-phenoxyoctane, (−)-*(4)*: $\alpha_D^{26} = -15.0°$ ($c = 5.0$, C_2H_5OH)[4].]

The generality of the method is evident from the examples given in Table 1. The alkoxyphosphonium salts *(5)* and *(6)*, which are derived from primary alcohols, were prepared at −78 °C and that from the secondary alcohol at −20 °C.

Table 1. Preparation of alkyl-aryl ethers and thioethers from alkoxy(dimethylamino)phosphonium hexafluorophosphates and potassium aryloxides and -thioxides.

Pot. salt of HOAr of HSAr	R in $(Me_2N)_3\overset{\oplus}{P}OR\,PF_6^{\ominus}$	ROAr or RSAr Yield [%]
2-Hydroxy-2'-nitrobiphenyl	Neopentyl	90
4-Nitrophenol	Neopentyl	42
4-Methoxyphenol	Neopentyl	66
Phenol	Neopentyl	75
2-Hydroxy-2'-nitrobiphenyl	1-Methylheptyl	81
4-Methoxyphenol	1-Methylheptyl	68
4-Nitrophenol	1-Methylheptyl	80
Phenol	1-Methylheptyl	99
Thiophenol	1-Methylheptyl	61
4-Methylthiophenol	1-Methylheptyl	68
Thiophenol	Benzyl	83
4-Methylthiophenol	Benzyl	98
4-Methylthiophenol	Allyl	97
Thiophenol	Allyl	90
Phenol	Allyl	79



(5) *(6)*

(7)

Benzyloxytris(dimethylamino)phosphonium hexafluorophosphate (5)

A solution of *(1)* (0.1 mol) in ether (30 ml) at −78 °C was added to a solution of benzyl alcohol (0.1 mol) and carbon tetrachloride (0.15 mol) in ether (100 ml), also at −78 °C. When the addition was completed the cold mixture was poured into an ice-chilled solution of NH_4PF_6 (0.1 mol) in water (40 ml) with immediate formation of a white solid. This solid was washed with ice-cold water (50 ml), then with ether (50 ml), and after drying over $CaCl_2$ (28.1 g; 68% yield) was finally recrystallized from ethanol (colorless plates, m. p. 124—126 °C, ^{1}H-NMR ($CDCl_3$): δ = 7.45 (s, 5 H), 5.25 (d, 2 H, $J_{PH} = 9.0$ Hz), 2.80 (d, 18 H, $J_{PH} = 2.80$ Hz).

Phenoxyneopentane (7)

Dimethylformamide (50 ml), dried over CaH_2, was added with stirring to powdered potassium hydroxide (0.02 mol). To the stirred mixture was added phenol (0.01 mol) followed by tris(dimethylamino)neopentyloxyphosphonium hexafluorophosphate (0.02 mol); the mixture was then heated under reflux for 15 h. After cooling to room temperature the reaction mixture was poured into water (100 ml) and extracted with ether (3 × 50 ml) and each extract was washed with water (3 × 30 ml). The combined ether layers were twice washed with an aqueous solution of sodium hydroxide, to remove unreacted phenol, and then dried over $MgSO_4$. Distillation of the residue after removal of solvent afforded *(7)* [1.24 g (75% yield), b.p. 55 to 58 °C/1.5 torr (literature value[5]: 82—83 °C/12 torr); ^{1}H-NMR ($CDCl_3$): δ = 7.40—6.80 (m, 5 H), 3.60 (s, 2 H), 1.0 (s, 9 H)].

Received: December 9, 1974 [Z 189 IE]
German version: Angew. Chem. *87*, 357 (1975)

CAS Registry numbers:
K 2-(2-nitrophenyl)phenoxide, 54738-99-7; K 4-nitrophenoxide, 1124-31-8; K 4-methoxyphenoxide, 1122-93-6; K phenoxide, 100-67-4; K thiophenolate, 3111-52-2; K 4-methyl(thiophenolate), 31367-69-8; tris(dimethylamino)neopentyloxyphosphonium PF_6^-, 54739-01-8; *(3)*, 54739-03-6; *(5)*, 54774-06-0; allyloxytris(dimethylamino)phosphonium PF_6^-, 54739-05-8; 2-neopentyloxy-2'-nitrobiphenyl, 54739-06-9; 4-nitrophenoxyneopentane, 14225-16-2; 1-methoxy-4-neopentyloxybenzene, 14225-17-3; *(6)*, 2189-88-0; 2-(2'-nitro-2-biphenyloxy)octane, 54739-07-0; 2-(4-methoxyphenoxy)octane, 54739-08-1; 2-(4-nitrophenoxy)octane, 54739-09-2; 2-phenylthiooctane, 13921-16-9; 2-(*p*-tolylthio)octane, 54739-10-5; benzylthiobenzene, 831-91-4; 4-benzylthiotoluene, 5023-60-9; 4-allylthiotoluene, 1516-28-5; 1-allylthiobenzene, 5296-64-0; 1-allyloxybenzene, 1746-13-0; *(1)*, 1608-26-0; (+)-*(4)*, 54739-11-6; (−)-*(4)*, 39998-99-7; *(R)*-(−)-2-octanol, 5978-70-1; benzyl alcohol, 100-51-6

[1] *A. J. Copson, H. Heaney, A. A. Logun*, and *R. P. Sharma*, J. C. S. Chem. Comm. *1972*, 315.

[2] *I. M. Downie, J. B. Lee*, and *M. F. S. Matough*, Chem. Commun. *1968*, 1350.

[3] *D. Brett, I. M. Downie, J. B. Lee*, and *M. F. S. Matough*, Chem. Ind. (London) *1969*, 1017.

[4] *J. Kenyon, H. Phillips*, and *V. Pittman*, J. Chem. Soc. *1935*, 1072.

[5] *B. Danrée* and *J. Seyden-Penne*, Bull. Soc. Chim. Fr. *1967*, 415; *B. Stephenson, G. Solladié*, and *H. S. Mosher*, J. Amer. Chem. Soc. *94*, 4181 (1972).

Valence Isomerization of Hexamethyl-*trans*-σ-trishomobenzene[1]

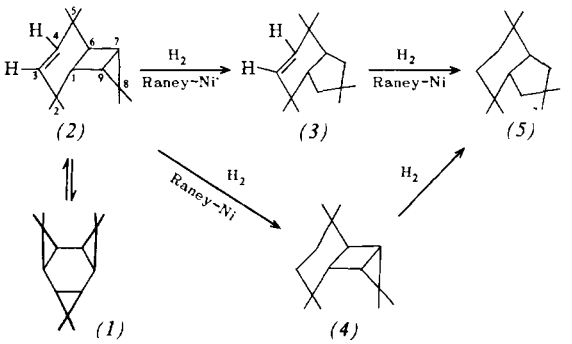
By *Paul Binger* and *John McMeeking*[*]

In contrast to previously known derivatives of *trans*-σ-trishomobenzene[3-5], hexamethyl-*trans*-σ-trishomobenzene *(1)*[2], which is readily accessible from 3,3-dimethylcyclopropene, already undergoes reversible valence isomerization associated with skeletal rearrangement above 120 °C.

After *ca.* 2 h at 200 °C, the tetracyclic compound *(1)* yields an equilibrium mixture of 7% *(1)* and 93% hexamethyl-*trans*-tricyclo[4.3.0.0^{7,9}]non-3-ene *(2)* (GC/MS) in which the two larger rings are *trans*-fused (^{1}H-NMR spectrum)[6]. The *trans*-

[*] Dr. P. Binger and Dr. J. McMeeking
Max-Planck-Institut für Kohlenforschung
433 Mülheim/Ruhr, Kaiser-Wilhelm-Platz 1 (Germany)

annelation of the C_4 ring follows from the splitting pattern of the two olefinic protons at $\tau = 4.80$ and 4.87 (AB problem, $J = 11$ Hz) and from the position (7.68) and the dd splitting ($J_{1,6} \approx 9$ Hz, $J_{1,9} \approx 5$ Hz) of the four-membered ring proton bound to C^1.



In the presence of Raney nickel, *(2)* rapidly takes up 1 mol of H_2 at room temperature. Rupture of the C^7—C^9 bond to form *(3)* is considerably faster than hydrogenation of the C=C bond to give *(4)*. After slow uptake of a second mol of H_2 at room temperature (*ca.* 30 h) a high yield of uniform hexamethyl-*trans*-bicyclo[4.3.0]nonane *(5)* is obtained.

The hydrocarbons *(3)* to *(5)*, and also *(2)*, were identified by mass and ^{1}H-NMR spectra[6]. *(3)* (MS: $M^{\oplus} = 206$) still possesses a *cis*-C=C bond [^{1}H-NMR: $\tau = 4.92$ (s, 2H)], in contrast to *(4)* (MS: $M^{\oplus} = 206$). In the ^{1}H-NMR spectrum of *(5)* (MS: $M^{\oplus} = 208$) only $>CH_2$, $\geqslant CH$, and CH_3 groups are to be seen.

The skeletal rearrangement of *(1)* to *(2)* involves cleavage of two cyclopropane bonds belonging to the cyclohexane ring. It is facilitated by an additional strain energy which is attributable to the spatial proximity of the geminal methyl groups to the *cis*-cyclopropane rings, and therefore takes place at temperatures about 400 °C lower than those required for other sterically unhindered *trans*-σ-homobenzene derivatives[5]. The uniform formation of the *trans*-isomer *(2)* suggests that the isomerization *(1)* → *(2)* might be a symmetry-allowed electrocyclic process ($2\sigma_s + 2\sigma_a$).

Procedure:

Compound *(1)* (14.6 g) is heated to 200 °C for 6 h. The resulting colorless liquid consists of (GC) 90.7% *(2)* and 6.9% *(1)*, the remainder being made up of three unknown compounds. Preparative gas chromatography afforded 11.2 g of 98.5% (GC) *(2)*, having m.p. 25—26 °C.

IR (neat): 1600 cm^{-1} (C=C); MS (70 eV): $m/e = 204$ ($M^{\oplus}$; rel. int. 5%), 189 (85), 161 (32), 147 (31), 133 (92), 119 (61), 110 (60), 105 (50), 95 (52), 91 (44), 83 (22), 79 (29), 77 (31), 69 (77), 55 (53), 43 (35), 41 (100); ^{1}H-NMR (neat, 100 MHz): $\tau = 4.80$ (d, $J = 11$ Hz, 1H), 4.87 (d, $J = 11$ Hz, 1H), 7.68 (dd, $J_{1,6} \approx 9$ Hz and $J_{1,9} \approx 5$ Hz, 1H), 8.47 (m, 2H), 8.75 (s, 3H), 8.83 (m, 1H), 9.02 (s, 3H), 9.11 (s, 3H), 9.16 (s, 3H), 9.18 (s, 3H), and 9.21 ppm (s, 3H).

On heating (4 h, 200 °C), compound *(2)* (98.5% (GC), 0.8 g) gives a mixture of (GC) 90.1% *(2)* and 6.6% *(1)*, the remainder consisting of four unknown compounds.

Received: January 30, 1975 [Z 194 IE]
German version: Angew. Chem. 87, 383 (1975)

CAS Registry numbers:
(1), 51898-92-1; *(2)*, 54832-80-3; *(3)*, 54832-81-4; *(4)*, 54832-82-5; *(5)*, 54832-83-6

[1] Systematic name: 3,3,6,6,9,9-hexamethyl-*cis,cis,trans*-tetracyclo-[6.1.0.0^{2,4}.0^{5,7}]nonane.

[2] *P. Binger, G. Schroth*, and *J. McMeeking*, Angew. Chem. *86*, 518 (1974); Angew. Chem. internat. Edit. *13*, 465 (1974).

[3] *H. Prinzbach* and *R. Schwesinger*, Angew. Chem. *84*, 988 (1972); Angew. Chem. internat. Edit. *11*, 940 (1972).

[4] *E. Vogel, H. J. Altenbach*, and *E. Schmidbauer*, Angew. Chem. *85*, 862 (1973); Angew. Chem. internat. Edit. *12*, 838 (1973).

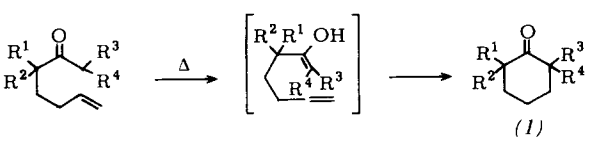
[5] *A. de Meijere, D. Kaufmann*, and *O. Schallner*, Tetrahedron Lett. *1974*, 3835.

[6] Interpretation of the ^{1}H-NMR spectrum of *(2)* was greatly facilitated by its 270 MHz spectrum. We are indebted to Dr. *G. Fritz* of Ciba-Geigy for recording this spectrum.

Reviews

Abstracts of selected progress reports and review articles

The thermal cyclization of unsaturated carbonyl compounds which find extensive use in the synthesis of C—C σ-bonds are summarily described in an article by *J. M. Conia* and *P. Le Perchec*. The reaction involves two steps, enolization (by catalytic [1,3]-H shift) and cyclization (by thermal enol-H shift). The method can be applied to the synthesis of numerous mono-, bi-, and polycycles as well as spiro and bridged carbonyl compounds—often in excellent yields. A discussion of the reaction mechanisms, necessary chain lengths, nature of the H acceptors and donors, orientation phenomenon of α-thermocyclization, and the stereochemistry and geometry

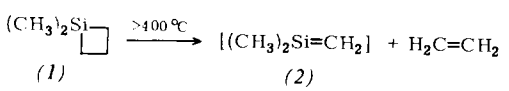


(1)

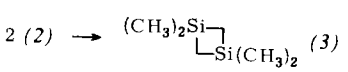
of the transition state is followed, *inter alia*, by an outline of the syntheses of cycloalkanones *(1)* and the thermal cyclization of doubly unsaturated carbonyl compounds. [The Thermal Cyclization of Unsaturated Carbonyl Compounds. Synthesis *1975* 1—19; 78 references]

[Rd 770 IE—M]

Unstable silicon analogs of unsaturated compounds are reviewed by *L. E. Gusel'nikov, N. S. Nametkin,* and *V. M. Vdovin*. Silacyclobutanes such as *(1)* pyrolyze to 1,3-disilacyclobutanes, such as *(3)*, and ethylene; the silicon-analogous isobutene *(2)*



(1) *(2)*



(3)

polymerizes on freezing-out. Kinetic and mass spectral data, as well as results of copyrolysis of *(1)* and 1-chloro-1-methylsilacyclobutane provide supporting evidence for the given reaction course. Dimethylsilanone is presented as example of a silicon-analogous ketone; it is formed on pyrolysis of an eight-membered cyclocarbosiloxane. [Unstable Silicon Analogs of Unsaturated Compounds. Accounts Chem. Res. *8*, 18—25 (1975); 78 references]

[Rd 774 IE—L]

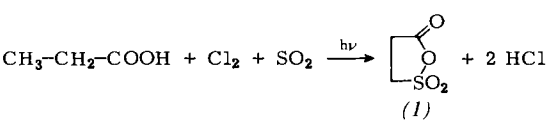
Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

For the industrial preparation of *p*-aminobenzoic acid a monoalkyl terephthalic ester, especially the monomethyl ester obtained as a by-product in the preparation of dimethyl terephthalate, is converted with ammonia into terephthalamide acid and the latter is subjected to a Hofmann degradation [DOS 2313580; Akzo GmbH, Wuppertal (Germany)]

[PR 260 IE—D]

3-Sulfopropionic anhydride (1,2-oxathiolan-5-one 2,2-dioxide) *(1)* is formed in good yield by a photochemical reaction of propionic acid with chlorine and sulfur dioxide if the conversion is carried out with less than 1 mol of chlorine per mol of propionic acid and with 0.95—7 times as much of sulfur dioxide by weight (referred to the weight of the chlorine).

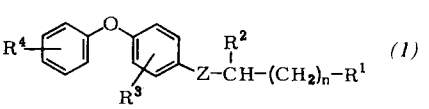


(1)

(1) is suitable, for example, for introducing hydrophilic groups into dye precursors. [DOS 2317601; BASF AG, Ludwigshafen (Germany)]

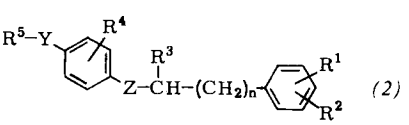
[PR 263 IE—D]

Metamorphosis inhibitors. Compounds of the general formula *(1)* and *(2)* are suitable for pest control.



(1)

$Z = O, S, >NR^5$; R^1 = if necessary, substituted phenyl; $R^2 = H, CH_3, C_2H_5$; $R^3, R^4 = H, CH_3, C_2H_5, OCH_3, OC_2H_5, NO_2$, halogen; $R^5 = H, CO{-}CH_3, CO{-}C_2H_5$; $n = 0, 1$.



(2)

$Y = -CH_2-, -N{=}N-, -CH_2-O-, -NH-, -CO-$, or direct bond; $Z = O, S$; $R^1, R^2 = H$, alkyl, Oalkyl, halogen, NO_2, Salkyl, *etc.*; $R^3 = H$, alkyl ($<C_4$); $R^4 = H$, alkyl ($<C_4$), halogen; R^5 = cyclohexyl, if necessary, substituted phenyl; $n = 0, 1$.

The following compounds are particularly noted: *(1a)*, $Z = O$, $R^1 = p\text{-}C_2H_5{-}C_6H_4$; $R^2 = R^3 = R^4 = H$; $n = 0$, and *(2a)*, $Y = -CH_2-$; $Z = O$; $R^1{-}R^2 = 3,4{-}O{-}CH_2{-}O-$; $R^3 = R^4 = H$; $R^5 = C_6H_5$; $n = 0$. [DOS 2418295 and 2418343; Ciba Geigy, Basel (Switzerland)]

[PR 265 IE—S]

Enzyme—Gewinnung—Analyse—Regulation (Enzymes: Isolation, Analysis and Control). By *A. Betz*. Verlag Chemie GmbH, Weinheim 1974. 1st edit., XII, 197 pp., 64 figs., 7 tables, bound, DM 28.80.

German textbooks on enzymes were hitherto a rarity in the bookshops, so the appearance of one by *Augustin Betz* on enzymology in the "chemie paperback" series is particularly welcome. This book is intended to provide the reader with basic knowledge of enzymology and is designed in the first place for students of biology and medicine. This purpose is fulfilled in every respect. All that is important about enzymes is summarized in eleven chapters: structure, biological function, mode of action and isolation, as well as applications in analysis, therapy, and industry. The presentation is very skilful and clear, and it is especially commendable that emphasis is repeatedly laid on techniques. For a new edition it remains only to hope that the chapter on allosteric enzymes will be made more detailed and that hydrophobic interactions will be described. The book can be most warmly recommended to all students who wish to enter the field of enzymology.

Horst Sund [NB 254 IE]

Organic Semiconductors. Dark- and Photoconductivity of Organic Solids. By *H. Meier*. Monographs in Modern Chemistry 2. Verlag Chemie GmbH, Weinheim 1974. 1st edit., XV, 661 pp., 150 figs., 70 tables, bound, DM 138.—.

Here, from the hand of a skilful researcher, we have a monograph in which the phenomena of photoconductivity in organic substances are placed in the foreground. There is undoubtedly a need for such a presentation, as physical processes in the field of biology and similar questions are matters of topical interest.

In the first part of the book the author has succeeded convincingly in picking up the sometimes complete analogies and the specific differences between the properties of inorganic crystals and those of solid organic substances. A chapter on the methods used for investigating organic substances, is followed by a second part which deals with electrical conductivity and chemical structure on a large number of examples.

In the third part the reader finds a treatment of dark- and photoconductivity, mainly from theoretical points of view. The fourth part gives applications from, *inter alia*, the fields of photobiological and industrial processes; photosynthesis, the processes of vision, conduction in membranes, and heterogeneous catalysts are only a few of the keywords. There is also a discussion of the extent to which inorganic materials can be replaced by organic compounds in electronic systems.

The author has succeeded in his aim of providing an intelligible presentation in spite of the high information density. Precise formulations in a text that has been kept brief are supplemented by numerous illustrations, more than 75 structural formulas and tables, and an unusually detailed bibliography with more than 2600 references. In this way it has been possible to make contact with the scientist who wants a review of this field, as well as providing the specialist interested in the properties of specific substances with useful ideas.

H. Pagnia [NB 255 IE]

Lehrprogramm Enzymkinetik (Enzyme Kinetics—A Learning Program). By *H. N. Christensen* and *G. A. Palmer*. Translated by *H. U. Wolf*. Pocketbook 23, Verlag Chemie GmbH, Weinheim 1974. 1st edit., VI, 134 pp., 51 figs., 10 tables, bound, DM 14.80.

This book by *Christensen* and *Palmer*, which now appears in excellent translation, has won a special place among student texts, being ideally suited to the treatment of enzyme kinetics for a course of self-study. It is intended equally for students of biology, chemistry and medicine, not only because such students should know about enzymes but also because the facts about enzyme kinetics can also be applied to pharmacological problems and to transport processes. The difficulty of the program increases continuously from relatively easy beginnings, and on reaching the end one has the feeling of having mastered enzymology. This applies not only to students but also to specialists whose student days are long past and who use the program as a refresher course—for them too it is excellently suited. Everything about enzyme kinetics is described: the derivation of the Michaelis-Menten equation, the importance of kinetic parameters and methods of their determination, the types of inhibition, allosteric enzymes (here the text could be made somewhat more detailed in a new edition), and also the pH and temperature dependence of enzyme-catalyzed reactions. The reader can check his progress from the problems. The book can be recommended unreservedly to all who wish to refresh their knowledge of enzyme kinetics or require supplementary information to lecture notes.

Horst Sund [NB 256 IE]

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 4036, ⟨140 36⟩, 4037, ⟨140 37⟩. Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim. Pappelallee 3. P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 4031, ⟨140 31⟩. Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 6
June 1975
Pages 375–444

Three-Dimensional Structure of the Actinomycins

By Helmut Lackner[*]

Many complicated three-dimensional structures can be formulated for the actinomycins, red chromopeptide antibiotics distinguished by pronounced antineoplastic activity, because of their unique constitutional type. Since these structures largely determine the specific activity of the actinomycin molecules in the host cells, knowledge of the structural forms occurring naturally in solution is a decisive prerequisite for detailed insight into the mode of biological action of the actinomycins. Investigations by several methods have shown that, in spite of their deviating primary structures, all important actinomycins assume only one very characteristic, pseudo-C_2-symmetrical, and remarkably stable three-dimensional structural type.

1. Introduction

Numerous Streptomycete strains isolated from soil samples produce orange-red chromopeptides—actinomycins—very active as antibiotics and cytostatics but highly toxic. They have been known since 1940 when *Waksman* and *Woodruff*[1] isolated actinomycin A, which incidentally was the first ever crystalline antibiotic. Since then more than thirty natural and a series of synthetic actinomycins have become available[2–4], all of which possess the same typical fundamental structure; two pentapeptide lactone rings (see Fig. 1b) linked to an aminophenoxazinone chromophore (Fig. 1a). This structure can be varied by alteration of the amino acids in the two peptide units (cf. Fig. 1b). *Brockmann*[2] has already reviewed the isolation and separation of actinomycins, the determination of their structure, and also the first total synthesis[5].

Actinomycins suppress the growth of gram-positive microorganisms such as *Bacillus subtilis* in concentrations as low as $<0.1\,\mu g/ml$; this is about the same activity as that of penicillins. However, the unusual toxicity of the actinomycins prevents their wider chemotherapeutic application. Thus, the lethal dose (LD_{50}) of actinomycin D in the mouse is 0.5 to 1 mg/kg (for phalloidin, the poison of the death cup mushroom, *Amanita phalloides*; the $LD_{50} \approx 2\,mg/kg$) and the maximum tolerated dose, spread over several days, is about 0.1 mg/kg.

The remarkable *cytostatic* properties of the antibiotic were first discovered in animal experiments (Ehrlich carcinoma, ascites tumors) and were later also demonstrated for some rarer tumor types in man (lymphogranulomatosis, Wilms' tumor, choriocarcinoma). Combined treatment by surgery, radiotherapy, and actinomycin has led to impressive successes, particularly for Wilms' tumor; in such treatment children receive 10 µg of actinomycin D *(1)* per kg of body weight per day for 8—10 days; the tolerance threshold for adults is still lower. It has not yet proved possible to broaden appreciably the extremely narrow margin between the effective and the dangerous doses (for penicillins it is 10^4 times as wide) by, for example, structural modification of the actinomycins or preparation of derivatives. More details about the structure-activity relationships and the application of actinomycins will be found in the extensive review by *Meienhofer* and *Atherton*[6].

The biological action of the actinomycins rests on their complex formation with the double-stranded helical deoxyribonucleic acids (DNA) of the cell (Fig. 2). Even *one* bound actinomycin molecule per *ca.* 1000 base pairs[7] produces selective 50% inhibition of DNA-dependent RNA synthesis and thus of protein biosynthesis. Higher actinomycin concentrations also inhibit DNA replication. In this attack on the very center of cell metabolism actinomycin does not differen-

[*] Priv.-Doz. Dr. H. Lackner
Organisch-Chemisches Institut der Universität
34 Göttingen, Tammannstrasse 2 (Germany)

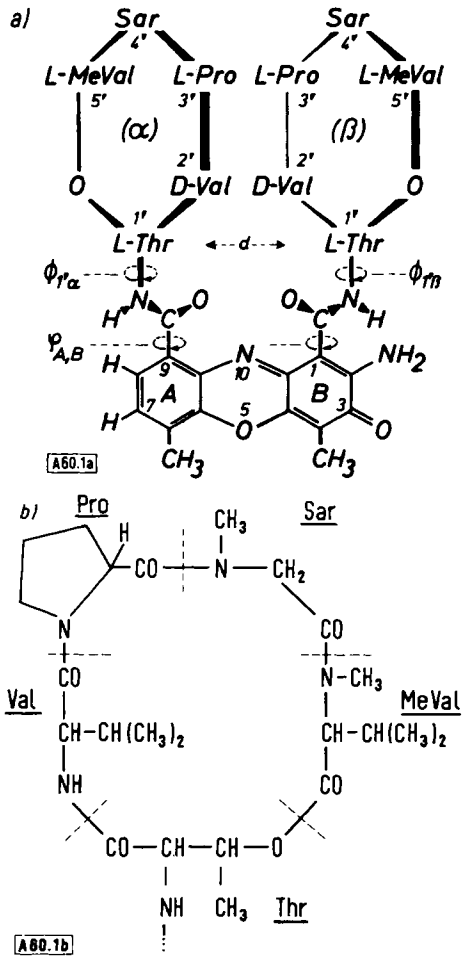


Fig. 1. a) Primary structure of actinomycin D *(1)*. This is the actinomycin that has been best studied and used most often. It is termed "C_1" in German-language literature; according to more recent proposals [6] it is also called [di-(2'-D-valine]actinomycin (abbreviated as Val_2-AM). b) Pentapeptide lactone ring, schematic. Val = valine, Pro = proline, Sar = sarcosine, MeVal = *N*-methylvaline, Thr = threonine. It should be noted that the NH groups in *(1)* still belong to the threonine residue. For the definition of φ and ϕ see Figs. 3 and 13.

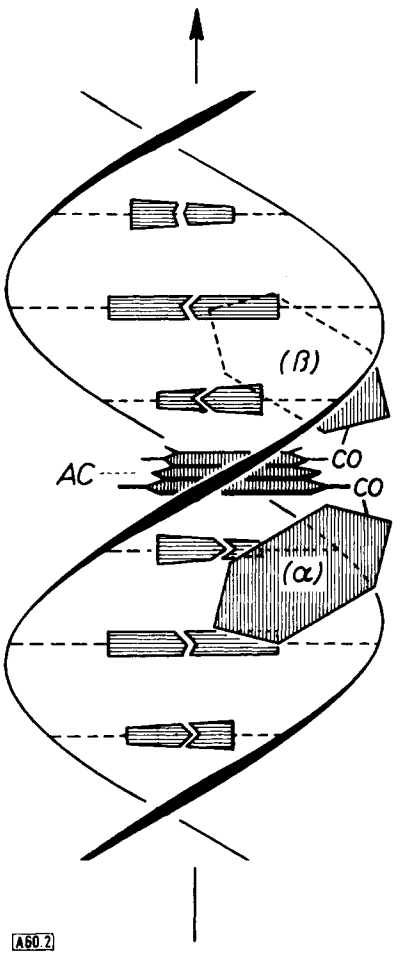


Fig. 2. The chromophore (AC) of an actinomycin molecule becomes intercalated between the guanine-cytosine pairs in the DNA double helix (see also Figs. 18 and 20). (α) and (β) = pentapeptide lactone groups.

tiate in principle between *e.g.* bacterial cells and cells of the host organism infected with the bacteria (penicillin does make this differentiation). Recognition of this phenomenon explains the high toxicity of the actinomycins and the pathological cell alterations that occur under their influence. Actinomycins are therefore being used increasingly in cell-biological investigations (virus replication, biosyntheses, *etc.*).

Discussion of the complex formation with DNA has concentrated mainly on two possibilities: a) addition of the actinomycin to the DNA by means of three hydrogen bonds from the chromophore to deoxyguanosine[8] and b) an intercalation model[7]. According to b), the actinomycin molecule selectively inserts itself with the chromophore between two neighboring guanine-cytosine base pairs in the DNA double helix (Fig. 2), where it is reversibly bound by hydrogen bonds (cf. Fig. 20), hydrophobic forces, and π-complexes. This leads not only to steric hindrance but also to local distortions of the DNA helix and thus to interference with information transfer (transcription) and the consequences mentioned above.

Concept b) also accords with, *inter alia*, hydrodynamic measurements (which indicate lengthening of the helix strand after complex formation), equilibrium-dialytic and kinetic findings (*e.g.* concerning the lifetime of the complex[7]), and recently with NMR[9-13] and X-ray analytical data[14-16].

The most detailed possible knowledge of the mode of formation and structure of the actinomycin-DNA complex is important if we are to understand the mode of action of actinomycins, to search for variants with greater therapeutic range, and to plan research on the introduction of actinomycins into molecular- and cell-biological work. The nature and the extent of the interactions within the complexes depend decisively on the three-dimensional structure of the actinomycin molecules in solution.

2. The Actinomycin Molecule

The primary structure of actinomycin D, confirmed by syntheses[5,17-21], is shown in Fig. 1: the chromophore, 2-amino-4,6-dimethyl-3-oxophenoxazine-1,9-dicarboxylic acid ("actinocin"), is linked to two pentapeptide lactone groups [(α) and (β)] by amide bridges. The peptide amino acid sequences $1'_\alpha$—$5'_\alpha$ and $1'_\beta$—$5'_\beta$ can be the same, as in actinomycin D *(1)*, or different; the terms *iso-* and *aniso-*actinomycins, respectively (cf. Fig. 16), are used for this differentiation. Because of the lack of symmetry in the chromophore, the (α)- and (β)-peptide lactone units are nonequivalent even when structurally identical.

If, for a start, one assumes similar, stable, and planar skeletal conformations for the two peptide rings (Fig. 3), then each ring can rotate independently around its N—C^{α}_{Thr} and the

C^1—CO or C^9—CO bond (Fig. 1). The amide bond between the chromophore and the peptide ring should remain in the energetically and sterically favored *trans*-form. The torsion angles $\phi_{1'\alpha}$ and $\phi_{1'\beta}$, together with φ_A and φ_B (Figs. 1 and 3) then determine the arrangements of the peptide planes relative to each other and to the plane of the chromophore. For example, variation of the angles φ_A, φ_B (Fig. 3) changes both the distance (d) between the peptide rings and their positions relative to the functional groups of the chromophore; both these are important parameters for the formation of the actinomycin-nucleotide complexes.

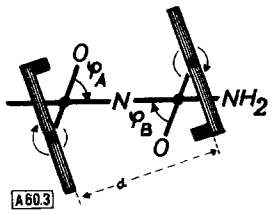


Fig. 3. The actinomycin D molecule (Fig. 1) drawn schematically from above (—N—NH_2 chromophore plane; ≡ plane of a peptide ring; ■ side chain, ● axes of rotation in the chromophore-peptide bridges).

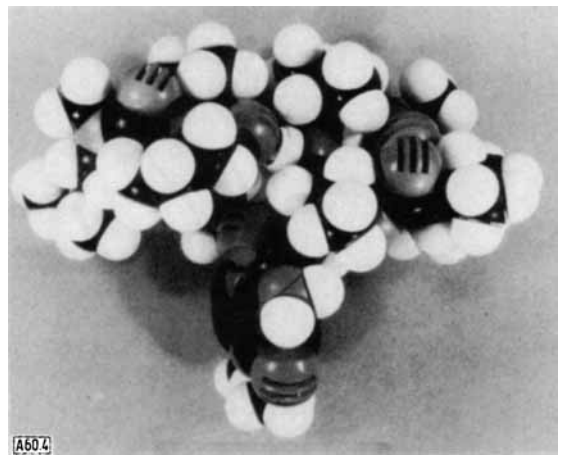


Fig. 4. CPK model of an actinomycin D molecule in the three-dimensional structure derived by X-ray analysis of the actinomycin-deoxyguanosine complex [14—16]. The chromophore, with the amino group in the front, projects downward; the (α)-peptide ring is on the left, the (β)-ring on the right; in the plane of the chromophore is one of the interannular CO---HN_{Val} hydrogen bonds that stabilize the structure.

According to molecular models, complete rotation or a quasicoplanar arrangement of the peptide rings is improbable for steric reasons. Rather, four rotation-isomeric fundamental structures (Figs. 5a—5d) come into consideration[22]. A change of conformation, such as a kink in the peptide planes (Fig. 5e), does not disturb this classification.

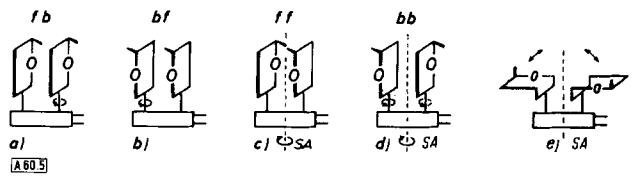


Fig. 5. Rotation-isomeric fundamental structures of an actinomycin molecule (SA = pseudo-C_2 symmetry axis). a) fb- (face-to-back), b) bf-, c) ff-, d) bb-structure, e) ff-structure with buckled peptide planes ("conformational change").

The primary aims of the investigations were therefore: a) determination of the, even in the *iso*-actinomycins *(1)*, not necessarily identical fundamental conformations of the (α)- and (β)-peptide lactone groups and b) elucidation of the spatial relation of the two peptide groups to the chromophore. In addition, it was interesting to consider the possible interactions between the (α)- and the (β)-peptide rings fixed in such close proximity to the chromophore [(α,β)-interannular interactions]. Since three-dimensional structures and their stability should be investigated particularly *in solution*, and earlier X-ray structure analyses[23] of this point had proceeded rather unsatisfactorily, NMR spectroscopy offered much the most promising method of investigation.

3. Conformations of the Free Pentapeptide Lactone Groups

For conformational studies of the peptide lactone groups the complicated actinomycin molecule *(1)* was replaced by synthetic derivatives of the simple pentapeptide lactone[19] (Fig. 6), which are practically "halved" actinomycins, since these can be more easily analyzed by NMR spectroscopy. The compounds *(2)*, called below *free* peptide lactones (*i.e.* not fixed pairwise to the actinocin residue), retain the amino-acid sequence of actinomycin D *(1)*—though others were also studied; the acyl groups are precursors of the chromophore.

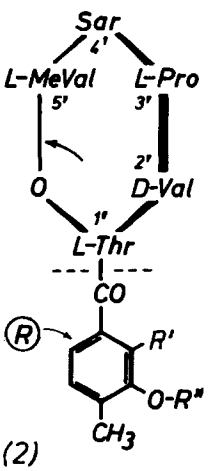


Fig. 6. "Free" pentapeptide lactones: *(2a)*, R′ = NO_2, R″ = $CH_2C_6H_5$; *(2b)*, R′ = NO_2, R″ = CH_3; *(2c)*, R′ = NH_2, R″ = H; *(2d)*, R′ = NO_2, R″ = $CH_2C_6H_5$, lactone ring opened (arrow); *(2e)*, R′ = NO_2, R″ = CH_3, lactone ring opened (arrow) (see also Fig. 1b).

Consideration of models, ^{1}H-NMR data[24], and the remarkable stereospecificity of the lactone ring closure *(2d)* → *(2a)*, and *(2e)* → *(2b)*[18, 24], lead one to expect that the 16-membered cyclopeptide ring would have *one* highly favored skeletal conformation. However, detailed ^{1}H- and ^{13}C-NMR measurements soon showed that while the free peptide lactone *(2)* did indeed assume one homogeneous conformation in deuteriochloroform[25], this is in no way coincident with that existing in actinomycin D. In the actinomycin, influences from the chromophore and possible interactions between the closely proximate peptide groups must stabilize a further conformational type. Whether the free peptide lactone could also form this type of conformation, or indeed other forms, perhaps in dependence upon the solvent, was next on the list for elucidation, together with the structures of these conformers.

Such investigations required particularly reliable identification of a large number of ^{1}H and ^{13}C-NMR signals (NCH_3,

C^{α}—H, NH, *etc.*). This was mainly achieved by means of synthetic peptides and actinomycins labeled with up to 15 deuterium atoms in selected parts of the molecule, *inter alia* specifically in the (α)- or the (β)-peptide chain[26].

3.1. Dependence of the Conformations on the Solvent

The behavior of the free pentapeptide lactone *(2)*, which was studied in solvents of various polarities ranging from benzene to water, showed interesting peculiarities that appeared neither with actinomycin (Section 4) nor with the linear pentapeptides *(2d)* and *(2e)* or their precursors.

The lactone ring closure *(2d)* → *(2a)* or *(2e)* → *(2b)*, being almost completely stereospecific, occurs only when the peptide chain has the LDL-L configuration sequence typical of actinomycins[18]. This reaction causes significant shifts in the ^1H and ^{13}C resonances. The resulting NMR spectra (cf. Fig. 8, spectrum C, and Fig. 11d) are very characteristic (NCH_3, $3\text{-}H_{Thr}$, $2\text{-}H_{Sar}$) of the cyclic peptide *(2)* and can be used for its reliable identification, for instance in biosynthetic studies, or for the rapid determination of cyclization yields. The spectra also show that in moist chloroform as the most favorable solvent[25] the free pentapeptide lactone *(2)* affords only *one*, very temperature-stable conformation. This we have designated the "C" conformation (cf. Section 3.2).

The "C" conformation also exists in benzene. However, in contrast to chloroform solutions, here an increase in the peptide lactone concentration (0.001 → 0.1 mol/l) causes rapidly progressing dimerization of the cyclopeptide *(2)*. This is shown, *inter alia*, by a doubling of the osmometrically determined molecular weight and a large number of proton signals[27]. From more accurate ^1H-NMR studies[24, 28] it can be concluded that an asymmetric fb- or bf-arrangement is formed (cf. Fig. 5).

When compared with the results for chloroform solutions, the spectra of the free pentapeptide lactone *(2)* in acetone show surprisingly large shifts of many ^1H- and ^{13}C-NMR signals (Fig. 8, C → A, and Fig. 11d → 11c), which greatly exceed normal solvent effects. The characteristic coupling constants which are, *inter alia*, indicators of the size of the bond torsion angles are altered, as are the temperature dependence of the δ(NH) values and the NH → ND exchange rates, which in turn permits conclusions about the nature of the hydrogen bonds. The findings can be explained only by far-reaching conformational changes in the peptide skeleton[28, 29]. In acetone, too, only *one* temperature-stable structure is formed, the "A" conformation. This "A" type is also formed in dimethyl sulfoxide, tetrahydrofuran, methanol, and similar solvents.

Acetone/chloroform mixtures contain the "A" and the "C" conformers side by side. Their relative amounts depend on the composition of the solvent and can be obtained directly from the ^1H-NMR spectrum which results from superposition of the spectra for the two individual conformers (Fig. 8, A + C). The two structures also occur in acetone or methanol containing from 5 up to >95% of water, but then always in about the same proportions. No indication of the existence of a third conformer type has been found under the usual experimental conditions.

3.2. The "C" Conformation

According to all the characteristic ^1H-NMR data the "C"-conformer of the free pentapeptide lactone *(2)* is stabilized by a strong intramolecular hydrogen bond with NH_{Val} as the donor[24]. If we first assume the energy-poorer *trans*-form for all the amide bonds in the peptide ring (b, e, h, k in Fig. 7), then Dreiding and the space-filling CPK molecular models show that the steric relationships are ideal for a stretched NH_{Val}---OC_{Sar} bond. All other H-bond acceptors are almost certainly excluded for steric reasons, even if individual amide groups are *cis*-oriented (Section 3.3). In view of this transannular H-bond (Fig. 7), the support to the structure given by the proline ring and consideration of the van der Waals atomic radii alone almost prove the skeletal conformation of the very compact (Fig. 4) peptide lactone ring.

Two limited variations are, however, still permitted for the lower part m to p of the ring. The sterically most favored structure, shown in Fig. 7, is in accord with all the ^1H- and ^{13}C-NMR data obtained so far. These concern *inter alia* the ring bonds c with the HN—$C^{\alpha}H_{Val}$ torsion angle $\phi_2^* \approx 150°$[30, 31], p (HC^{α}—$C^{\beta}H_{Thr} \approx 90°$), and h, i ($CO_{Pro}$ and H^{α}_{Sar} "peri"-situated) and also the torsion angle ϕ_1^* (≈180°) and the C^{α}—C^{β} bonds of the valine and methylvaline groups.

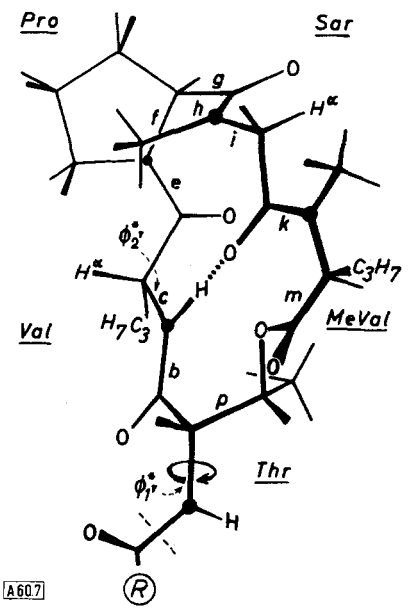


Fig. 7. The "C"-conformation of the free pentapeptide lactone *(2)*. Ⓡ: cf. Fig. 6. Definition of φ*: see Fig. 13; ● N atoms.

It is admitted that the assumption of an *all-trans*-amide allocation may be subject to doubt, since there are only rather small *trans/cis*-energy differences for peptide bonds leading to *N*-alkylamino acids such as proline, sarcosine, and methylvaline (e, h, k in Fig. 7), but this provides the most likely interpretation not only of the very stable intramolecular H-bond but also of all other findings, in particular those arising from the conformational change of the pentapeptide lactone from the "C" into the "A"-type and *vice versa* (Section 3.3). Conformation energy calculations by *De Santis et al.*[32] confirm the possibility of the formation of the proposed NH_{Val}---OC_{Sar} bridge but at the same time favor the *cis*-form for the Val → Pro and the Pro → Sar bonds, and this is not compatible with the NMR and model data[33].

3.3. The "A" Conformation

As mentioned above, the solvent change from chloroform to acetone causes a change in the skeletal conformation of

the free pentapeptide lactone *(2)* and hence marked changes in the ^{1}H- and ^{13}C-NMR spectra. In the ^{1}H-NMR spectra (Fig. 8, C→A) it becomes clear, *e.g.* from the entire behavior of the NH_{Val}-proton, that the transannular H-bond of the "C"-conformer is cleaved in acetone and—since the NH then lies exposed in space—becomes intermolecularly built-in into the solvent (Fig. 10)[28]. The 2-H signals of sarcosine, methylvaline, and proline, assigned unambiguously by directed deuterium labeling, are shifted to partly quite unusual values, and the NCH_3 signals of methylvaline and sarcosine change places. The 2-H triplet of proline becomes a pseudodoublet in acetone, and this is typical of a change of the Val→Pro amide bond from *trans* to *cis*[34,35]. The Pro→Sar bond apparently also changes to the *cis* form, as is indicated, in analogy with model compounds[26,38], by the smaller geminal 2-H_2 coupling constant of sarcosine (18→14 Hz)[39].

fixed (α)- and (β)-peptide lactone rings of the dissolved actinomycin molecule (Section 4).

Meanwhile, the conformation of the peptide lactone ring in a crystalline actinomycin-D/deoxyguanosine complex had become known through X-ray structure analyses[14-16] (cf. Section 7 and Fig. 20). Since here too the Val→Pro→Sar sequences proved to be *cis,cis*-bonded, the next step was clearly to extend the peptide lactone structure existing in the crystal tentatively to the "A"-conformer of the dissolved cyclopeptide *(2)*.

The structure in Fig. 9 departs considerably from that of the "C"-conformer (Fig. 7). Thus, as a result of the *cis*-amide bond between valine and proline the CO and the NH group of the valine are twisted out of the peptide ring and are now able to form H-bonds to the solvent, thus stabilizing the structure, in agreement with the NH_{Val} NMR data. The

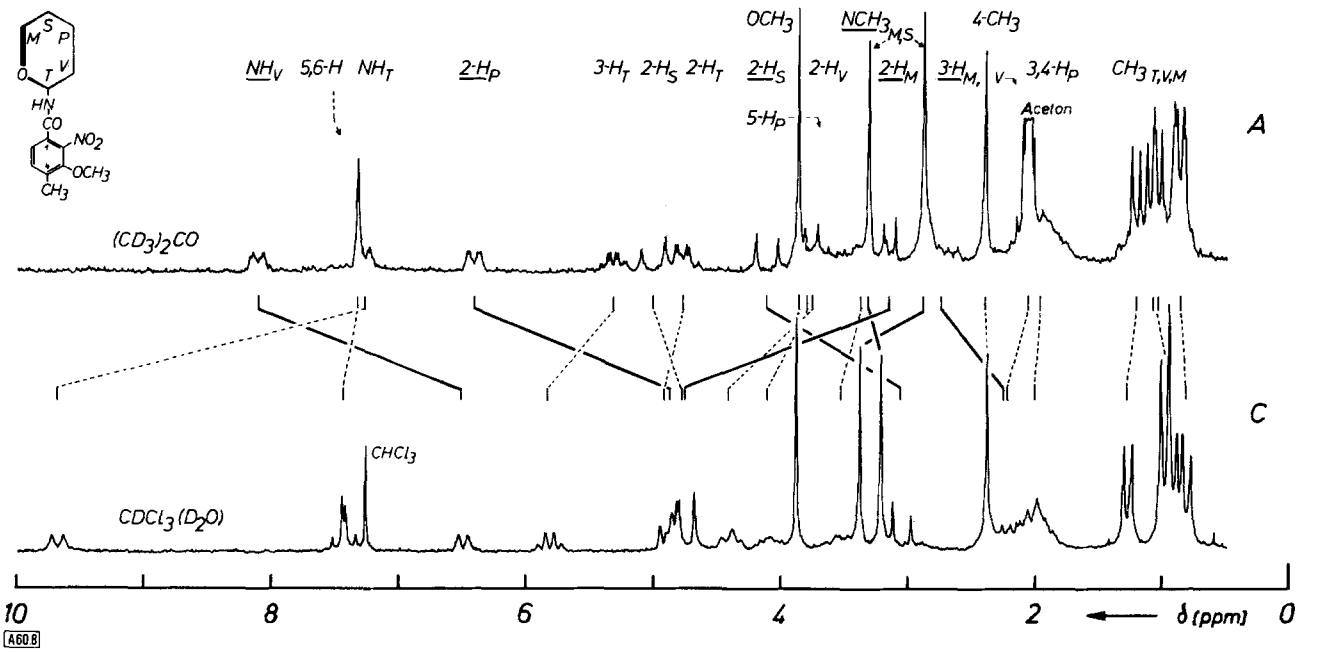


Fig. 8. Comparison of the 100 MHz ^{1}H-NMR spectra of the free pentapeptide lactone *(2d)* in [D_6]-acetone ("A"-conformation) and [D]-chloroform ("C"-conformation). T, V, P, S, M = threonine, valine, proline, sarcosine, *N*-methylvaline (for precise assignment cf. [26]). Internal standard: tetramethylsilane. Instrument: Varian HA-100.

The ^{13}C-NMR data for the pentapeptide lactone (cf. Fig. 11d→11c) support these findings. Thus, it follows also from the position of the ^{13}C-NMR signals of proline (C^{β}_{P}, C^{γ}_{P}), in accord with model investigations[35-37], that the Val→Pro amide bond of *(2)* is *trans* in chloroform but *cis* in acetone. The NCH_3 signals of sarcosine and methylvaline are also shifted beyond their cross-over point, and the signal of C^{2}_{MeVal} (C^{γ}_{M}) reaches the unusual value of δ = 72 (cf. Fig. 11c).

The NMR spectrometric findings as a whole do not yet permit any detailed structural proposal for the "A"-conformer of the pentapeptide lactone *(2)*, which is much more labile in consequence of the loss of the transannular H-bridge, but among other things they show that: 1) The "A"-form apparently contains a *cis,cis*-bonded Val→Pro→Sar sequence, which is a strong argument for an all-*trans*-amide structure of the "C"-conformer (Fig. 7); 2) the characteristic ^{1}H- and ^{13}C-NMR data for the "A"-conformer of *(2)* agree surprisingly well with those of the peptide lactone units in actinomycin D *(1)* (cf. Fig. 11c→11b), which means that the "A"-conformation of the *free* pentapeptide lactone *(2)* exists also in the

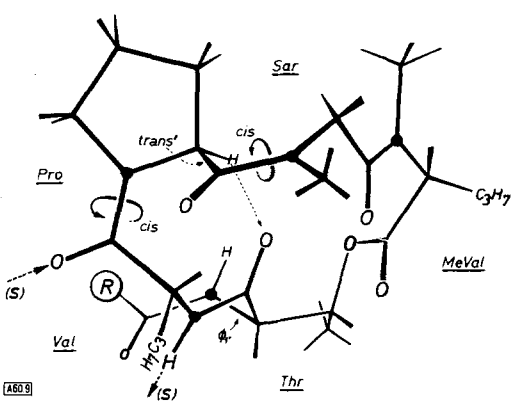


Fig. 9. The "A"-conformation of the free pentapeptide lactone *(2)*, drawn according to the structure of the actinomycin-D-deoxyguanosine complex determined by X-ray analysis[14-16]. For Ⓡ cf. Fig. 6; Ⓢ = solvent; ● = N atoms.

trans'-proline-carbonyl and the *cis*-Pro→Sar bond cause further change in the geometry of the peptide ring, so that, for example, the 2-H of proline comes directly next to the

carbonyl oxygen of threonine, and this may explain the unusual position of its ^{1}H-NMR signal ($\delta = 6.4$). It is also interesting that the C^{α}-N_{Thr} bond (ϕ_1) and thus also the plane of the chromophore R now lie not *in* the plane of the peptide ring as in the "C"-conformer but almost perpendicular to it (cf. Fig. 10). All in all, the NMR findings found so far for *(2)* in acetone (bond angles, *etc.*) are consistent with this structure, so that Fig. 9 seems to represent very well the skeletal conformation "A" of the free pentapeptide lactone *(2)*.

4. The Conformation of the Peptide Lactone Groups in Actinomycin

As was indicated above, the question of what happens to the "A"- and "C"-conformers of the free pentapeptide lactone on the latter's inclusion in an actinomycin molecule could clearly be answered. Actinomycin D *(1)* is formed by oxidative condensation of two molecules of the peptide lactone derivative *(2c)* in methanol/water. In this solvent *(2c)* exists to approximately equal proportions in the "A"- and the "C"-form (Fig. 10). Only the "A"-conformer is taken over into the actinomycin, as follows unambiguously from comparison of the ^{1}H-NMR data[28, 29, 40] and is demonstrated particularly convincingly by the ^{13}C-NMR spectra[41]

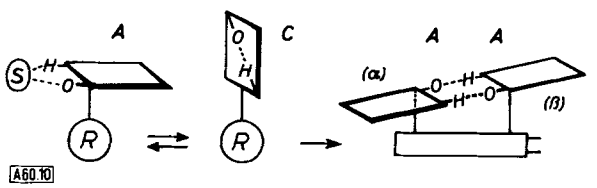


Fig. 10. Transformation of the free pentapeptide lactone *(2c)* into an actinomycin molecule *(1)* with stabilization of the "A" conformation of the peptide skeleton. Ⓢ = solvent.

The shifts shown in Figs. 11d and 11c (chloroform→acetone) for the ^{13}C-NMR signals of the free pentapeptide lactone *(2a)* correspond to those of the ^{1}H-NMR signals from *(2b)* (Fig. 8) and illustrate the conformational change of the free cyclopeptide *(2)* from the "C"- into the "A"-type. However, the positions of the ^{13}C-NMR signals are substantially identical for the "A"-conformer and for actinomycin D (Fig. 11c→Fig. 11b); thus, the peptide lactone groups have the skeletal conformation "A" also in the actinomycin molecule, but now, as shown in Fig. 11a, this conformation cannot be reconverted into the "C"-type by the reverse solvent change acetone→chloroform, as it can for the *free* peptide lactone.

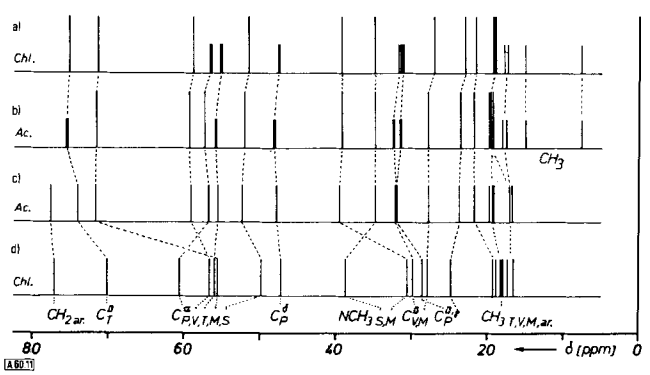


Fig. 11. ^{13}C-NMR spectrum of the peptide lactone units of actinomycin D a) in $CDCl_3/D_2O$, b) in [D_6]-acetone; c) ^{13}C-NMR spectrum of the free pentapeptide lactone *(2a)* in [D_6]-acetone, d) in $CDCl_3/D_2O$. T, V, P, S, M = threonine, valine, proline, sarcosine, *N*-methylvaline. Compare the complete spectrum of *(1)* in Fig. 17.

According to numerous further ^{1}H-NMR studies[9, 10, 42, 43] the "A"-conformation of the actinomycin peptide ring, locked as it were into the molecule as a whole, remains unchanged in benzene, pyridine, dimethylformamide, and up to methanol and water, and also when the temperature and concentration are changed. The cause of this very surprising structural stability must be sought not only in the "clamping" and orientation by the chromophore but also in the mutual buttressing of the two (α)- and (β)-peptide lactone rings deriving from two strong interannular H-bonds (Fig. 10) between them. According to the ^{1}H-NMR data[9, 40, 42, 43], the donor in *both* rings is again the NH_{Val} group. The solvent can no longer act as an acceptor, as with the free "A"-conformers, but instead the acceptor will be the neighboring peptide ring which is already fixed in a favorable position by the common actinomycin chromophore (Fig. 10, cf. Section 5)[44].

The ^{13}C-NMR spectra of actinomycin D illustrated in Figs. 11a, 11b, and 17 show further that there is almost complete superposition of the signals from carbons situated in the same positions in the (α)- and the (β)-peptide chain (*homologous* C atoms). Minimal deviations (short double lines in Fig. 11) result from the dissymmetry of the chromophore. Analogous remarks apply to the NMR signals of the protons[9, 26, 28] independently of the solvent and temperature. This indicates that the two peptide lactone groups of a dissolved *iso*-actinomycin such as D behave almost identically, not only in the skeletal-conformational type ("A") but also in the overall three-dimensional structure and that, as explained in Section 5, these groups must have an axially symmetrical mutual arrangement (Fig. 10).

5. The Three-dimensional Arrangement of the Peptide Lactone Groups in Actinomycin D

As explained in Section 2, the position of the two actinomycin peptide rings in relation to the chromophore is defined by the three bonds in the chromophore-peptide bridges (Fig. 1) and their torsion angles (Fig. 3). There the amide linkages should be fixed in the *trans*-form by the steric conditions.

The orientation of the C^9—CO and C^1—CO bonds in the chromophore (φ_A, φ_B in Figs. 12 and 13) can only rarely be determined by NMR spectrometry. In model compounds with only *one* amino acid or peptide residue, as in *(3a)* and *(4a)* or *(3b)* and *(4b)*[45], both carbonyl oxygens are very probably in the plane of the chromophore (φ_A, $\varphi_B \approx 0°$, 180° or 180°, 0° respectively); this follows from ^{1}H-NMR

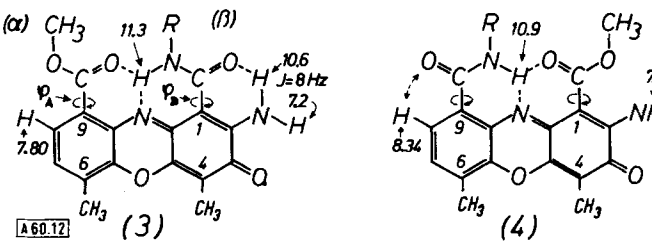


Fig. 12. Illustration of the arrangement of the carbonyl groups of the chromophore (torsion angles φ_A, φ_B).—*(3a)*, *(4a)*: R—NH = Thr(OCH_3); *(3b)*, *(4b)*: R—NH = pentapeptide lactone [45]; *(3c)*, *(4c)*: as (a), but 2-OH in place of 2-NH_2. *(3d)*: as *(a)*, but in (α) Thr(OCH_3) in place of OCH_3. The ^{1}H-NMR values (δ) inserted are for *(3a)* and *(4a)* (in $CDCl_3$).

data (Fig. 12), where *(3a)* shows a rare geminal H—N—H coupling[46].

A hydroxy instead of the 2-amino group [*(3c), (4c)*][45] favors the coplanar arrangement fixed by H-bonds for the carbonyl groups of the chromophore [δ(2-OH) = 15.95 or 14.6]. However, this is usually prevented if a *second* bulky amino acid or peptide group replaces the (α)- or the (β)-methoxy group [*(3d), (1)*]. In actinomycins such as D the carbonyl groups are therefore always twisted out of the plane of the chromophore[47]. They must be arranged transoidally, as in Fig. 13 (cf. below).

Information about the N—C^{α} bonds in the two threonine groups (torsion angles $\phi_{1'\alpha}$, $\phi_{1'\beta}$) is given by the HN—C^{α}H coupling constants, which in turn depend on the HN—C^{α}H angles $\phi^{*}_{1'\alpha}$, $\phi^{*}_{1'\beta}$ (Fig. 13)[30]. For the free peptide lactone *(2)* ϕ^{*} is found to be about 180°, with a sterically favorable *anti*-orientation of the hydrogen atoms. In actinomycin D $\phi^{*}_{1'\alpha}$ and $\phi^{*}_{1'\beta}$ amount, as drawn in Fig. 13, to about 150° ($J_{CH,HN}$ = 7.0 Hz; $CDCl_3$) and are thus of the *same* magnitude[40]. Here again according to the model the antiperiplanar arrangement of the protons is very strongly favored. ^{1}H-NMR studies in other solvents[9, 42] lead to similar results. If structural variation is introduced into both peptide groups of actinomycin D or into the chromophore (Fig. 16), then $\phi^{*}_{1'\alpha}$ and $\phi^{*}_{1'\beta}$ change within the range of 120—180° ($J_{CH,NH}$ = 2 to 9 Hz) but always remain equal to one another.

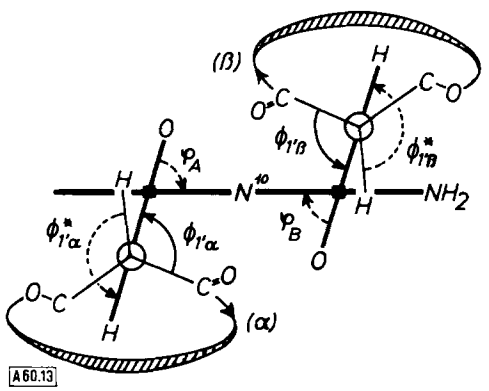


Fig. 13. Arrangement of the peptide lactone groups in the actinomycin molecule and torsion angles of the bonds in both chromophore-peptide bridges (molecule seen from the peptide side; Fig. 1 from above). —N—NH_2 chromophore plane; ■ carbonylcarbon atoms C-1 and C-9; (difference between ϕ and ϕ^{*} = 60°). The sketch shows the natural, transoid, C_2-axial-symmetric arrangement of the peptide groups.

Quite apart from any steric hindrance, the torsion angle pairs φ_A, φ_B and $\phi_{1'\alpha}$, $\phi_{1'\beta}$ cannot assume just any values; rather, the bonds in the chromophore-peptide bridges must always be so arranged that the steric position of the (α)- and (β)-peptide rings permits the formation of two important characteristics of the actinomycin structure (Section 4): a) the axial-symmetric arrangement of the peptide lactone groups and b) their conformational stabilization by the reciprocal H-bridges that determine the distance between the peptide rings (Figs. 10 and 14).

The general finding that also the ^{1}H-NMR signals of homologous nuclei in the (α)- and the (β)-peptide rings are almost superposable, even when these are exposed (side-chain protons), shows that each of the two peptide rings is magnetically shielded in the same way by both the adjacent peptide and (within limits) by the chromophore. This means that homologous groups of atoms "see" their respective neighbor peptide with the same aspect (cf. Fig. 20). This already shows the C_2-axial-symmetric arrangement of the peptide rings, which necessarily includes the chromophore (Figs. 13 and 14). Because of the dissymmetric actinocin chromophore the whole actinomycin molecule has pseudo-C_2-symmetry, with the symmetry axis passing through N^{10} and O^5 (Fig. 1) or, in Figs. 13 and 14, perpendicular to the plane of the paper through N^{10} (see also Figs. 5c and 5d). This arrangement of the peptides, and the finding that the torsion angles $\phi_{1'\alpha}$, $\phi_{1'\beta}$ are found to be always equal for *iso*-actinomycins (see above), have as a consequence that φ_A and φ_B are also approximately equal (Fig. 13).

The two (α,β)-interannular structurally identical hydrogen bonds originating from the NH_{Val} groups (Figs. 10 and 14) require also that the peptide rings be arranged with their "faces" turned toward each other (cf. the ff-form in Fig. 5c). On the basis of the peptide conformation "A" illustrated in Fig. 9, one must regard the acceptors in the H-bonds as being, also in solution, the "opposing" valine-carbonyl groups of the neighboring peptides (conformational-energy calculations and IR findings[32], consideration of models). Numerous ^{1}H-NMR studies[9, 27, 41, 42], as well as ORD data[49] and investigations of actinomycin D variants[28], all show that the two H-bonds are not only of the same type but also surprisingly stable in the usual solvents including water.

All the characteristic structural features of the actinomycin molecule discussed above—the fixed dimensions of the chromophore, the excentrically mobile chromophore-peptide bridges, the conformationally determinable, axial-symmetrically disposable peptide rings, the two H-bonds that determine their separation, *etc.*—together provide unequivocal evidence for the three-dimensional structural type of the actinomycins (Figs. 14 and 20). A key part is played here by the two hydrogen bonds, since by their locked-in position in the final molecule they practically bolt together the skeletal conformation and the position of the peptide lactone rings and thus the entire three-dimensional structure (cf. Section 6).

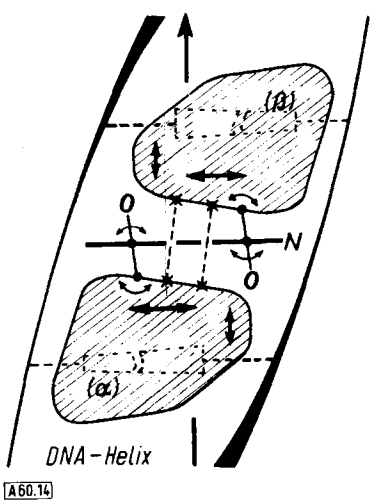


Fig. 14. Sectional drawing of an actinomycin molecule inserted in the DNA helix, seen from the peptide side (cf. Fig. 4). ×---× (α,β)-interannular hydrogen bonds. ● points of rotation.

The sectional sketch (Fig. 14) of such an actinomycin D molecule shows that the structure, although fixed in principle, yet remains flexible. For example, limited changes in the position of the H-bond partners (×) resulting from conformational deviations of the peptide lactones in actinomycins with different amino acids (Fig. 6) can easily be compensated by mutual shifts of the (α)- and (β)-peptide rings (straight double-headed

arrows). As is indeed observed for some actinomycins, where $\phi^{*}_{1'\alpha} \approx \phi^{*}_{1'\beta}$ varies between 120 and 180°, this implies twisting of the bonds in the chromophore-peptide bridges (Fig. 14, curved double-headed arrows), in such a way that the position of the peptides again becomes optimal for the formation of (α,β)-interannular H-bonds. The three-dimensional structural type is then retained.

When arranged as in Fig. 14 with a twist from left to right toward the top, in the sense of a *P*-helix, the peptide lactone groups fit fairly well into the small groove in the DNA double strand which also twists to the right (Fig. 2). An alteration of the spatial arrangement of the peptide rings should thus also influence the stability of the reversible actinomycin-DNA complexes[7], providing a reasonable explanation for the considerable differences sometimes observed between the physiological activities of actinomycin D variants[6, 7]. Large changes in the positions of the peptide rings must completely prevent intercalation of the actinomycin into the DNA helix (Fig. 2); and indeed *enantio*-actinomycin D, which is the mirror image of *(1)*[50], as well as the (*na, enantio*)-actinomycin D *(6a)* and its (α,β)-isomer both containing only *one* enantiomeric peptide ring (cf. Fig. 15)[29, 51], are inactive[52]. If these views are correct, the DNA complex can be formed only by an actinomycin with the transoid structure shown in Fig. 13, which, moreover, is the only one that allows formation of the (α,β)-interannular hydrogen bonds.

6. Stability of the Three-Dimensional Structure

According to Fig. 14 the pseudo-C_2-symmetrical three-dimensional structure described above for the actinomycin D molecule should be only slightly sensitive to minor changes in the primary structure of the peptide lactone groups. The extent to which such "structural faults" can still be tolerated and the sensitivity with which NMR spectra respond to changes in the three-dimensional structure have been illustrated by studies of some further actinocin-bispeptides and actinomycins.

From numerous concordant ^{1}H-NMR studies it could be concluded that the three-dimensional structure of actinomycin D remains intact in spite of changes in the solvent (benzene[42], chloroform, acetone[9, 24], up to methanol, dimethylformamide, and water[9, 10] or salt solutions[10]), in temperature, concentration[29, 42], or the pD value[10]. Only under extreme conditions, *e.g.* on dissolution in hexafluoroacetone sesquihydrate, were the (α,β)-interannular H-bonds apparently broken. According to CD measurements[49], this is presumably followed by rotation of the carbonyl groups of the chromophore (torsion angles φ_A, φ_B) together with rotation of the peptide rings through 180°; these changes provide a second transoid structural form (Fig. 13, with the (α)-peptide ring toward the top and the (β)-ring toward the bottom) and also stabilization of that form by new peptide-solvent H-bonds; according to the NMR spectra the typical three-dimensional structure is then lost.

Modification of the *fundamental* structure of actinomycin D is very detrimental to mutual stabilization of the conformations of the peptide chains. Opening of even one lactone bond [*(5a), (5b)* and their methyl esters[45]; Fig. 15] causes the two peptide groups to assume different conformations that are again strongly solvent-dependent[53]. This can be recognized by the appearance of about 15 instead of four NCH_3 ^{1}H-NMR signals ($CDCl_3$) and bands specific for the "C"-conformer of the free pentapeptide lactone *(2)* (Fig. 8)[54]. Apparently, however, the cyclic peptide unit in *(5a)* or *(5b)* nevertheless prearranges the neighboring linear peptide to some extent in a suitable conformation, since the yield on relactonization to actinomycin D is remarkably high at 55 or 67%, respectively [25—30% is found for the free pentapeptide *(2d)* → *(2a)* and actinomycin D acid *(5c)* → *(1)*[19]]. If, however, the peptide lactone ring in *(5a)* or *(5b)* is replaced by its enantiomer *(6c)*, then the neighboring linear peptide with the natural configuration cyclizes only to the extent of 5%; the resulting crystalline (*na,enantio*)-actinomycins *(6a)* and *(6b)*[29, 51] exist, like the actinomycin acid monolactones *(5a)* and *(5b)*, in heterogeneous again very solvent-dependent structures. For steric reasons the (α)- and (β)-peptide rings that are now mirror images of one another can no longer form the H-bonds necessary for stabilizing the structure. It remains to be discovered whether rotational isomers in the sense of Figs. 5a—5d are formed in this case.

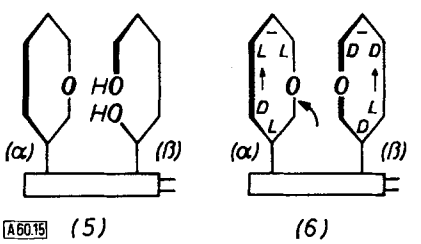


Fig. 15. Actinocin-bispeptides with conformationally heterogeneous peptide chains. *(5a)* actinomycin-D acid (α)-lactone; *(5b)* (α)- and (β)-peptide groups of *(5a)* interchanged; *(5c)* (α)-peptide ring of *(5a)* also opened (actinomycin-D acid). *(6a)* (α-*na*, β-*enantio*)-actinomycin D; *(6b)* (α)- and (β)-peptide rings of *(6a)* interchanged; *(6c)* peptide ring with the natural configuration in *(6a)* or *(6b)* opened at the lactone bond.

Expansion of the peptide rings (insertion of glycine as a sixth amino acid[2, 18]) also prevents the formation of the characteristic three-dimensional structure, as does inclusion of configurationally "false" or structurally very different amino acids. An example of this is tetra-*N*-demethyl-actinomycin D *(7f)* (Fig. 16)[55], which contains four additional NH groups that can compete with NH_{Val} in the formation of H-bonds and whose peptide lactone rings are considerably more mobile as a result of the absence of the *N*-methyl groups. Alteration of the natural configurational sequence LDL-L (Fig. 1) generally suffices to prevent the ring closure reaction, since this is to

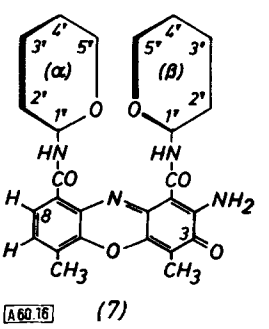


Fig. 16. Selected structural variants of actinomycin D *(1)* (Fig. 1). *(7a)* L-serine in place of L-threonine in 1_α and 1_β; *(7b)* D-*allo*-isoleucine in place of D-valine in 2_α (actinomycin i-C_2); *(7c)* D-*allo*-isoleucine in place of D-valine in 2_β (actinomycin C_2); *(7d)* D-*allo*-isoleucine in place of D-valine in $2'_\alpha$ and 2_β (actinomycin C_3); *(7e)* L-4-oxoproline in place of L-proline in 3_β (actinomycin X_2); *(7f)* glycine in place of sarcosine in $4'_\alpha$ and 4_β, also L-valine in place of *N*-methyl-L-valine in $5'_\alpha$ and 5_β; *(7g)* 2-Cl in place of 2-NH_2 (2-deamino-2-chloro-actinomycin D); *(7h)* 4,6- and 1,9-substituents interchanged (pseudo-actinomycin D).

a large extent stereospecific[18]. All the compounds of types *(5)* and *(6)* have in common that, according to their NMR spectra, they do not assume the three-dimensional structure typical of actinomycin D and are accordingly completely inactive bacteriostatically.

If the alterations to the primary structure are restricted to the *amino-acid side chains* of the actinomycin D molecule, a considerable range of variations is still possible for the peptide lactone units without preventing them from forming the skeletal conformation "A" and stabilizing it by (α,β)-interannular H-bonds corresponding to Fig. 14. This is shown by the large number of active natural and synthetic peptide analogs of actinomycin D[2-4, 6, 18] (Fig. 16). There the changes mainly concern the amino acids 2' (valine→*allo*-isoleucine, leucine, alanine), 3' (proline→sarcosine, 4-oxoproline, 4-hydroxyproline *etc.*), and 5' (methylvaline→methylalanine, methylisoleucine), but also 1' (threonine→serine, α,β-diaminobutyric acid[56]). Introduction of amino acids with less bulky side chains or replacement of the lactone by lactam bonds[56] leads to reduced and sometimes greatly diminished physiological activity, clearly because of a somewhat more mobile peptide skeleton and smaller changes in the positions of the peptide rings corresponding to Fig. 14. In all cases, however, it follows unambiguously from numerous ^{1}H- and ^{13}C-NMR measurements[26, 28, 57] that the characteristic three-dimensional structural type is retained. This is also true for the *aniso*-actinomycins *(7e)* with more strongly differing (α)- and (β)-peptide groups and for variants with altered chromophores such as *(7g)* and *(7h)*[58, 59].

The *^{1}H-NMR spectra* respond particularly sensitively to changes in the three-dimensional structure or the surroundings (solvent, neighboring peptide, *etc.*) of an actinomycin molecule or peptide ring. In this way it is possible, by means of typical signal shifts, to differentiate with certainty between (α,β)-position-isomeric *aniso*-actinomycins such as i-C_2 *(7b)* and C_2 *(7c)* whose structures differ only minimally[26, 28]. This cannot be done by chromatography or by other physical methods.

In *iso*-actinomycins that are sterically looser [*(7a)*] or have modified chromophores [*(7g)*, *(7h)*] one can discern improved symmetry in the peptide arrangement compared with *(1)* and also apparently greater stability of the (α,β)-interannular H-bridges (δNH_{Val}: +0.5—0.8 ppm). Since the signals of important actinomycins such as D were assigned separately to the (α)- and the (β)-peptide ring[28], each peptide ring can be examined individually for changes in structure or surroundings. In principle it can be decided in this way whether interactions of an actinomycin with a complex-partner occur on the (α)- or the (β)-side (the environment of the peptides are then different) or whether, as in the case of the oligonucleotides (cf. Fig. 18) they occur axial-symmetrically.

The signals of the generally more strongly shielded *carbon atoms* preferentially permit conclusions about the skeletal conformations (Fig. 11) and the molecular symmetry. If these change one can usually, as for the free peptide lactone *(2a)* (Figs. 11c and 11d), check the behavior of each separate carbon atom—unequivocal identification of the signals is naturally a prerequisite for this purpose[61]. Also, in the ^{13}C-NMR spectrum of actinomycin D (Fig. 17; cf. Figs. 11a and 11b) all 62 carbon signals can be recognized, insofar as they are not exactly superposed on grounds of symmetry for homologous nuclei in the (α)- and (β)-peptide rings (*e.g.* at δ = 34 for the N-methyl C-atoms of the two sarcosine residues). For *aniso*-actinomycins such as *(7e)* the changes in symmetry occurring are distinctly recorded, although the type of the spectrum (Fig. 17) remains unchanged.

NMR spectroscopic investigations of more than twenty actinomycin D variants and numerous other actinocin-peptides agree in showing that a) all the important actinomycins, including those with differing peptide rings, such as *(7e)*, form the same characteristic pseudo-C_2-symmetrical three-dimensional structural type (Fig. 14) and b) formation of this structure requires two intact pentapeptide lactone groups that are not too flexible, are altered only within certain limits, and contain the natural configurational sequence LDL-L[62]. Alterations to the chromophore system, as in *(7g)* and *(7h)*, do not normally destroy the peptide structure, although they decisively influence the bonding of the whole molecule to DNA[7].

7. NMR and X-Ray Structure Analyses of Complexed Actinomycin D

A point of particular interest for the mode of action of actinomycins is the three-dimensional structure that they assume in the actinomycin-DNA complex. Since NMR-investi-

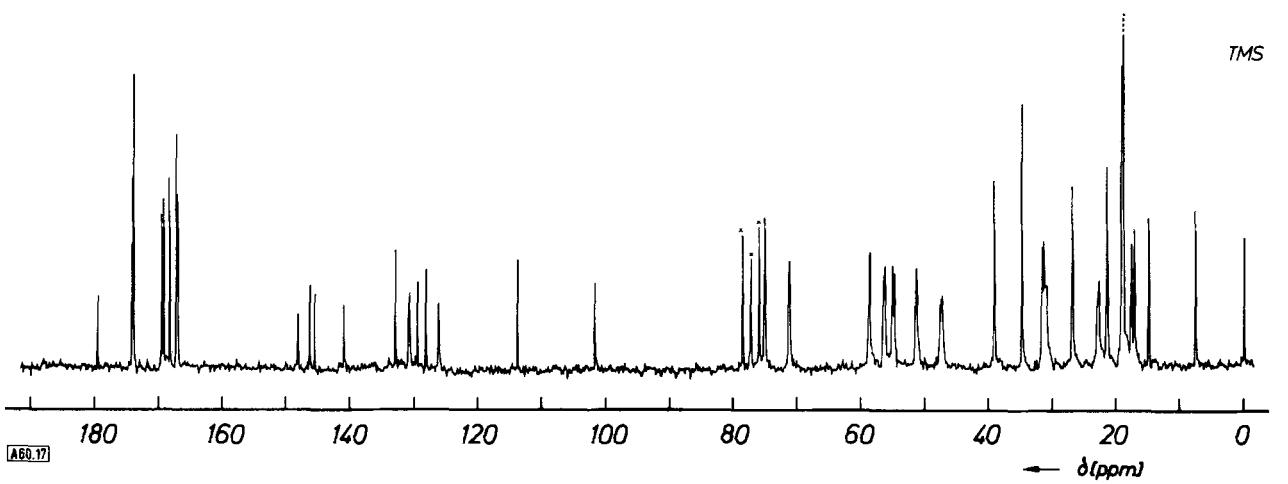


Fig. 17. ^{13}C-FT-NMR spectrum of actinomycin D *(1)* in deuteriochloroform. For the assignment of the peptide-carbon signals (0—80 ppm) see Fig. 11a; the signals of the twelve ring-carbon atoms of the phenoxazinone system occur at 100—150 and 180 ppm, and those of the twelve amide- and lactone-carbonyl groups around 170 ppm. x = solvent peaks. Internal standard: tetramethylsilane. Instrument: Varian XL-100-15 [60].

gations of the DNA complex are too difficult [minimal actinomycin concentrations per base pair (Section 2), interference by NMR signals from the DNA, *etc.*], small nucleotides with the complex-forming bases guanine and cytosine—*i.e.* DNA fragments—were used for these studies.

Preliminary ^{1}H-NMR measurements at 220 MHz[9] showed that even 2'-deoxyguanosine-5'-monophosphate and actinomycin D in water (D_2O) form a 2:1 complex. Characteristic shifts in the chromophore and NH_{Thr} signals, together with almost unchanged positions of the signals from the peptide groups, led to the assumptions that a) one complex-partner is attached at each of the two sides of the actinocin group plane-parallel with its base, b) like the actinomycin molecule, the complex is pseudo-C_2-symmetric (Fig. 18a), and c) the conformation and the arrangement of the peptide rings are barely disturbed.

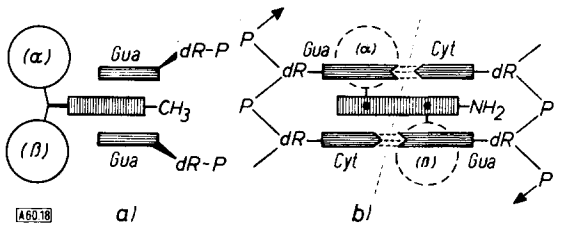


Fig. 18. Formation of pseudo-C_2-symmetric (1:2)-actinomycin-nucleotide complexes a) with 2'-deoxyguanosine-5'-phosphate [9], b) with two guanine-(Gua)-cytosine(Cyt) base pairs of di- or hexanucleotides (after [12, 13]). The actinomycin chromophore in a) is seen from C-7, C-8 and in b) from the 4- and 6-methyl groups; (α), (β) = peptide rings; dR = 2-deoxyribose residue; P = phosphate group.

More detailed high-field ^{1}H- and ^{31}P-NMR studies of the bonding of actinomycin D to various deoxynucleotides[11, 12] have confirmed and extended these views. Thus, it was found that here too pseudo-C_2-symmetric 1:2 complexes are formed (Fig. 18b) and that guanine-cytosine base pairs are strongly favored complex-partners, as had already been known for DNA. The influences of the chromophore ring current and of the magnetic anisotropic groups on the NMR signals of specific nucleotide nuclei ("complexing shifts") provided evidence for the more precise arrangement of the nucleotides. The deoxy*hexa*nucleotide with the self-complementary base sequence ATGCAT[13, 63] already existing in the form of a double helix binds actinomycin D in the sense of Fig. 18b, as expected, between the GC and the CG pairs. By this process the melting point of the double helix—*i.e.* its decomposition into two single strands— is significantly increased as a result of the additional "clamping". The overall stereomodel that results for the actinomycin-oligonucleotide complex in solution (Fig. 18b) corresponds to the structure proposed for the DNA complex as a result of X-ray analysis[14-16] (see below), as shown in Fig. 20.

Actinomycin molecules without any complex-partner associate in cold water, but without any resulting change in conformation or orientation of the peptide lactone groups[9, 10]. The behavior of the ^{1}H-NMR signals of the chromophore indicates the formation of dimers of the kind shown in Fig. 19, their equilibrium constants[10] correlating with those derived from centrifuge measurements[64]. Such dimers do not occur in organic solvents [contrast the dimerization of the free peptide lactone *(2)* in benzene; Section 3.1] and explain the surprisingly high solubility of actinomycins in cold (4 °C) water[65].

Fig. 19. Dimerization of an actinomycin in water (after [10]).

It was soon found[23] that normal actinomycin crystals were too unstable for X-ray structure analysis. It was not until actinomycin or 7-bromoactinomycin D[66] was co-crystallized with 2'-deoxyguanosine in a 1:2 ratio that crystal forms well suited for X-ray analysis were obtained, so that decisive progress in understanding the three-dimensional structure of actinomycin D became possible[14-16]. Like the nucleotide complexes studied by NMR spectroscopy, the 1:2 complexes investigated proved to be pseudo-C_2-symmetric. The two peptide rings arranged *transoid* in the sense of Figs. 13 and 14 contain the *cis,cis*-linked Val→Pro→Sar sequence discussed in Section 3 above. They stabilize their characteristic conformation (Figs. 9 and 20) by means of the hydrogen bonds between (α)-NH_{Val} and (β)-CO_{Val} and between (β)-NH_{Val} and (α)-CO_{Val} as described above. Contributions to stabilization of the whole complex are provided by two further H-bond pairs from actinomycin to the two deoxyguanosine (G) molecules, namely 2-NH_{2G}---OC_{Thr} and NH_{Thr}---N-3_G (Fig. 20), as well as by hydrophobic bonds and H-bonds to attached water molecules. Fig. 20 shows the three-dimensional structure derived by this X-ray analysis for an actinomycin D molecule inserted between two guanine-cytosine base pairs of a DNA double helix.

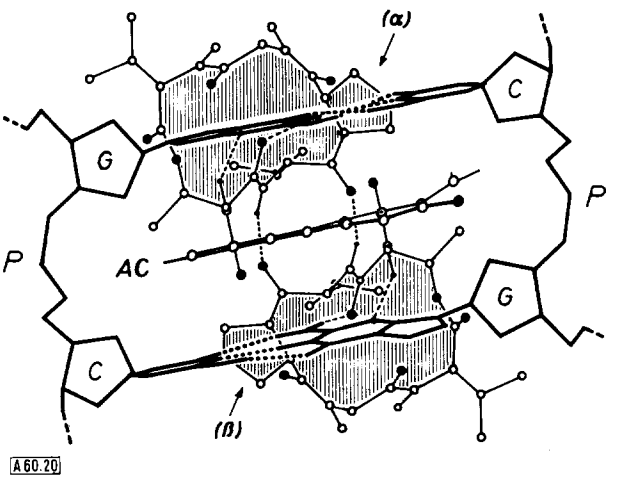


Fig. 20. Three-dimensional arrangement of an actinomycin D molecule between the guanine-cytosine base pairs of a DNA double helix (drawn in accord with the structure proposed by *Sobell* and *Jain* [14—16]). G = deoxyguanosyl; C = deoxycytidyl; P = phosphate groups. AC = actinocin residue (chromophore) (Figs. 1 and 2) seen from the 4- and 6-methyl groups (cf. also Fig. 4 from the bottom) Shaded areas = (α)- and (β)-peptide lactone rings. ● Oxygen atoms of the actinomycin.

8. Concluding Remarks

The three-dimensional structural model of the crystalline (1:2)-actinomycin-D-deoxyguanosine complex, determined by X-ray analysis and forming the basis of Fig. 20, is consistent with all the NMR findings for actinomycin-deoxynucleotide complexes in aqueous solution[9, 11-13]. From the NMR data for the actinomycin partners it can be seen that the type of the three-dimensional structure in *free* actinomycin, which is itself very resistant to changes in its environment, remains

stable also in the complexes. Since furthermore, in agreement with calculations of conformational energy[32], numerous structure-specific NMR data for actinomycin D and the free pentapeptide lactone ("A" type) are in accord with the above model, we can assume that the three-dimensional structure of actinomycin D in solution corresponds very widely to that of the crystalline complex (Fig. 20); it can be extended to the most important natural and synthetic actinomycins[67].

Fig. 4 (Section 2) shows a space-filling model of actinomycin D *(1)* based on the structure illustrated in Fig. 20. The peptide rings are axially symmetrical on each side of the chromophore plane and lie "flat" (cf. the ff-form in Fig. 5e and also Fig. 10). The molecule, with its conformation so skilfully stabilized (one of the interannular H-bonds is in the middle) is structurally very well balanced and compact. Thus, when there are local conformational distortions, such as the (β)-proline ring being changed to 4-oxoproline in *(7e)*, they propagate—as indicated by NMR data—to very distant parts of the molecule (the chromophore or the neighboring peptide group): molecular interactions occurring there, *e.g.* insertion of the chromophore between the DNA base pairs, are thereby indirectly influenced. Whether, and how far, the three-dimensional structure of the actinomycin molecule complexed with a complete DNA double strand is still altered remains to be tested, for the data so far available are based on analysis of short-chain model complexes in which the partners can arrange themselves with relatively little constraint. NMR studies on the deoxyhexanucleotide[113], itself present as double helix, were performed with this aim in mind and confirmed the structures already established (Fig. 20).

Because of the unique structural type of the actinomycins, comparison with other specific DNA blockers is limited essentially to the chromophore. The antibiotics that should be mentioned in this context, namely those of the mitomycin and anthracycline groups (Daunomycin, Rhodomycin), as well as some acridine derivatives, are also cytostatically very active and some of them are used in treatment of leukemia in spite of their high toxicity. Like *(1)*, they intercalate between the base pairs of the DNA double helix but carry no peptide groups on the chromophore (benzoquinone or anthraquinone derivatives)—anthracyclines carry rare sugars instead. Mitomycins clamp the DNA strands irreversibly, unlike the actinomycins (Fig. 18b)[68].

A uniform, stable, three-dimensional structural model thus exists for more than a hundred known actinomycins and actinomycin derivatives; this brings to a degree of conclusion the investigations into the structure of the actinomycins that began with *Brockmann*'s elucidation of the constitution of actinomycin C_3 *(7d)*. How far the antitumor properties first described more than 20 years ago[69] can be developed and better exploited with the aid of the detailed knowledge of the three-dimensional structure must be answered by further research.

Our own work cited in this report was carried out with experimental collaboration of Frau M. Köppler and Frau E. Salkowski. The author is indebted to Professor H. Brockmann for his intense interest and very generous financial support.

Received: October 3, 1974 [A 60 IE]
German version: Angew. Chem. *87*, 400 (1975)
Translated by Express Translation Service, London

[1] *S. A. Waksman* and *H. B. Woodruff*, Proc. Soc. Exp. Biol. Med. *45*, 609 (1940).

[2] *H. Brockmann*, Fortschr. Chem. Org. Naturst. *18*, 1 (1960); Angew. Chem. *72*, 939 (1960).

[3] *S. A. Waksman:* Actinomycin; Nature, Formation, and Activities. Interscience, New York 1968.

[4] *E. Katz* in *D. Gottlieb* and *P. D. Shaw:* Antibiotics, Biosynthesis. Springer, New York 1967, Vol. II, p. 276.

[5] *H. Brockmann* and *H. Lackner*, Naturwissenschaften *47*, 230 (1960); *51*, 384 (1964); Chem. Ber. *100*, 353 (1967).

[6] *J. Meienhofer* and *E. Atherton*, Advan. Appl. Mikrobiol. *16*, 203 (1973).

[7] *W. Müller* and *D. M. Crothers*, J. Mol. Biol. *35*, 251 (1968).

[8] *L. Hamilton, W. Fuller*, and *E. Reich*, Nature *198*, 538 (1963).

[9] *B. H. Arison* and *K. Hoogsteen*, Biochemistry *9*, 3976 (1970).

[10] *N. S. Angerman, T. A. Victor, C. L. Bell*, and *S. S. Danyluk*, Biochemistry *11*, 2402 (1972).

[11] *T. R. Krugh* and *J. W. Neely*, Biochemistry *12*, 1775, 4418 (1973).

[12] *D. J. Patel*, Biochemistry *13*, 1476, 2388 (1974).

[13] *D. J. Patel*, Biochemistry *13*, 2396 (1974).

[14] *H. M. Sobell, S. C. Jain*, and *T. D. Sakore*, Nature New Biol. *231*, 200 (1971).

[15] *S. C. Jain* and *H. M. Sobell*, J. Mol. Biol. *68*, 1 (1972).

[16] *H. M. Sobell* and *S. C. Jain*, J. Mol. Biol. *68*, 21 (1972).

[17] *H. Brockmann* and *J. H. Manegold*, Chem. Ber. *100*, 3814 (1967).

[18] *H. Brockmann* and *H. Lackner*, Chem. Ber. *101*, 1312 (1968).

[19] *H. Brockmann* and *H. Lackner*, Chem. Ber. *101*, 2231 (1968).

[20] *J. Meienhofer*, J. Amer. Chem. Soc. *92*, 3771 (1970).

[21] *J. Meienhofer, Y. Sano*, and *R. Patel* in *B. Weinstein* and *S. Lande:* Peptides: Chemistry and Biochemistry, Marcel Dekker, New York 1970, p. 419.

[22] *H. Lackner*, Tetrahedron Lett. *1970*, 2807.

[23] *H. G. Bachmann* and *W. Müller*, Nature *201*, 261 (1964); *M. F. Perutz*, *ibid. 201*, 814 (1964).

[24] *H. Lackner*, Tetrahedron Lett. *1970*, 3189.

[25] Chloroform dissolves all the actinomycins, peptide lactones, and their precursors equally well and is currently the best solvent for comparative studies. "Moist" deuteriochloroform: the solution to be measured is shaken for a short time with a few drops of deuterium oxide and then centrifuged.

[26] *H. Lackner*, Chem. Ber. *104*, 3653 (1971).

[27] As the concentration of *(2)* is increased the original monomer spectrum becomes overlaid by another which finally reaches equal intensity. The signals of the latter spectrum are mostly at higher field values and should be derived from the inner protons of the dimer that are situated *between* the two peptide rings and are thus additionally shielded.

[28] *H. Lackner*, Habilitationsschrift, Universität Göttingen 1972.

[29] *H. Lackner* in *J. Meienhofer:* Chemistry and Biology of Peptides. Proc. 3rd Amer. Peptide Symp. Ann Arbor Science Publ., Ann Arbor, Michigan 1972, p. 147.

[30] *V. F. Bystrov, S. L. Portnova, V. I. Tsetlin, V. T. Ivanov*, and *Yu. A. Ovchinnikov*, Tetrahedron *25*, 493 (1969).

[31] According to models, the synperiplanar orientation ($\phi^{\S} \approx 0°$) also derivable from $J_{CH,NH} = 8.3$ Hz is extremely unlikely—and similarly for the "A" conformation. For the definition of ϕ^* see Fig. 13.

[32] *P. De Santis, R. Rizzo*, and *G. Ughetto*, Tetrahedron Lett. *1971*, 4309; Biopolymers *11*, 279 (1972).

[33] The *trans*'-form must be borne in mind as possibly replacing the *cis*'-C^{α}—CO orientation (bond g) for the proline group in Fig. 7, since, in contradiction to the results from models and some NMR data, calculation of the conformational energy [32] shows them to be also apparently favored. This is currently being studied by ^{13}C-NMR measurements.

[34] *C. M. Deber, D. A. Torchia*, and *E. R. Blout*, J. Amer. Chem. Soc. *93*, 4893 (1971); *D. A. Torchia, S. C. K. Wong, C. M. Deber*, and *E. R. Blout*, *ibid. 94*, 616 (1972).

[35] *F. A. Bovey* in *J. Meienhofer:* Chemistry and Biology of Peptides. Proc. 3rd Amer. Peptide Symp. Ann Arbor Science Publ., Ann Arbor, Michigan 1972, p. 3.—*D. E. Dorman* and *F. A. Bovey*, J. Org. Chem. *38*, 2379 (1973).

[36] *R. Schwyzer* in *J. Meienhofer*: Chemistry and Biology of Peptides. Proc. 3rd Amer. Peptide Symp. Ann Arbor Science Publ., Ann Arbor, Michigan, 1972, p. 141.

[37] *R. Schwyzer, Ch. Grathwohl, J. P. Meraldi, A. Tun-Kyi, R. Vogel*, and *K. Wüthrich*, Helv. Chim. Acta *55*, 2545 (1972); *K. Wüthrich, A. Thun-Kyi*, and *R. Schwyzer*, FEBS Lett. *25*, 104 (1972). The cyclopentapeptide Gly-L-Ala-Gly-Gly-L-Pro considered here can also assume two conformations.

[38] *J. Dale* and *K. Titlestad*, Chem. Commun. *1970*, 1403; J. C. S. Chem. Comm. *1972*, 225.

[39] IR measurements were of little value for deciding the *cis/trans*-assignment; the optical rotations of the "A" and the "C" conformer differ considerably.

[40] *H. Lackner*, Tetrahedron Lett. *1971*, 2221.

[41] *H. Lackner*, Tetrahedron Lett. *1975*, in press.

[42] *T. A. Victor, F. E. Hruska, C. L. Bell,* and *S. S. Danyluk*, Tetrahedron Lett. *1969*, 4721; *T. A. Victor, F. E. Hruska, K. Hikichi, S. S. Danyluk,* and *C. L. Bell*, Nature *223*, 302 (1969).
[43] *F. Conti* and *P. De Santis*, Nature *227*, 1239 (1970).
[44] The NH→ND exchange, for example, is almost as slow as in the "C"-conformer of *(2)*.
[45] *H. Lackner*, Chem. Ber. *103*, 2476 (1970).
[46] *H. Kamei*, Bull. Chem. Soc. Jap. *38*, 1212 (1965).
[47] A structure based on *(3a)* has also been proposed [48] for actinocin-bis(threonine methyl ester) *(3d)*. However, the finding that *(3d)* shows a normal $\delta(NH_2)$ value of 7.1 and that its 2-deamino-2-hydroxy derivative shows a δ(2-OH) value of 10.8 [*(3a)*: $\delta(NH_2)=10.6/7.2$; *(3c)*: $\delta(OH)=15.9$] alone indicates considerable disturbance of the coplanar arrangement of the carbonyl groups in *(3d)*. It is true that the assumption of a 9-CO---HN_{Thr} or 1-CO---H_2N hydrogen bond (Fig. 12) in dissolved actinomycin D *(1)* [32, 42] explains some of the findings, but this is not in accord with other NMR data, particularly those for actinomycin derivatives such as *(7g)*.
[48] *B. Anastasi, F. Ascoli, P. Costantino, P. De Santis, R. Rizzo,* and *M. Savino*, Biochemistry *12*, 1834 (1973).
[49] *F. Ascoli, P. De Santis, M. Lever,* and *M. Savino*, Biopolymers *11*, 1173 (1972).
[50] *H. Brockmann* and *W. Schramm*, Tetrahedron Lett. *1966*, 2331.
[51] *H. Lackner* and *E. Schäfer*, to be published.
[52] Steric hindrance is, of course, only one of the reasons for the inactivity of these actinomycins. It is relevant, for example, that the three-dimensional relationships no longer permit the formation of hydrogen bridges between the guanosine groups of the DNA and the threonine group of the now enantiomeric peptide chains [14–16]; cf. Section 7.
[53] Similar remarks apply to seco-actinomycins (one peptide ring opened between sarcosine and methylvaline). The conformations of actinomycin acids *(5c)* are very complex and hitherto unknown.
[54] NCH_3 signals for the (α)- and (β)-peptide chains are assigned on the basis of spectra of (α,β)-specifically *N*-methyl-deuteriated actinomycin acid lactones [26].
[55] *C. W. Mosher* and *L. Goodman*, J. Org. Chem. *37*, 2928 (1972).
[56] *E. Atherton* and *J. Meienhofer*, J. Amer. Chem. Soc. *94*, 4759 (1972).
[57] *H. Lackner*, unpublished results.
[58] *H. Brockmann, H. Gröne,* and *G. Pampus*, Chem. Ber. *91*, 1916 (1958).
[59] *H. Brockmann* and *E. Schulze*, Tetrahedron Lett. *1971*, 1489.
[60] I am grateful to Dr. *F. Wehrli* and Mr. *K. Hiltbrunner* (Varian AG, Zug) for most of the ^{13}C-NMR spectra of the pentapeptide lactones, actinomycins, and deuterioactinomycins.
[61] Dr. *S. Braun*, Organisch-Chemisches Institut der Technischen Hochschule, Darmstadt, kindly measured numerous selectively proton-decoupled ^{13}C-NMR spectra.
[62] Some actinomycins contain sarcosine in place of L-proline as amino acid 3'. They have the configurational sequence LD--L and also assume the characteristic three-dimensional structure, even if in apparently somewhat more labile form.
[63] A = adenine, T = thymine, G = guanine, C = cytosine.
[64] *D. M. Crothers, S. L. Sabol, D. I. Ratner,* and *W. Müller*, Biochemistry *5*, 1817 (1968).
[65] As the water cools from 25 to 0–4 °C the solubility of the actinomycins increases by 2–3 powers of ten: *K. H. Schulmeyer*, Diplomarbeit, Universität Göttingen 1961.
[66] *H. Brockmann, J. Ammann,* and *W. Müller*, Tetrahedron Lett. *1966*, 3595.
[67] That actinomycin D and its variants have the same three-dimensional structural type is also shown by the formation of the DNA complex of actinomycin C_3 *(7d)*, which is formed analogously to that of actinomycin D: *R. Schara* and *W. Müller*, Eur. J. Biochem. *29*, 210 (1972).
[68] *D. Gottlieb* and *P. D. Shaw*: Antibiotics. Mechanism of Action. Springer, New York 1967, Vol. 1, p. 211.
[69] *G. Schulte*, Z. Krebsforsch. *58*, 500 (1952); *Ch. Hackmann, ibid. 58*, 607 (1952).

The Photochemistry of Organic Solids

By Mendel D. Cohen[*]

During the years that he was at the Weizmann Institute of Science the late *G. M. J. Schmidt* initiated and developed a very vital research program on the relationship between the structures of organic crystals and the reactions which occur in these crystals. As the program developed the "solid-state group" became larger and more diversified—X-ray crystallographers, organic chemists, spectroscopists, and even theoreticans had their contributions to make. Professor Schmidt died in 1971. As one of the members of this group, I here present a review of recent developments in parts of the field of interest to me.

Of the reactions of organic crystals which have been studied thus far a large number are induced by light and other radiation. This is because radiation, unlike most chemical reactants, can readily penetrate the surface of the crystal, and thus reach the sites one wishes to activate. It is my aim in this article to point out some of the principles operative in the photochemistry of organic crystals. I shall choose examples to illustrate these principles and will not attempt to cover all the various types of reactions and systems which have been studied.

It is appropriate at this stage to pay tribute to the memory of another great scientist who recently passed away—*Theodor Förster*. Many of the ideas which I develop here are extensions of Professor *Förster*'s earlier work, as are so many of the recent developments in photochemistry.

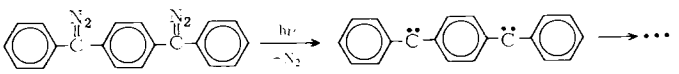
1. Dichroic Systems

The first, and most often forgotten, law of photochemistry states that only the light absorbed by the system can bring about reaction. In this context crystals are of special interest since the chromophoric groups therein are either all aligned parallel to one another, or have only a few relative orientations. The former case is particularly easily distinguished since the crystal will be strongly dichroic, *i.e.* will strongly absorb only light having its electric vector parallel to the chromophores. Thus, if the molecules are photolabile, reaction will be induced by such light, but not by light with its electric vector perpendicular to the chromophores.

[*] Prof. Dr. M. D. Cohen
Patricia Bildner Professor of Solid State Chemistry
Department of Structural Chemistry
The Weizmann Institute of Science
Rehovot (Israel)

A good example of this effect was reported by *Murray* and *Trozzolo*[1, 2]: they studied the photolysis of the dichroic crystals of various diazo compounds (Scheme 1). The appearance of the crystals under the polarizing microscope is illus-

Scheme 1.



trated in Figure 1a; the chromophoric (diazomethylene) linkages are all aligned (parallel or antiparallel) in the molecular orientation shown. Irradiation of a polycrystalline sample with polarized light brings about decomposition only of those crystals suitably oriented to absorb this radiation (Fig. 1b).

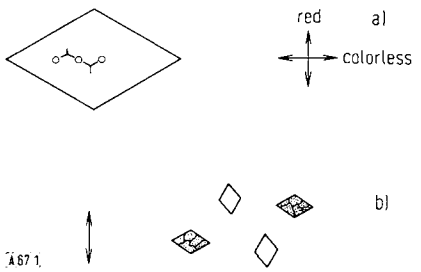


Fig. 1. a) Crystal shape and color in plane-polarized light, for the diazo compound of Scheme 1. b) Appearance of polycrystalline sample of this compound after irradiation with light plane polarized as shown (after [1]).

An interesting application of this effect has become apparent from recent studies of the visual process[3, 4]: a schematic view of part of the outer segment of an isolated rod from a vertebrate retina is shown in Figure 2a. The rod contains a large number of discs lying parallel to one another, and normal to the rod axis. The visual pigment is associated with these discs. Microscopic examination of a rod shows it to be highly dichroic; the absorption is strong when the electric vector is parallel to the disc, but weak when the electric vector is parallel to the rod axis. This shows that the chromophores are aligned parallel to the discs. On the other hand, when the rod is viewed along its axis the absorption is isotropic, suggesting that the chromophores are randomly distributed in this projection. Now supposing that the rod is irradiated from its circular end by light plane-polarized in the x-direction (Fig. 2b), we would expect that only those chromophores with components along this direction would be bleached so that the rod would become dichroic. In fact it was found that the residual absorption remains isotropic after such partial bleaching. However, if the chromophores were first "fixed" by treating the rod with glutaraldehyde,

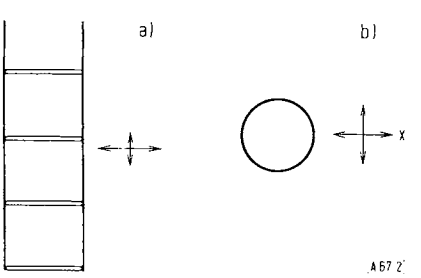


Fig. 2. Schematic representation of part of retinal rod, showing discs and relative absorptions of light plane polarized as shown. Viewed normal to (a) and along (b) rod axis.

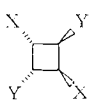
the bleaching did give rise to dichroism[3]. This suggests that the chromophores rotate parallel to the disc, as was confirmed by partial bleaching of native rods with nanosecond pulses of light, when it was found that dichroism is indeed induced but decays in a few microseconds[4]. These observations have important implications concerning the structure of the disc membrane, and possibly also with regard to the mechanism of generation of the nerve impulse.

In crystals having overlapping optical transitions of different polarization the photochemistry might be dependent on the direction of polarization of the irradiating beam. To my knowledge, however, no studies have been reported on such systems.

2. Lattice Control in (2+2)-Photocyclodimerizations

In order to enable development of the arguments to be given in later sections it is desirable to recall the results of such dimerizations. A wide variety of crystalline olefins have been studied; these include *trans*-cinnamic acids and their amides, and a number of dienes, chalcones, and stilbenes[5–7]. These materials can be classified into three types according to the geometric relationships between neighboring molecules in their crystal structures, and to their photochemical behavior (Scheme 2).

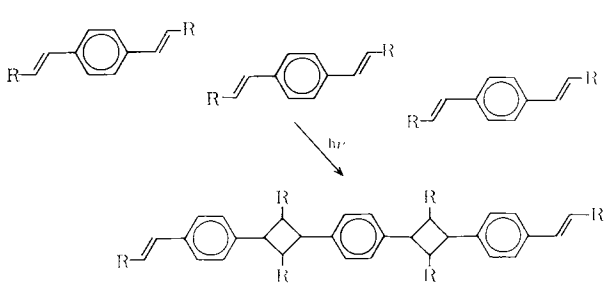
Scheme 2.

Packing type	Structure	Photoproduct
β	X···C=C⊲Y X···C=C⊲Y	
α	X···C=C⊲Y Y···C=C⊲X	
γ	X···C=C⊲Y X···C=C⊲Y	no reaction

We see that the structure of the monomer crystal determines whether or not reaction occurs, and the stereochemistry of the product, if any. Further, from the similarity of the atomic positions in the parent crystal and in the product molecule it is concluded that the reaction involves combination of nearest neighbor monomer molecules.

Hasegawa et al.[8] have studied the solid-state polymerization of divinyl monomers and find that in many cases polymers with cyclobutanes along their backbones are formed (Scheme 3). These reactions also appear to proceed under lattice control.

Scheme 3.



Recently some descriptions have been given[9, 10] of (2+2) photocyclodimerizations in two-component systems. The stereochemistries of the products are as expected for lattice-controlled reactions in substitutional solid solutions.

The term "topochemical" has been used to describe such crystal-structure control of reactions in the solid[11].

3. Where Does Reaction Occur in a Crystal?

In considering reactions, particularly photochemical ones, in the solid it is important to recall that all real crystals contain finite populations of impurity molecules and of structural defects of various sorts. We illustrate a hypothetical real crystal in Figure 3. Here P symbolizes an impurity molecule and the dashed lines indicate defects.

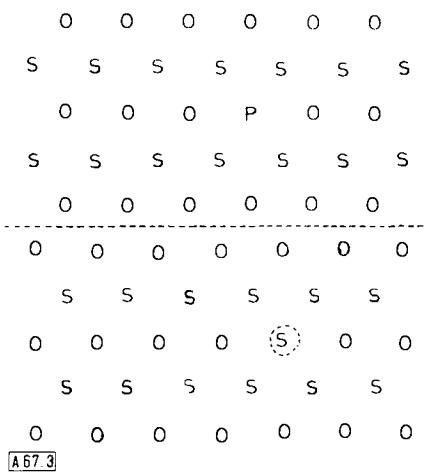


Fig. 3. Imaginative representation of a real two-component crystal. O and S are the components, P impurities, and broken lines indicate structural faults.

Let us irradiate such a crystal: since the vast majority of the molecules are not impurity molecules and are not at structurally defective sites, the light will essentially all be absorbed by the perfect part of the crystal. Anthracene containing tetracene impurity at a concentration of about 10^{-4} M/M will serve as an example. Anthracene molecules absorb the light, yet it is found that most of the emission is from tetracene. The explanation lies in the rapid transmission of the excitation energy through the anthracene until it is trapped by the impurity.

We can generalize from this case: in an arbitrary crystal if the rate of transfer of energy is high enough compared to the rates of reaction in, or emission from, perfect parts of the crystal then this energy can reach impurities or defects and give rise to photoreaction or emission at these sites. The results of processes occurring in the perfect crystal or at defect sites may or may not be distinguishable.

A case which has been extensively studied by *Ludmer* in our laboratory is the (4+4)-photodimerization of 9-cyanoanthracene[12]. Crystals of the starting material are composed of stacks of parallel molecules; on the basis of this structure (cf. Scheme 2, β type) we would expect the product to be the *cis*-dianthracene. However, it is the *trans*-dimer which is actually formed[13, 14]. (In solution, too, only the *trans*-dianthracenes are generally formed; yet in several cases the *cis*-dimers are known to exist (see [12]). Thus the *cis*-isomer can be formed in principle, but the *trans*-form is formed much more rapidly.) How does this come about?

Together with *Thomas* and *Williams* we have investigated the type of structural defects prevalent in crystals of 9-cyanoanthracene, and found that defective regions are present in which adjacent molecules lie antiparallel rather than parallel[15, 16]. Similar studies by *Desvergne et al.*[17] on 1,8-dichloro-9-methylanthracene and 1,8-dichloro-10-methylanthracene reveal the presence of defect sites in which adjacent molecules are closely spaced and strongly overlapped, which is not true of the perfect structures. In all three cases reaction at the defect sites would give the products actually observed, which differ from the products, if any, expected on the basis of the crystal structures.

In the case of 9-cyanoanthracene we have shown that the photoreaction does not occur uniformly through the crystal but only at specific sites, and there is strong circumstantial evidence that these sites of reaction are the structural defects described above[12]. It therefore appears that energy is absorbed in the bulk of the crystal and is transferred to suitable faults where reaction occurs. According to this model, if we incorporate into the crystal suitable impurity molecules that can trap the mobile energy this should inhibit the reaction by preventing the energy from reaching potential sites of reaction. We have demonstrated this effect with a variety of impurity molecules in 9-cyanoanthracene[6, 12].

There is an interesting biological analog to the above. One of the principle causes of radiation damage in biological systems is the intrastrand combination of thymine residues in DNA to give the "photodimer". Recently two groups have shown[18, 19] that in multiply damaged DNA the dimers are not formed at random along the chain but in clusters. It is not clear whether the first dimerization in each cluster occurs at random, or whether there are faulty sites in the DNA at which the reaction occurs preferentially. However, the subsequent steps are clearer: the energy is absorbed in undamaged zones but is mobile and brings about further reaction at sites adjacent to the primarily damaged ones, possibly because of high atomic mobility there[18]. The growth of the cluster is analogous to the development of product nuclei in a solid-state reaction.

In systems such as discussed here, where energy transfer precedes reaction, we expect to find that the rate of reaction is sensitive to the purity and structural quality of the crystal, and to factors such as the size and history of the crystal, and the nature of the ambient atmosphere. Also different wavelengths of light may produce different effects because of their different depths of penetration, leading to different probabilities of surface trapping of the mobile excitation.

One of the characteristics of reactions in such systems is that they involve an induction period, which is sensitive to the quality of the crystal. If a reaction in a particular system shows no induction period this indicates that either there is no transfer of energy preceding reaction, or that there are no special sites at which reaction occurs preferentially.

In 9-cyanoanthracene the *cis*-dimer, expected on the basis of the crystal structure, is not found. The situation is different in the cinnamic acids and related materials where only products allowed by the crystal structure are obtained. In the latter systems, a knowledge of the structures of the products provides no indication of whether or not energy transfer precedes reaction. However, there is an alternative experimental approach which gives this information.

Consider a mixed crystal (solid solution) of molecules O and S which yield products P_O and P_S, respectively, in solid-state reactions. If there is no energy transfer the relative yields of these products are determined by the concentrations and absorption coefficients of O and of S and by the quantum yields of their reactions. On the other hand, the transfer of energy prior to reaction will change the distribution of the excitation energy between O and S and therefore also the relative product yields. Thus these yields provide a measure for the energy transfer.

We have carried out such studies with systems of two cinnamic acids, two cinnamides, and two stilbenes[9, 10, 20]. In all the systems the yields show that there is little or no transfer of energy, so that the reactions must be localized near the site of light absorption. It should be pointed out, however, that our analysis of the results assumes that the two components form solid solutions with one another. This seems very probable because of the demonstrated topochemical control involved. However, we have not yet been able to prove to our satisfaction that such solutions are indeed formed, and the conclusions must therefore be considered as tentative.

4. Consequences of the Limited Mobility in Solids

Cohen and *Schmidt*[11] explained their results on topochemically controlled dimerization in terms of a "Topochemical Principle" which states that reactions in solids take place with a minimum of atomic and molecular movement. It is worthwhile considering the implications of this principle.

Figure 4 shows a hypothetical β-structure of the olefin of Scheme 2. The fact that the dimerization is a topochemical one means that the product-determining step is controlled by the parent lattice. This in turn implies that, at least up to the transition state, the reaction complex maintains close contact with its environment in the crystal.

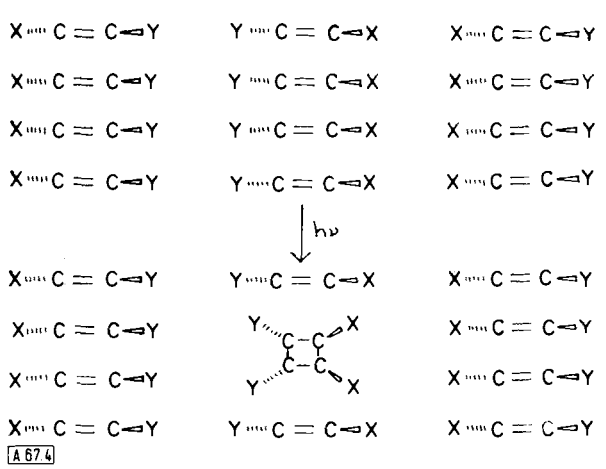


Fig. 4. Structure of a β-type olefin crystal before and after formation of one molecule of photodimer.

We now introduce the concept of a "reaction cavity". The molecules which are going to participate directly in a solid-state reaction occupy a space of a certain size and shape in the starting crystal. This is the reaction cavity, which is surrounded by the contact surface of the molecules inside it with the surrounding molecules. The above topochemical principle can be interpreted to mean that those reactions which proceed under lattice control do so with minimal distortion of the surface of the reaction cavity. In particular, the formation of voids within the cavity or of extrusions from it are energetically unfavorable since they involve, respectively, a large decrease of attractive forces or increase of repulsive ones (Fig. 5).

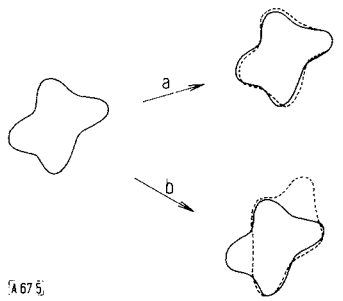


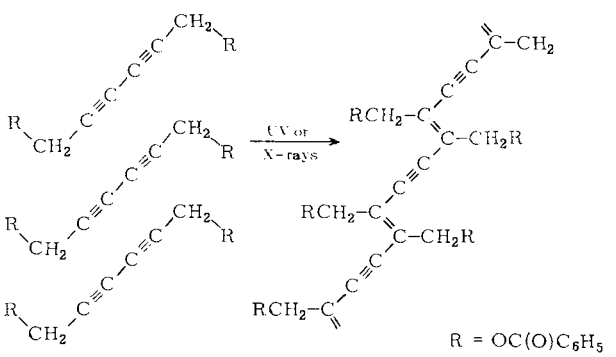
Fig. 5. The reaction cavity before reaction (full line) and in the transition state (broken line) for energetically favorable (a) and unfavorable (b) reactions.

In some cases this fitting of the reaction complex to the surrounding crystal continues beyond the transition state to the product, so that the product molecules are produced as substitutional solute in the parent crystal. As the degree of conversion of reactant to product increases a point is reached in most systems where the solubility limit is exceeded and the product crystallizes out in its own structure. Among the cinnamic acids we have observed cases where conversions of up to 50% are reached before this recrystallization occurs.

Consequently a topochemically controlled reaction will, prior to the recrystallization step, give rise to product molecules in that conformation which best fits them to solid-solubility in the reactant crystal. This effect will be most marked when the product molecule is intrinsically readily deformable.

This effect has been most clearly demonstrated in lattice-controlled polymerization, where it leads to formation of polymers of extended conformation, in keeping with the prediction of *Morawetz*[21]. Some beautiful examples have been given by *Wegner et al.*[22] in the reactions of 1,3-diacetylenes; one of these is represented in Scheme 4.

Scheme 4.



In this system polymerization probably proceeds *via* a rotation of each molecule about its center of mass so that a minimal interference with the rest of the lattice results. The above reactant 2,4-hexadiynylene bis(benzoate) has been found to exist in three crystal forms. In form I polymer molecules are formed at random in the monomer lattice, there is no change in density during reaction, and complete conversion can be achieved without a phase change since the polymer as formed is crystallographically isomorphous with the starting

monomer. Structure II, however, gives rise to a non-isomorphous polymer, which means that the reaction is not completely topochemically controlled; reactant crystals remain single only up to 10% conversion. With further conversion the parent crystal lattice becomes more and more distorted, and at 30% conversion disruption halts reaction. In form II the sites of initiation of reaction may be random, but since the initial chains do not fit the monomer structure they cause distortion in their surroundings and it becomes energetically favorable for further reaction to occur near earlier-formed polymer. This implies in turn that there is prior transfer of energy and that this transfer is more rapid than the rate of reaction in the undistorted crystal. Also in form I, if the reaction rate in the perfect crystal is not appreciably higher than the rate in form II, such transfer of energy must occur. Since this does not lead to aggregation of the polymer this indicates that the surroundings of already-formed chains are so little distorted that they do not provide preferential sites for further reaction. In keeping with this analysis one would expect appreciably longer induction periods in II than in I. This appears to be the case[22].

We would expect pronounced lattice control of polymerization when the monomer molecules bear long aliphatic chains which would presumably determine the crystal structure of the monomer as well as the structure of the polymer. Systems of this sort which have been studied include vinyl stearate[23], lauryl methacrylate[24], and cetyl vinyl ether[25]. In the last case *Hardy et al.* argued, on the basis of the absence of an induction period in the solid-state reaction, that the lattice geometry forces isomorphism upon the polymer up to a certain conversion.

In the case of "small molecule reactions" lattice control of the conformation of the product is less clearly established. *McCollough, Paul,* and *Curtin*[26, 27] have described the (thermal) reaction of picryl ethers of some benzophenone oximes which leads to *N*-substituted benzanilides. They point out that practically no change in molecular volume is involved, so that if the product is formed in an appropriate conformation it will readily be incorporated into the parent structure. On the basis of this known structure the authors point out which conformation would be appropriate.

Such conformational mimicry[28] associated with ready solid solubility may be important in solid-state *cis-trans* isomerization. Irradiation of planar *trans*-cinnamic acids gives dimers only. However, in the case of *cis*-acids and of sterically hindered *trans*-acids isomerization is frequently observed. Thus *ortho*-methoxy-*cis*-cinnamic acid gives the centric dimer along with *trans*-acid. For this system *Ron* and *Schmidt*[5, 29] have provided evidence that the isomerization is the primary reaction, resulting in a solid solution of the *trans*- in the *cis*-acid; this eventually breaks up into crystals of *cis*-acid and crystals of *trans*-acid which undergo dimerization. It is known that the *cis*-acid is markedly non-planar[30]; the *trans*-acid can dissolve in it because it can adopt a similar conformation, and therefore *cis*→*trans* isomerization is feasible. However, the *trans*-acid in its own crystal is presumably near-planar; the solubility of the *cis* in the *trans* crystal is therefore very limited and isomerization in that structure is energetically unfavorable. On the other hand, crystals of *trans*-acids, the molecules of which are so hindered as to be markedly non-planar, can incorporate high concentrations of the *cis*-isomer and *trans*→*cis* isomerization may then occur. This could be the case for β-methyl-*trans*-cinnamic acid which gives both the *cis*-isomer and the centric dimer[5, 31]. It is significant that in *cis*-planar molecules such as muconic acids containing one or more *cis*-linkages there is no sign of photoisomerization, the only photoproducts being cyclobutane dimers or oligomers[32, 33].

Having dealt with the limitations imposed on changes in the shape and size of the reaction cavity we now ask how this constrains the movements of the contents of the cavity and thus gives rise to the specificity of the solid-state reaction. For some of the systems treated above the answer is obvious, but let us turn to more complex cases.

Consider first the model system described by *McBride*[34] where the contents of the cavity consist of two hydrogen acceptors and a molecule which can donate two hydrogen atoms; let the donor be partially deuterated (Fig. 6). The paths for the two transfers are geometrically different so that the transition states interact differently with their crystal environments. As a result of this "transition state perturbation" the relative yields of the two products from the solid-state reaction will differ from those of reaction in non-crystalline media.

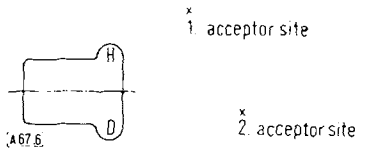


Fig. 6. Model system having two-proton donor and two acceptor sites (after [34]).

However, as *McBride* points out[34], there can be a second factor determining the relative yields in the crystal. Suppose there is only one acceptor site, say the first one in Figure 6. Then only the protium and not the deuterium is in the right position for transfer. If, however, the donor molecule rotates about the dotted line shown, then the two isotopes are alternately brought into this position. When the rate of this rotation is high compared to that of the transfer process then the relative yields of protium and deuterium transfer will be independent of the rotation rate and be determined by the primary isotope effect. On the other hand at low enough rates of rotation this rate determines the relative yields.

Thus the relative yields of the products from a solid-state reaction may be determined by transition-state perturbation or by the rate of a diffusion process which establishes the right geometries for reaction. This diffusion may be rotational, as above, or translational, in which case it modifies the size and shape of the reaction cavity.

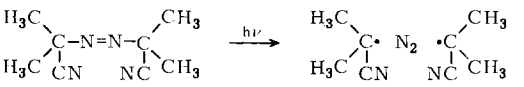
Examples of diffusion control are provided by systems showing strong cage effects. Of these we mention the photolysis of 1,1,3-triphenylacetone, studied by *Quinkert et al.*[35]. The primary photoproducts are $Ph_2CH^{\bullet}$, $PhCH_2^{\bullet}$ and CO. The radicals are formed in close proximity and if they cannot diffuse apart they will react with one another; if they can

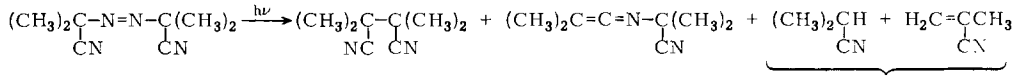
Scheme 5.

$$Ph_2HC-\overset{O}{\overset{\|}{C}}-CH_2Ph \xrightarrow[-CO]{h\nu} (PhCH_2)_2 + Ph_2CH-CH_2Ph + (Ph_2CH)_2$$

benzene solution		1	:	2	:	1
crystal	:	–		only		–

Scheme 8.



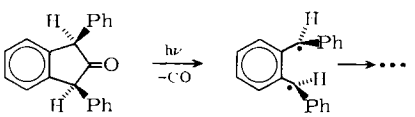


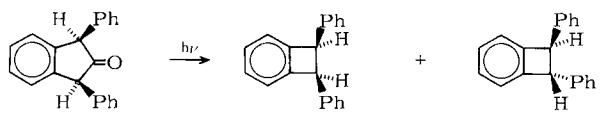
	combination		disproportionation
solution:	40%	55%	5%
crystal:	5%	0%	95%

diffuse apart they can react with radicals from another cage. Comparative results for solid and for solution are given in Scheme 5.

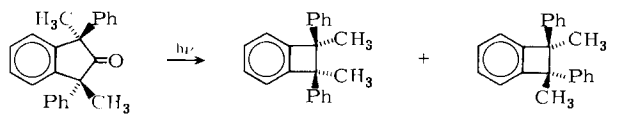
Rotational-diffusion limitation of product distribution from a solid-state reaction may occur when a flexible intermediate is involved. Again we take an example investigated by *Quinkert et al.*, the photolysis of 2-indanones[36]. Previously it had been shown that this reaction involves an intermediate, probably a diradical[37]. The product distribution will then depend on whether or not rotation can occur prior to ring closure. Some results for this system are given in Scheme 6.

Scheme 6.





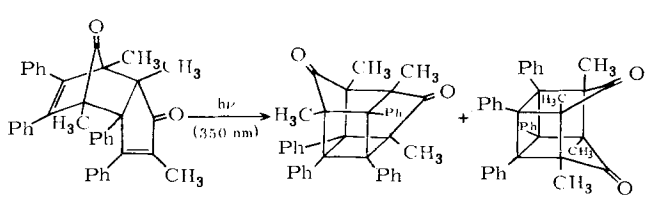
ether solution:	11%	89%
crystal :	95%	5%



ether solution:	9%	91%
crystal :	14%	86%

A less documented example is provided by the photolysis of the dimer of 2,5-dimethyl-3,4-diphenylcyclopentadienone. *Fuchs*[38] showed that this leads to two cage products. Subsequently *Houk* and *Northington*[39] obtained evidence that the reactant molecule is of *endo*-configuration and determined the yields of products from solution and crystal reactions (Scheme 7).

Scheme 7.



	normal	abnormal
acetonitrile solution:	–	70%
crystal :	43%	15%

The authors point out that the formation of the "abnormal" product requires an intermediate step, possibly dissociation to an excimer, followed by a rotation of part of the system. Apparently the rotation is inhibited in the crystal.

While the above three sets of results could perhaps be explained largely on the basis of "viscosity effects", this is clearly not so in the photolysis of azobis(isobutyronitrile) (AIBN). *McBride et al.* determined the product yields for this reaction in the crystal and in fluid and rigid solutions[40]. The primary reaction and results of further reactions are given in Scheme 8.

The crystal structures of the reactant (AIBN is dimorphic) were subsequently elucidated[41] and the factors affecting the relative yields discussed. One structure is represented in Figure 7.

The authors argue that an important factor in determining the molecular packing is the dipole-dipole attraction of the antiparallel nitrile groups. The path leading to the ketenimine, although it possibly might not much distort the reaction cavity, is energetically unfavorable because it counteracts the dipole-dipole attraction. However, the disproportion reaction can proceed without disrupting the cavity or the nitrile framework: One of the radicals formed can rotate about its C—C—N axis so that a methyl replaces the nitrogen, and hydrogen transfer follows (Scheme 9).

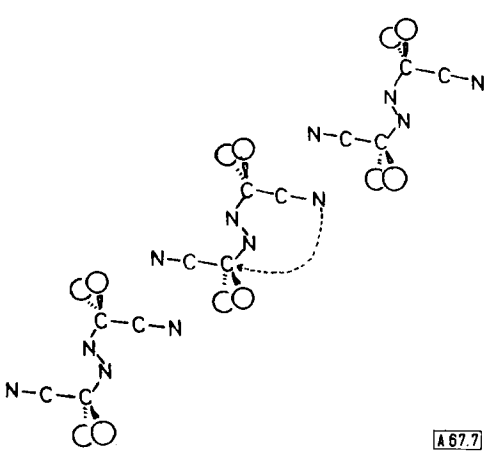
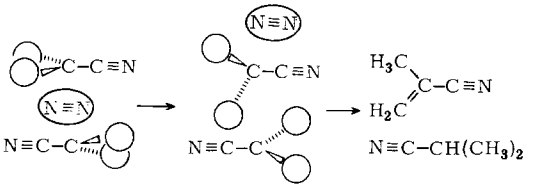


Fig. 7. Part of the crystal structure of one form of dimorphic azobis(butyronitrile), AIBN. The broken line shows the path to ketenimine (after [41]).

This rotational diffusion is slow enough to determine the rate[42].

Scheme 9.



5. Asymmetric Synthesis in Chiral Crystals

The earlier work on cyclodimerization (cf. Section 2) demonstrated the control of the crystal lattice on the course of reaction. The question then arose as to whether a more refined type of control could be achieved: consider a reaction which converts a prochiral molecule into a chiral product. If this reaction occurs in a chiral crystal, will this result in the preferential formation of one enantiomeric product rather than the other? (A chiral crystal is one whose symmetry elements do not interrelate enantiomeric objects.)

The answer is yes, although in the systems studied thus far the lattice is not so dominant as it is, for example, in determining the selectivity in the dimerization of cinnamic acids. In the case of the (thermal) addition of gaseous bromine to 4,4'-dimethylchalcone the enantiomeric excess achieved is of the order of 5 to 15 %[43, 44], while in the solid-state photoaddition of 1-(2,6-dichlorophenyl)-4-(2-thienyl)-1,3-butadiene to the corresponding -4-phenylbutadiene this excess is of the order of 70 %[45].

As previously, we can picture the reaction as occurring in a cavity in the crystal. There are contacts between the contents of the cavity and its surroundings, and these contacts cannot be much modified during the reaction if this is to be energetically feasible. Because of the chirality of the structure these contacts are asymmetric; the result is that the forces directing the reaction towards one enantiomer differ from those directing it towards the other. (This picture of the asymmetric cavity is reminiscent of the recent work of *Wulff et al.*[46] who produced a synthetic polymer having asymmetric pockets as an enzyme analog and showed that it could be used for resolution of a racemic substrate.)

It should be pointed out that even before the reaction the surroundings provide an asymmetric force field, so that the contents of the cavity must be to some extent chiral. For this reason the transition states leading to the two products are not strictly enantiomeric, but rather diastereoisomeric.

Green, Lahav, and *Schmidt*[47] have analyzed the relationship between the symmetry of a monomer crystal and the possibility of achieving asymmetric synthesis by a dimerization reaction within it. In the case of dienes there is the possibility of achieving reaction between non-equivalent double bonds. In this case in a chiral crystal there is a major difference between the paths leading to enantiomeric products, and very high optical yields may be expected. Initial experiments on such systems have been very promising[48].

6. Excimers

It is now twenty years since *Förster* and *Kasper*[49, 50] observed an anomalous long-wavelength emission from pyrene in solution and explained it as originating from an electronically excited bimolecular complex (excimer). This system has since been the subject of extensive experimental and theoretical studies, so that it can now be considered as reasonably well understood. As far as its geometry is concerned the excimer is believed to have its two constituent molecules lying parallel, strongly overlapped, and with interplanar distance of about 3.2 Å (typically the interplanar distance between aromatic molecules in the ground state is about 3.5 Å).

The excimer phenomenon is now well established for a wide variety of materials both in solution and in crystals of suitable structure. Some of the materials also undergo photodimerization. From the geometric point of view it is reasonable to suggest that the excimer is an intermediate on the path to dimer formation. However, this suggestion has been confirmed only very recently: *Ferguson* and *Mau*[51] used single crystals of anthracene photodimer. By irradiation with high energy light they split some of the dimer molecules into pairs of monomers, and then studied the fluorescence and redimerization of these pairs on long-wavelength irradiation at various temperatures. Their results show conclusively that the excimer is competitively deactivated by fluorescence and dimerization, and that the dimerization reaction proceeds exclusively *via* the excimer.

A further property of excimers is of importance in solid-state photochemistry: In those excimer-forming crystals which have been studied there occurs transfer of energy from excimer to neighboring-pair, so that the excimer energy is mobile. This has been demonstrated for pyrene, particularly by *Klöpffer*[52]; we have recently given[53] a theoretical interpretation of the mechanism of this transfer. *Ludmer*[12] has shown that such transfer also occurs in crystalline anthracenes such as 9-cyanoanthracene.

In a material such as the last-named we picture the dimerization reaction as proceeding as follows: Exciting light is absorbed by any monomer or pair of adjacent monomers and is localized by excimer formation. This localization is not complete because the energy can be transferred from pair to pair by thermal activation (the energy required is appreciably less than the dissociation energy of the excimer). The transfer continues until radiative or non-radiative deactivation occurs, or the energy reaches an appropriate structural defect where reaction occurs. The major part of the emission originates from sites other than those of reaction.

Since, in the crystal, excimer formation involves a relatively small change in the geometry of the pair it should be a reaction particularly suited to the solid state. It is of interest that even here the lattice imposes constraints. We have shown[53] that the spectroscopic results for pyrene can be explained only if one assumes that excimer formation involves not only close approach of the two molecules, but also a relative displacement parallel to the molecular planes. *Warshel* and *Huler*[54] have made detailed calculations of the potential surfaces of pyrene crystals in their ground and excited (*i.e.* containing an excimer) states, assuming that on excimer formation the rest of the crystal is undistorted. The authors show that whereas in the isolated excimer the molecules are completely overlapped, in the crystal there is an "in-plane" displacement of about 0.7 Å. My rough estimate based on the data given reveals that in the crystal the energy of a completely overlapped pair is about 10 kcal mol^{-1} higher than that of the displaced pair, at the same interplanar spacing. This then gives some qualitative idea of the energy involved in

the force interactions with the surroundings of the reaction cavity.

The calculations[55] on the single-component analog of the diphenylbutadiene system, which has been used for asymmetric photodimerization[45] (cf. Section 5), also deserve mention. This material shows excimer emission (which should be circularly polarized[56]), and in the light of the results obtained by *Ferguson* and *Mau*[51] it is reasonable to assume that the excimer state is passed through on the path to the photodimer. *Warshel* and *Shakked* calculated energies and geometries for the path: "crystal" $\xrightarrow{h\nu}$ "crystal containing excited monomer" → "crystal containing excimer". The second step can pass along two paths, corresponding to attack of the excited monomer on its upper or lower neighbors. The calculations show that while the excimer is the same, irrespective of which path is followed (in one case an inversion of the primarily excited molecule occurs), the gradients of the two paths are nevertheless different. This can then explain why there are different rates of production of the two enantiomeric products.

There is one interesting open question concerning excimers and photodimerization: it has been postulated[57, 58] that production of non-topochemical dimers in some systems arises through mutual rotation of the two molecules of an excimer. Thus, for example, 9-cyanoanthracene could be pictured as forming a *cis*-excimer which is transformal into a *trans*-excimer, which finally gives the *trans*-dimer. Whereas such a rotation is energetically unlikely in the bulk of the crystal, it may not be so at or near defects. If this is the case then it is relative freedom of movement near the defect which is important, rather than the specific structure of the defect as we have suggested[15, 16]. While I find our explanation preferable (see ref.[12]) it is nevertheless of interest that others have also postulated relative rotation in the excimer in another context[39]. Whatever the case may be, this discussion highlights an important feature[59], namely that the energetics of molecular movement are likely to be sensitive to the site in the crystal—a factor which may prove to be of significance in a variety of reacting systems.

In the light of the above remarks on excimers one may expect that exciplexes, too, may play an important role in some solid-state reactions. No photochemical reactions proceeding *via* exciplexes in solids have been described thus far; however, the formation of exciplexes in 9-cyanoanthracene doped with perylene has been described[6, 12].

Received: October 7, 1974 [A 67 IE]
German version: Angew. Chem. 87, 439 (1974)

[1] *R. W. Murray* and *A. M. Trozzolo*, Microchem. J. Symp. Ser. 2, 233 (1962).
[2] *R. W. Murray* and *A. M. Trozzolo*, J. Org. Chem. *29*, 1268 (1964).
[3] *P. K. Brown*, Nature (London) New Biol. *236*, 35 (1972).
[4] *R. A. Cone*, Nature (London) New Biol. *236*, 39 (1972).
[5] *G. M. J. Schmidt*, Pure Appl. Chem. *27*, 647 (1971).
[6] *M. D. Cohen* in *J. S. Anderson, M. W. Roberts*, and *F. S. Stone*: Reactivity of Solids. Chapman and Hall, London 1972, p. 456.
[7] *M. D. Cohen* and *B. S. Green*, Chem. Brit. 9, 490 (1973).
[8] For example, *M. Hasegawa, Y. Sazuki*, and *T. Tamaki*, Bull. Chem. Soc. Jap. *43*, 3020 (1970).
[9] *J. D. Hung, M. Lahav, M. Luwisch*, and *G. M. J. Schmidt*, Isr. J. Chem. *10*, 585 (1972).
[10] *M. D. Cohen, R. Cohen, M. Lahav*, and *P. L. Nie*, J. C. S. Perkin II *1973*, 1095.
[11] *M. D. Cohen* and *G. M. J. Schmidt*, J. Chem. Soc. *1964*, 1996.
[12] *Z. Ludmer*, Ph. D. Thesis, Weizmann Institute of Science, Rehovot 1974.
[13] *D. P. Craig* and *P. Sarti-Fantoni*, Chem. Commun. *1966*, 742.
[14] *E. Heller* and *G. M. J. Schmidt*, Isr. J. Chem. *9*, 449 (1971).
[15] *M. D. Cohen, Z. Ludmer, J. M. Thomas*, and *J. O. Williams*, Chem. Commun. *1969*, 1172.
[16] *M. D. Cohen, Z. Ludmer, J. M. Thomas*, and *J. O. Williams*, Proc. Roy. Soc. (London) *A 324*, 459 (1971).
[17] *J. R. Desvergne, J. M. Thomas, J. O. Williams*, and *H. Bouas-Laurent*, J. C. S. Perkin II *1974*, 363.
[18] *N. N. Shafranovskaya, E. N. Trifinov, Yu. S. Lazurkin*, and *M. D. Frank-Kamenetskii*, Nature (London) New Biol. *241*, 58 (1973).
[19] *C. F. Brunk*, Nature (London) New Biol. *241*, 74 (1973).
[20] *M. D. Cohen* and *R. Cohen*, unpublished results.
[21] *H. Morawetz*, J. Polym. Sci. *C 12*, 79 (1966).
[22] *J. Kaiser, G. Wegner*, and *E. W. Fischer*, Isr. J. Chem. *10*, 157 (1972).
[23] *H. Morosoff, H. Morawetz*, and *B. Post*, J. Amer. Chem. Soc. *87*, 3035 (1965).
[24] *A. Chapiro* and *L. Perec*, J. Chim. Phys. Physicochim. Biol. *63*, 842 (1966).
[25] *Gy. Hardy, K. Nyitrai, F. Cser, Gy. Cselik*, and *I. Nagy*, Eur. Polym. J. *5*, 133 (1969).
[26] *J. D. McCullough, Jr., D. Y. Curtin*, and *I. C. Paul*, J. Amer. Chem. Soc. *94*, 874 (1972).
[27] *J. D. McCullough, Jr., I. C. Paul*, and *D. Y. Curtin*, J. Amer. Chem. Soc. *94*, 883 (1972).
[28] *M. D. Cohen*, J. Chem. Soc. *B 1968*, 373.
[29] *I. Ron*, Ph. D. Thesis, Weizmann Institute of Science, Rehovot 1971.
[30] *Y. Leser* and *D. Rabinovich*, unpublished results.
[31] *S. E. Filippakis, L. Leiserowitz, D. Rabinovich*, and *G. M. J. Schmidt*, J. C. S. Perkin II *1971*, 1750.
[32] *M. Lahav* and *G. M. J. Schmidt*, J. Chem. Soc. *B 1967*, 312.
[33] *C. K. Hu, M. Lahav, D. Rabinovich*, and *G. M. J. Schmidt*, to be published.
[34] *J. M. McBride*, personal communication.
[35] *G. Quinkert, K. Opitz, W.-W. Wiersdorff*, and *J. Weinlich*, Tetrahedron Lett. *1963*, 1863.
[36] *G. Quinkert, T. Tabata, E. A. J. Hickmann*, and *W. Dobrat*, Angew. Chem. *83*, 212 (1971); Angew. Chem. internat. Edit. *10*, 199 (1971).
[37] *G. Quinkert, J. Palmowski, H.-P. Lorenz, W.-W. Wiersdorff*, and *M. Finke*, Angew. Chem. *83*, 210 (1971); Angew. Chem. internat. Edit. *10*, 198 (1971).
[38] *B. Fuchs*, J. Amer. Chem. Soc. *92*, 2544 (1971).
[39] *K. N. Houk* and *D. T. Northington*, Tetrahedron Lett. *1972*, 303.
[40] *A. B. Jaffe, K. J. Skinner*, and *J. M. McBride*, J. Amer. Chem. Soc. *94*, 8510 (1972).
[41] *A. B. Jaffe, D. S. Malament, E. P. Slisz*, and *J. M. McBride*, J. Amer. Chem. Soc. *94*, 8515 (1972).
[42] *J. M. McBride*, J. Amer. Chem. Soc. *93*, 6302 (1971).
[43] *K. Penzien* and *G. M. J. Schmidt*, Angew. Chem. *81*, 628 (1969); Angew. Chem. internat. Edit. *8*, 608 (1969).
[44] *B. S. Green* and *L. Heller*, Science *185*, 525 (1974).
[45] *A. Elgavi, B. S. Green*, and *G. M. J. Schmidt*, J. Amer. Chem. Soc. *95*, 2058 (1973), and unpublished results.
[46] *G. Wulff, A. Sarhan*, and *K. Zabrocki*, Tetrahedron Lett. *1973*, 4329.
[47] *B. S. Green, M. Lahav*, and *G. M. J. Schmidt*, Mol. Cryst. Liq. Cryst. *29*, 187 (1975).
[48] *L. Addadi, M. D. Cohen*, and *M. Lahav*, J. C. S. Chem. Comm., in press.
[49] *Th. Förster* and *K. Kasper*, Z. Phys. Chem. N. F. *1*, 275 (1954).
[50] *Th. Förster*, Angew. Chem. *81*, 364 (1969); Angew. Chem. internat. Edit. *8*, 333 (1969).
[51] *J. Ferguson* and *A. W.-H. Mau*, Mol. Phys. *27*, 77 (1974).
[52] *W. Klöpffer, H. Bauser, F. Dolezalek*, and *G. Mandorf*, Mol. Cryst. Liq. Cryst. *16*, 229 (1972).
[53] *M. D. Cohen, E. Klein, Z. Ludmer*, and *V. Yakhot*, Chem. Phys. *5*, 15 (1974).
[54] *A. Warshel* and *E. Huller*, Chem. Phys. *6*, 463 (1974).
[55] *A. Warshel, E. Huller, D. Rabinovich*, and *Z. Shakked*, J. Mol. Struct. *23*, 175 (1974).
[56] *I. Z. Steinberg* in *R. Chen* and *H. Edelhoch*: Concepts in Biochemical Fluorescence. Marcel Dekker, New York 1974.
[57] *A. Kawada* and *M. M. Labes*, Mol. Cryst. Liq. Cryst. *12*, 133 (1970).
[58] *E. J. Baum* in *J. N. Pitts Jr.*: Excited State Chemistry. Gordon and Breach, New York 1970, p. 121.
[59] Cf. *G. Friedman, E. Gati, M. Lahav, D. Rabinovich, G. M. J. Schmidt*, and *Z. Shakked*, J. C. S. Chem. Comm., in press.

Ternary Cu^{2+} Complexes: Stability, Structure, and Reactivity

By Helmut Sigel[*]

The driving forces leading to the formation of ternary Cu^{2+} complexes are outlined; they are (i) statistical reasons, (ii) neutralization of charge in the mixed-ligand complexes, (iii) steric factors (bulky groups, ring size of chelates), and (iv) formation of π bonds. The last point is important for achieving a large stability, as well as for the observation of discriminating qualities. An additional stability increase may possibly be achieved through a direct interaction between the two ligands bound to the same metal ion, *i.e.* Schiff base formation, hydrogen bonding or a charge-transfer relation. The latter leads to distinct structures, *i.e.* metal ion-bridged charge-transfer complexes. The relation between stability and structure on the reactivity of mixed-ligand complexes is emphasized. The relevance of the results for mixed-ligand complexes containing metal ions other than Cu^{2+} is briefly outlined.

1. Introduction

Apart from under artificial conditions in laboratories, metal ions and ligands never exist in pure and isolated form. Under biological and environmental conditions multiligand-multimetal ion equilibria dominate strongly, *i.e.* mixed-ligand or higher order complexes[1] are formed. Per definition, the most simple of these species, *i.e.* a ternary complex[2], will consist of a metal ion and two different ligands, other than the solvent. Such ternary complexes are important in analytical chemistry[3] and metal ion catalyzed reactions[4, 5]; they appear in biological fluids[7], create specific structures[8–10], and manifest themselves as enzyme-metal ion-substrate complexes[11]. Thus, it becomes understandable why mixed-ligand systems have recently been receiving more and more attention[12]. At present, ternary Cu^{2+} complexes are by far the best studied group. It is the aim of this short review to outline briefly the basic conditions for the formation of ternary complexes and to show, with examples, how certain properties regarding structure and reactivity can only be achieved by forming mixed-ligand complexes[**].

2. Stability of Ternary Cu^{2+} Complexes

Cu_{aq}^{2+} has a distorted octahedral structure which arises from the Jahn-Teller effect. Four of the coordinated H_2O are situated in an equatorial square plane about the central Cu^{2+}, while the remaining two H_2O are located at a greater distance along the central axis perpendicular to the square plane[13]. In its complexes Cu^{2+} shows a strong preference for square-planar (or grossly distorted octahedral) structures[14] as can be judged from their stabilities[15, 16] and catalytic behavior[17, 18]. That is, the strong donor atoms are bound in the tetragonal plane[20], and the coordination tendency of the axial positions is very low[21, 22]. This holds also for the ternary Cu^{2+} complexes[19, 21], and H_2O possibly bound to an apical position is not specifically considered.

2.1. Characterization of Stability and Statistical Effects

There are two common ways to express on a quantitative basis the stability of ternary complexes[2, 21, 23]. Both methods are independent of the basicity of the ligands, A and B, and in both some of the following general definitions are used[*]:

$$Cu + A \rightleftharpoons CuA \qquad K_{CuA}^{Cu} = [CuA]/([Cu][A]) \qquad (1)$$

$$CuA + A \rightleftharpoons CuA_2 \qquad K_{CuA_2}^{CuA} = [CuA_2]/([CuA][A]) \qquad (2)$$

$$Cu + 2A \rightleftharpoons CuA_2 \qquad \beta_{CuA_2}^{Cu} = [CuA_2]/([Cu][A]^2) \qquad (3)$$

$$Cu + A + B \rightleftharpoons CuAB \qquad \beta_{CuAB}^{Cu} = [CuAB]/([Cu][A][B]) \qquad (4)$$

$$CuA + B \rightleftharpoons CuAB \qquad K_{CuAB}^{CuA} = [CuAB]/([CuA][B]) \qquad (5)$$

$$CuB + A \rightleftharpoons CuBA \qquad K_{CuBA}^{CuB} = [CuAB]/([CuB][A]) \qquad (6)$$

$$\log K_{CuAB}^{CuA} = \log \beta_{CuAB}^{Cu} - \log K_{CuA}^{Cu} \qquad (7)$$

$$\log K_{CuBA}^{CuB} = \log \beta_{CuAB}^{Cu} - \log K_{CuB}^{Cu} \qquad (8)$$

The ternary complexes CuAB and CuBA [cf. Eqs. (5) and (6)] are identical for labile species in solution.

(i) The one approach is based on the "disproportionation" constant, X, as defined by Eq. (9); $\log X$ may be calculated according to Eqs. (10) or (11).

$$CuA_2 + CuB_2 \rightleftharpoons 2CuAB \qquad (9)$$

$$X = [CuAB]^2/([CuA_2][CuB_2])$$

$$\log X = 2\log \beta_{CuAB}^{Cu} - (\log \beta_{CuA_2}^{Cu} + \log \beta_{CuB_2}^{Cu}) \qquad (10)$$

$$\log X = (\log K_{CuBA}^{CuB} - \log K_{CuA_2}^{CuA}) + (\log K_{CuAB}^{CuA} - \log K_{CuB_2}^{CuB}) \qquad (11)$$

For statistical reasons the value expected for X [Eq. (9)] is 4, *i.e.* $\log X = 0.6$[24–26], and the statistical value for one of the terms within brackets in Eq. (11) is 0.3 log units. Hence, under purely statistical conditions one would expect the ternary complex to be formed to the extent of 50% while the binary parent complexes should occur to the extent of 25% each.

(ii) The other approach compares the difference in stability, $\Delta \log K$, *e.g.*, for the reaction between CuA or $Cu(aq)^{2+}$ and the ligand B. On the basis of the properties of a cyclic system[2, 27] one can define Eq. (12). Consequently, the influence of both ligands in a ternary complex is mutual and of the same size; both ligands are either stabilized or destabili-

[*] Priv.-Doz. Dr. H. Sigel
Institut für Anorganische Chemie der Universität
CH-4056 Basel, Spitalstrasse 51 (Switzerland)

[**] It is not intended here to give a detailed list of data (these may easily be found in the cited references) but rather to present some few characteristic examples.

[*] Charges are omitted in all equations. Equations (1)–(3) hold analogously for ligand B.

zed in their coordination to the same metal ion. The difference, $\Delta \log K$, is the result from the substraction of two constants, and must therefore also be a constant; this corresponds to Eq. (13).

$$\Delta \log K = \log K^{CuA}_{CuAB} - \log K^{Cu}_{CuB} = \log K^{CuB}_{CuBA} - \log K^{Cu}_{CuA} \quad (12)$$

$$CuA + CuB \rightleftarrows CuAB + Cu \quad (13)$$

Since more coordination positions are available for bonding of the first ligand to a given multivalent (hydrated) metal ion than for the second ligand $\log K^{Cu}_{CuA} > \log K^{CuA}_{CuA_2}$ usually holds, *i. e.* one expects to observe negative values for $\Delta \log K$. The difference, $\log K^{CuA}_{CuA_2} - \log K^{Cu}_{CuA}$, is generally about -0.5 to -0.8 log units for monodentate ligands and about -1 to -2 log units for bidentate ligands[15]. Another, probably more satisfactory, approach is to determine statistical values for $\Delta \log K$. In the case where A and B are bidentate ligands, there are twelve edges of a regular octahedron (oh) available for the first entering ligand but only five for the second[*] *i. e.* the statistical factor is $^5/_{12}$ and, accordingly, $\Delta \log K_{oh} = -0.4$. For a square-plane (sp) one obtains a factor of $^1/_4$, *i. e.* $\Delta \log K_{sp} = -0.6$. However, for the distorted octahedron (do) of Cu^{2+}_{aq} the statistical value is more difficult to assess: Considering the Jahn-Teller inversion to be rapid[29], there are eight (or even twelve) equivalent attacking positions for the first ligand, while the value for the second ligand can vary from one to four (or even five) depending on the relative rates of inversion. Hence, the statistical value is between $^1/_8$ (or even $^1/_{12}$) and $^4/_8$, *i. e.* $\Delta \log K_{do} = -0.9$ (or -1.1) to -0.3. In the present case of Cu^{2+}_{aq} and ligands that introduce a strong ligand field, we consider the statistical expression, $\Delta \log K_{do/Cu} = -0.9$, as the most appropriate one[**]. Hence, an experimentally determined value of $\Delta \log K > -0.9$ indicates that in Eq. (13) the ternary complex is favored.

Depending on the kind of study either one or the other approach [Eqs. (9)—(11) or (12)—(13)] may be preferable. The calculation of $\log X$ requires knowledge of $K^{CuA}_{CuA_2}$ and $K^{CuB}_{CuB_2}$, but these are often unknown[8, 23, 30]. Furthermore, as the complexes CuA_2 and CuB_2 do not lie on the reaction pathway for formation of CuAB, extraneous factors may enter into $K^{CuA}_{CuA_2}$ and $K^{CuB}_{CuB_2}$, and then appear in $\log X$ [Eq. (11)]. Electrostatic effects also contribute differently to $\log X$ and $\Delta \log K$[21]. To a first approximation electrostatic factors cancel in the $\Delta \log K$ formulation when either ligand possesses a zero charge. In the $\log X$ expression electrostatic factors cancel only when the charges of the two ligands are equal to each other. Hence, for most ligands of interest, the $\Delta \log K$ formulation is also less dependent upon ionic strength[21] (cf. also Ref. [10]), but the statistical value depends upon the coordination number of the metal ion and the denticity of the ligands. Overall, it appears that the main advantage of the log X formulation is its firm statistical basis, while that of $\Delta \log K$ is that only the corresponding binary 1:1 complexes contribute to its formulation [Eqs. (12), (13)].

For a given system with known equilibrium constants, one may tentatively say: to judge the conditions in a solution which contains the same or a smaller amount of ligands, compared to the concentration of the metal ion, $\Delta \log K$ is preferably used, while reasoning on a solution containing excess of ligands is best based on $\log X$. Obviously, this is the consequence of the fact that the one method relies on the binary 1:1 complexes [Eqs. (12), (13)] and the other on the binary 1:2 complexes [Eqs. (9), (10)].

2.2. Neutralization of Charge

Neutralization of charge is expected to be one of the driving forces leading to the formation of ternary complexes. This is confirmed by Eqs. (14) and (15)[*]. The reaction of the two charged binary parent complexes in Eq. (14) leads to

$$Cu(En)^{2+}_2 + Cu(Ox)^{2-}_2 \rightleftarrows 2\,Cu(En)(Ox) \quad \log X = 0.94^{[31, 32]} \quad (14)$$

$$Cu(En)^{2+}_2 + Cu(P_2O_7)^{6-}_2 \rightleftarrows 2\,Cu(En)(P_2O_7)^{2-} \quad \log X = 2.3^{[35]} \quad (15)$$

$$Cu(En)^{2+} + Cu(Ox) \rightleftarrows Cu(En)(Ox) + Cu^{2+} \quad \Delta \log K = -0.79^{[31]} \quad (16)$$

the neutral ternary complex, Cu(En)(Ox). This means, coulombic effects (enthalpy) and the release of orientated solvent molecules (entropy) favor the formation of the mixed-ligand complex[36]. Equation (16) (cf. with $\Delta \log K_{do} = -0.9$) confirms the above mentioned (Section 2.1) small influence of electrostatic effects on $\Delta \log K$.

2.3. Influence of Steric Factors

Such an influence is obvious from Eqs. (17) through (20).

$$Cu(En)^{2+}_2 + Cu(Et_2en)^{2+}_2 \rightleftarrows 2\,Cu(En)(Et_2en)^{2+} \quad \log X = 1.83^{[37]} \quad (17)$$

$$Cu(En)^{2+} + Cu(Et_2en)^{2+} \rightleftarrows Cu(En)(Et_2en)^{2+} + Cu^{2+} \quad \Delta \log K = -1.40^{[37]} \quad (18)$$

$$Cu(En)^{2+}_2 + Cu(Ida)^{2-}_2 \rightleftarrows 2\,Cu(En)(Ida) \quad \log X = 1.9^{[38]} \quad (19)$$

$$Cu(En)^{2+} + Cu(Ida) \rightleftarrows Cu(En)(Ida) + Cu^{2+} \quad \Delta \log K = -2.3^{[38]} \quad (20)$$

Steric hindrance in one of the binary 1:2 parent complexes, say CuA_2, increases the stability of the ternary complex, CuAB. The bulky ethyl groups of *N,N'*-diethylethylenediamine in the 1:1 complex favor more the coordination of ethylenediamine than a second ligand of the same kind; in accord with this $\log X$ of Eq. (17) exceeds the statistical value of 0.6. On the other hand, Eq. (18) shows that under 1:1 conditions a $\Delta \log K$ value is obtained that is below the statistically expected value of -0.9. In other words: in Eq. (18) the left hand side with the two "ternary complexes with H_2O as

[*] Cf. footnote 31 in Ref. [28].—From a kinetic point of view this "static" approach may not seem very satisfactory, since coordination of the first ligand group is usually rate determining. However, mono- and bidentate ligands actually show rather different values [2, 15] for $\log K^{CuA}_{CuA_2} - \log K^{Cu}_{CuA}$, in accord with the reasoning used above.

[**] In binary 1:2 complexes the reverse reaction is favored by a factor of 2 compared with the 1:1 complex, hence one has to add -0.3 log units to the above statistical values.

[*] Abbreviations: Bipy = 2,2'-bipyridyl; Dhns = 6,7-Dihydroxynaphthalene-2-sulfonate; En = ethylenediamine; Et_2en = *N,N'*-diethylethylenediamine; Gly = glycinate; Ida = iminodiacetate; Mal = malonate; Men = 1,2-diaminopropane; Ox = oxalate; Phen = 1,10-phenanthroline; Prop = 1,3-diaminopropane; Pyr = pyrocatecholate; Tir = (Tiron) 1,2-dihydroxybenzene-3,5-disulfonate. AMP, ADP and ATP, adenosine 5'-mono-, 5'-di- and 5'-triphosphate; the 5'-di- or 5'-triphosphates of inosine, guanosine, cytosine, uridine, and thymidine are IDP, ITP, GDP, GTP, CDP, CTP, UTP, and TTP.

the second ligand"[21] is favored. Similar reasoning holds for Eqs. (19) and (20): the removal of a coordinated acetate residue is possible ($\log X > 0.6$) under conditions where the ligands are in excess compared to the metal ion, while with low ligand concentrations the mixed-ligand complex is not favored ($\Delta \log K < -0.9$).

Besides bulky groups or a "surplus" of donor atoms, the ring-size of chelates may influence the formation of ternary complexes. As a tentative rule it is concluded[31, 39] that mixed-ligand chelates containing a five- and a six-membered ring are favored compared to those containing two rings of equal size (cf. Section 2.7). Moreover, it appears that ternary chelates containing two six-membered rings are somewhat more stable than the corresponding complexes with two five-membered rings (cf. Table 1).

Table 1. Influence of the chelate-ring size on the stability of ternary Cu^{2+} complexes [31]; $I = 0.1$, $NaClO_4$; 25 °C.

Equilibrium		$\log X$	$\Delta \log K$ [a]
$Cu(En)_2^{2+} + Cu(Ox)_2^{2-}$	$\rightleftharpoons 2\,Cu(En)(Ox)$	0.94	−0.79
$Cu(En)_2^{2+} + Cu(Mal)_2^{2-}$	$\rightleftharpoons 2\,Cu(En)(Mal)$	2.31	−0.76
$Cu(Prop)_2^{2+} + Cu(Ox)_2^{2-}$	$\rightleftharpoons 2\,Cu(Prop)(Ox)$	3.14	−0.35
$Cu(Prop)_2^{2+} + Cu(Mal)_2^{2-}$	$\rightleftharpoons 2\,Cu(Prop)(Mal)$	2.55	−1.30

[a] Cf. Eqs. (12) and (13).

2.4. Formation of π Bonds

It had already been recognized several years ago that the presence of an aromatic amine is crucial for a high stability of a ternary complex[2]. This has been repeatedly confirmed[8–10, 23, 27, 30, 40], and was attributed to π back-bonding from the metal ion to the aromatic amine[2, 23]. This is in accord with the results of Table 2: the stability of the ternary complexes, (amine)Cu(pyrocatecholate), decreases with decreasing π acceptor qualities of the amines[40, 41]. That the π system of the ligand with O donors also has some influence on the stability can be seen by comparing the results of Eq. (14) with the last system given in Table 2. The occurrence of cooperative effects[23, 40] between the π systems of two ligands[42] bound to the same metal ion was also demonstrated in Cu^{2+} systems containing an aromatic amine, 2,2'-bipyridyl or 1,10-phenanthroline, and pyrocatecholate derivatives with electron-withdrawing or electron-donating substituents[43]. Further evidence for π back-bonding and the transmission of electronic effects through bonding orbitals in mixed-ligand complexes was obtained from electronic spectra, ESR parameters[19], and CD studies[21] (cf. also Ref. [44]).

Table 2. Influence of the π acceptor capability of the amine in (amine)Cu(pyrocatecholate) complexes [40]; $I = 0.1$, $NaClO_4$; 25 °C.

Ligand A	$\Delta \log K$	$\log X$	$pK^{H}_{H_2A}$	pK^{H}_{HA}
2,2'-Bipyridyl	+0.43	6.15	−0.2	4.49
4-(2'-Pyridyl)imidazole	+0.11	5.47	1.33	5.49
2-Picolylamine	−0.11	4.64	2.05	8.70
4-Aminomethylimidazole	−0.35	3.46	4.73	9.35
Ethylenediamine	−0.76	2.65	7.10	9.89

The described π back-bonding effects are certainly closely connected with the observation of a discriminating behavior[2, 23] of binary Cu^{2+}-*aromatic* amine 1:1 complexes[8]: ligands with O donors, like phenolates[23, 43], carboxylates[42, 45–47], phosphates[27, 41], *etc.*[42, 46, 47], are preferably bound. The systems of Fig. 1[23, 31, 39, 48a] demonstrate this for the Cu^{2+}-2,2'-bipyridyl 1:1 complex, *i. e.* pyrocatecholate or oxalate forms more stable complexes with $Cu(bipyridyl)^{2+}$ than 1,2-diaminobenzene or ethylenediamine. For "mixed" N/O ligands, like *o*-aminophenolate or glycinate, the $\Delta \log K$ and $\log X$ values are about midway between those observed for pure O and N donors[23, 49, 50]. In contrast *aliphatic* amine-Cu^{2+} complexes, like $Cu(En)^{2+}$, show no discriminating qualities.

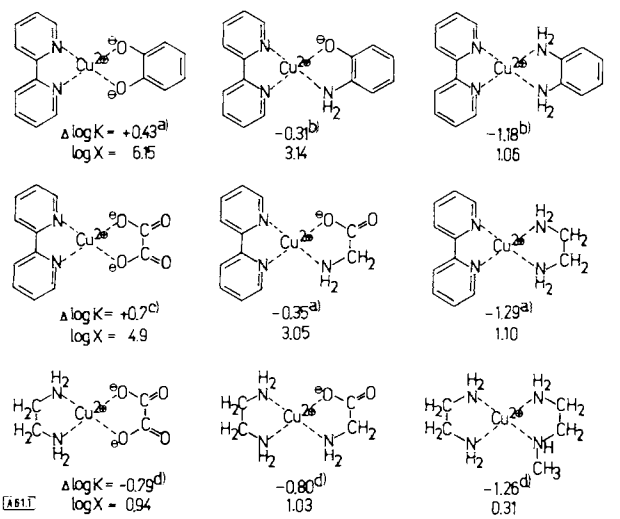


Fig. 1. The discriminating qualities of $Cu(2,2'\text{-bipyridyl})^{2+}$; the data are from refs.: a) [23], b) [48a], c) [39], and d) [31].

The other most surprising fact is that *positive* $\Delta \log K$ values are observed (cf. Fig. 1 and Table 2): ligands containing oxygen as donor atoms form more stable complexes with $Cu(bipyridyl)^{2+}$ than with Cu^{2+}_{aq}, *i. e.* the equilibrium in Eq. (13) is displaced to the right. The high stability of these ternary complexes is confirmed by the correspondingly large $\log X$ values[*].

2.5. Other Factors

Other factors possibly influencing the stability of mixed-ligand complexes are the following:

1. Schiff base formation within the coordination sphere of the metal ion, *e. g.* between an amino acid and pyruvate, leads to a ligand of higher denticity and thus to a larger stability compared with the complexes of the simple ligands[53].

2. Charge-transfer interaction between two suitable ligands within a ternary complex can also occur (for examples see Section 3.2).

3. Hydrogen bond formation between the two ligands bound to a metal ion, as known for example from the binary bis(dimethylglyoximato)Ni^{II} complex, also appears possible in ternary complexes, especially in biological systems where ligands like proteins and nucleic acids participate in complex formation.

[*] With regard to the $\log X$ formulation one could be tempted to argue [21] that the octahedral *cis*-diaquo-$Cu(Bipy)_2^{2+}$ complex [51, 52] is an inappropriate reference for the square planar ternary complexes. This is not so because $Cu(Bipy)_2^{2+}$ *exists* and thus Eq. (9) is a thermodynamic reality. [Furthermore, as certainly $\log K^{Cu(Bipy)}_{cis\text{-}Cu(Bipy)_2} \geq \log K^{Cu(Bipy)}_{trans\text{-}Cu(Bipy)_2}$ the values of $\log X$ (cf. Eq. (11)) may rather be considered too small, hence all given conclusions are valid in any case.] However, for certain comparisons, like ESR parameters or electronic spectra [19], *cis*-$Cu(Bipy)_2^{2+}$ is indeed not a usable reference.

All these latter factors have in common that ligands forming the higher order complex are not only bridged *via* the central metal ion but are also directly "linked" together.

2.6. Ligand-Basicity and Mixed-Ligand Complex Stability

For binary complexes it is well-known that for a series of structurally related ligands a straight line is observed, if *e.g.* $\log K^{Cu}_{CuA}$ is plotted *versus* pK^{H}_{HA}[54]. Apart from a few exceptions[55] complex stability increases with increasing basicity of the ligands. The same is true for ternary complexes if $\log \beta^{Cu}_{CuAB}$ or $\log K^{CuB}_{CuBA}$ is plotted *versus* pK^{H}_{HA} $(+pK^{H}_{H_2A})$; examples are 2,2'-bipyridyl-Cu^{2+}-carboxylate[9, 42, 45–47], 2,2'-bipyridyl-Cu^{2+}-aminoacetate[8, 56], and 2,2'-bipyridyl-Cu^{2+}-peptide systems[30]. However, in the case of ternary complexes a further dependence, namely between $\Delta \log K$ or $\log X$ and pK^{H}_{HA} $(+pK^{H}_{H_2A})$, is observable[57]. This is surprising since $\Delta \log K$ and, likewise, $\log X$ are only *indirectly* dependent on ligand basicity (cf. Section 2.1)[21], because none of the species occurring in Eqs. (9) and (13) can react directly with a proton, as is possible in the case of the free ligands A or B occurring in Eqs. (1) to (6). The dependence of $\Delta \log K$ or $\log X$ on the ligand basicity is especially remarkable if an aromatic amine is involved; in this case slopes of any kind are possible (cf. Fig. 2). Obviously, the basicity of these ligands is influenced by the π electron distribution even though H is bound only by a σ bond; that complex stability is dependent upon π electron distribution is well-known (Section 2.4)[55]. It should also be noted that the amines of Table 2 are *not* "related" enough for a straight line to be observed on plotting $\log K^{Cu}_{Cu(amine)}$ or $\log \beta^{Cu}_{Cu(amine)(Pyr)}$ *versus* $pK^{H}_{H_2A}+pK^{H}_{HA}$, whereas linear plots are observed with the corresponding $\Delta \log K$ or $\log X$ values.

The importance of these plots from the practical standpoint is that they afford a means for estimating the stabilities of ternary complexes that have not yet been studied (for possible pitfalls cf. Ref. [57]). For example, from the known values of the histamine-Cu^{2+}-ethylenediamine and histamine-Cu^{2+}-serinate systems—the latter ligand coordinates glycine-like[16]—the constants, $\log X$ (or $\Delta \log K$), for the histamine-Cu^{2+}-oxalate system may be estimated. In general, it is more favorable to use $\log X$ for the estimation because here differences are more significant. Obviously, with $\log X$ and the tabulated data[15] of the binary complexes all data of interest for the ternary system can be calculated. This method appears especially valuable for the estimation of stabilities of ternary complexes containing metal ions other than Cu^{2+}, because for these not many constants have as yet been determined[8, 16, 58, 59]. Constants estimated in this way certainly lead to more reliable conclusions than the simple use of statistical values.

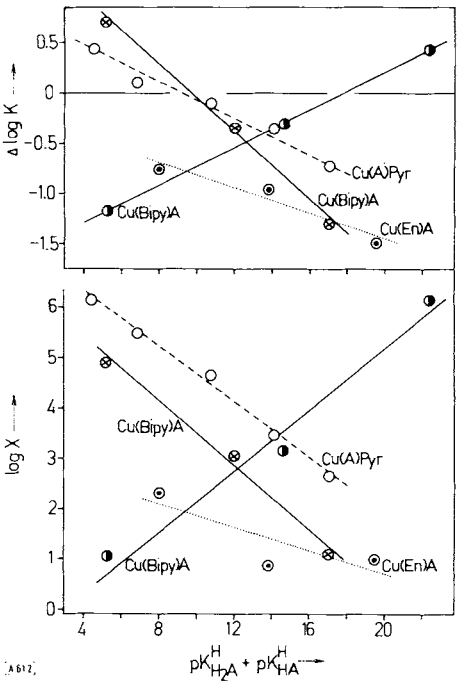


Fig. 2. Relation between $\Delta \log K$ (upper part) or $\log X$ (lower part) and $pK^{H}_{H_2A}+pK^{H}_{HA}$ for the ternary complexes Cu(A)Pyr where A = 2,2'-bipyridyl, 4-(2'-pyridyl)imidazole, 2-picolylamine, 4-aminomethylimidazole or ethylenediamine (in the figure from the left to the right) and Pyr = pyrocatecholate (○; cf. Table 2) [40], Cu(Bipy)A where A = oxalate, glycinate and ethylenediamine and Bipy = 2,2'-bipyridyl (⊗) [23, 39], Cu(En)A where A = malonate, β-alaninate and 1,3-propylenediamine and En = ethylenediamine (◉) [31], and Cu(Bipy)A where A = 1,2-diaminobenzene, *o*-aminophenol and pyrocatecholate (◑) [23, 48a].

2.7. Conclusions

Among the common driving forces (Sections 2.1 to 2.4) leading to mixed-ligand complexes π bond formation is the

Table 3. Comparison of the stability of some representative ternary Cu^{2+} complexes ($I = 0.1$; 25 °C).

Ligand A	Ligand B	$\Delta \log K$	$(\log K^{Cu}_{CuA} - \log K^{CuA}_{CuA_2})$	$(\log K^{Cu}_{CuB} - \log K^{CuB}_{CuB_2})$	$(\log K^{CuB}_{CuBA} - \log K^{CuA}_{CuA_2})$	$(\log K^{CuA_B}_{CuA_B} - \log K^{CuB}_{CuB_2})$	$\log X$	Ref.
Bipy	Pyr	+0.43	2.40	2.89	2.83	3.32	6.15	[23]
Bipy	Ox	+0.7	2.40	1.24	3.10	1.90	4.9	[39]
Bipy	Gly	−0.35	2.40	1.35	2.05	1.00	3.05	[23]
Bipy	En	−1.29	2.40	1.28	1.11	−0.01	1.10	[23]
En	Pyr	−0.76	1.28	2.89	0.52	2.13	2.65	[40]
En	Ox	−0.79	1.28	1.24	0.49	0.45	0.94	[31]
En	Gly	−0.80	1.28	1.35	0.48	0.55	1.03	[31]
En	Men	−1.26	1.38	1.45	0.12	0.19	0.31	[31] [a]
En	Ida	−2.3	1.51	5.03	−0.8	2.7	1.9	[38] [b]
Phen	Pyr	+0.35	2.50	2.89	2.85	3.24	6.09	[43]
Phen	Tir	−0.09	2.50	3.14	2.41	3.05	5.46	[43]
Phen	Dhns	+0.82	2.50	3.82	3.32	3.64	6.96	[43]
Statistical values:		−0.9	(1.2)	(1.2)	0.3	0.3	0.6	[c]

[a] Calculated from the results of *Näsänen* and *Koskinen* as described in Ref. [31].
[b] These values correspond to 30 °C.
[c] Cf. Sections 2.1 and 2.7, and the footnote [**] on p. 395.

most effective one, which results even in positive values for $\Delta \log K$. The data of Table 3 show that quite generally the largest contribution to $\log X$ arises from the ligand which has the greatest difference in stability between the 1:1 and 1:2 complexes[23]. This difference [Eq. (21)] reflects the stability of

$$\mathrm{CuA} + \mathrm{CuA} \rightleftharpoons \mathrm{CuA_2} + \mathrm{Cu} \qquad \Delta \log K_{21(\mathrm{A})} = \log K^{\mathrm{CuA}}_{\mathrm{CuA_2}} - \log K^{\mathrm{Cu}}_{\mathrm{CuA}} \tag{21}$$

CuA (or similarly CuB) towards "disproportionation"[*]. The connection between Eqs. (12) and (13) and Eq. (21) is obvious. The relation between $\Delta \log K$ [Eq. (12)] and $\log X$ [Eq. (11)] is given in Eq. (22)[21]. The statistically expected value for

$$\log X - 2\Delta \log K = (\log K^{\mathrm{Cu}}_{\mathrm{CuA}} - \log K^{\mathrm{CuA}}_{\mathrm{CuA_2}}) + (\log K^{\mathrm{Cu}}_{\mathrm{CuB}} - \log K^{\mathrm{CuB}}_{\mathrm{CuB_2}}) \tag{22}$$

the term, $\log X - 2\Delta \log K$, is 2.4 (cf. Section 2.1), and $\Delta \log K_{21(\mathrm{A})} = -{}^1/_2(\log X - 2\Delta \log K) = -1.2$ (cf. also footnote [**] on p. 395). This value also corresponds favorably with many of those observed for simple non-"*aromatic*" ligands (cf. Table 3 and Ref. [15]). Additionally, it is worth noting that the difference of the two terms on the right side of Eq. (22) is equal to the difference of the two terms on the right side of Eq. (11) [cf. Eq. (23)].

$$(\log K^{\mathrm{Cu}}_{\mathrm{CuA}} - \log K^{\mathrm{CuA}}_{\mathrm{CuA_2}}) - (\log K^{\mathrm{Cu}}_{\mathrm{CuB}} - \log K^{\mathrm{CuB}}_{\mathrm{CuB_2}}) = (\log K^{\mathrm{CuB}}_{\mathrm{CuBA}} - \log K^{\mathrm{CuA}}_{\mathrm{CuA_2}}) - (\log K^{\mathrm{CuA}}_{\mathrm{CuAB}} - \log K^{\mathrm{CuB}}_{\mathrm{CuB_2}}) \tag{23}$$

Hence, considering the differences in stability between the 1:1 and 1:2 Cu^{2+} complexes for the ligands, A and B, and taking into account the factors outlined in Sections 2.2 to 2.4 one may tentatively answer the question of the tendency of formation of the corresponding ternary complex, CuAB. Finally, in order to develop a feeling for the concentrations of the several species present in a mixed-ligand system three examples with representative stabilities of CuAB are given in Fig. 3. In this connection it must be noted that, for example, the concentration of the ternary complex, 2,2'-bipyridyl-Cu^{2+}-α-aminoacetate, reaches about 94% of the total Cu^{2+} present, while the binary complex, Cu^{2+}-α-aminoacetate, in the corresponding binary system reaches only about 67%[60]. Thus, in the binary system, the concentrations of Cu^{2+} and the 1:2 complex are still relatively high (each about 16%), while in the mixed-ligand system the ternary complex dominates very strongly.

Having the factors discussed in mind, one begins to realize why even "simple" binary Cu^{2+} systems can be seemingly complicated. For example, the Cu^{2+}-histidine 1:2 complex is actually an internal ternary complex, *i.e.* one histidine is bound histamine-like and the other glycine-like[8, 21, 61] to the square coordination sphere of Cu^{2+}. Similarly, in the square-plane around Cu^{2+} in the corresponding *S*-methylcysteine 1:2 complex there are two N, one O, and one S donor[62].

Finally, the observation of positive $\Delta \log K$ values leads to the question whether the enhanced stability is due to an increased rate of complex formation or to a reduced rate

[*] Here is also the origin of the rule (cf. Section 2.3) that ternary complexes containing a 5- and a 6-membered chelate are usually more stable than the corresponding 5-,5- or 6-,6-membered complexes because $\Delta \log K_{21(\mathrm{A})}$ is commonly more negative for binary 6-membered chelates than for 5-membered ones.

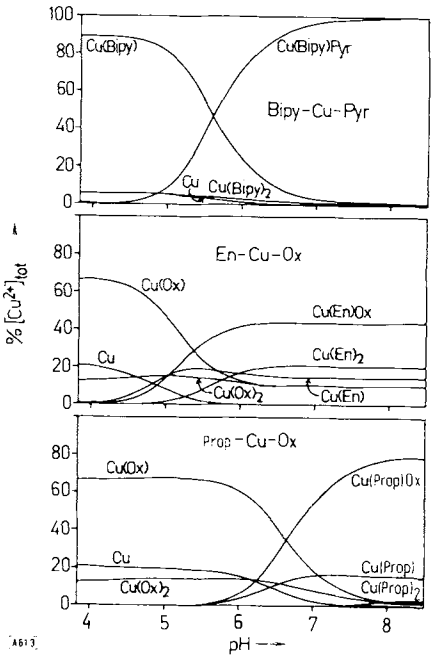


Fig. 3. Dependence of concentration (given as the percentage of the total Cu^{2+} present) on pH for the various species in an aqueous solution ($I = 0.1$; 25 °C) of Cu^{2+}, 2,2'-bipyridyl (Bipy), and pyrocatecholate (Pyr) [upper part; cf. the first system of Table 2; Cu(Pyr) reaches its maximum concentration at pH 6 with 1.2%; $Cu(Pyr)_2^{2-}$ is less than 0.1% at pH <8.5] or Cu^{2+}, ethylenediamine (En), and oxalate (Ox) [middle part: cf. Eqs. (14) and (16)] or Cu^{2+}, 1,3-propylenediamine (Pr), and oxalate [lower part: cf. Table 1]. All data were computed with the constants given in the literature (Bipy/Pyr [23], En/Ox [31], Pr/Ox [31]) for concentrations of 10^{-3} M for each reactant; hydrolysis was neglected in these calculations.

of dissociation. So far no unequivocal answer can be given since it has not yet been possible to study $Cu(Bipy)^{2+}$-O donor systems; however, some conclusions may be drawn from the results of Eqs. (24) and (25)[28]. As the charges of

$$\mathrm{Cu^{2+}} + \mathrm{Gly^-} \underset{22\,\mathrm{s^{-1}}}{\overset{4\cdot 10^9\,\mathrm{M^{-1}s^{-1}}}{\rightleftharpoons}} \mathrm{Cu(Gly)^+} \tag{24}$$

$$\mathrm{Cu(Bipy)^{2+}} + \mathrm{Gly^-} \underset{19\,\mathrm{s^{-1}}}{\overset{1.6\cdot 10^9\,\mathrm{M^{-1}s^{-1}}}{\rightleftharpoons}} \mathrm{Cu(Bipy)(Gly)^+} \tag{25}$$

the corresponding species are identical, and the reverse rate constants are also about the same, the forward rate constants can be compared directly if that of Eq. (24) is "corrected" by a statistical factor of ${}^1/_8$ (cf. Section 2.1). Hence, we obtain an additional factor of about 3 for the formation of the ternary complex. Analogous results have been obtained for the 2,2'-bipyridyl-Cu^{2+}-alaninate system[63, 64].

3. Structural Aspects

3.1. Displacement of Ligand Groups

The displacement of ligand groups during the formation of a ternary complex is quite common [*e.g.* Eqs. (19) and (20)], but it is important to realize that this fact may drastically change the qualities of a system. An example of this is given in Table 4 where binary Cu^{2+}-peptide complexes are compared with ternary 2,2'-bipyridyl-Cu^{2+}-peptide complexes[30]. The deprotonation of the first amide group—systems 1 to 5—occurs in the binary complexes from pH 4 through 7, while in *all* the ternary complexes the proton is displaced at pH ≈ 8. Furthermore, in *all* the ternary systems only the first amide

group is deprotonated while in the suitable binary systems up to three amide groups are deprotonated (for the structures cf. Ref. [30])[8]. These differences result from the coordination of 2,2'-bipyridyl, leading to only two available coordination positions at Cu^{2+} for the peptides (which should also influence the hydrolysis of the peptides).

pyrimidine residues participate in complex formation, the acidification is considerable.

Summarizing, by the formation of mixed-ligand complexes, created from ligands that have in total more binding sites than necessary to saturate the coordination sphere of the metal ion, new qualities can be achieved. These include *e.g.*,

Table 4. Equilibrium constants of binary Cu^{2+}-peptide and ternary 2,2'-bipyridyl-Cu^{2+}-peptide systems ($I=0.1$; 25 °C).

No.	Ligand (L)	pK^{H}_{HL}	$\log K^{Cu}_{CuL}$	pK^{H}_{CuL}	$pK^{H}_{Cu(L-1H)}$	$pK^{H}_{Cu(L-2H)}$	$\log K^{Cu(Bipy)}_{Cu(Bipy)L}$	$pK^{H}_{Cu(Bipy)L}$	$\Delta\log K$
1	Glycine amide [50]	8.04	5.40	7.01			5.01	7.71	−0.39
2	Diglycine [48b, 30] [a]	8.15	5.55	3.99			5.09	7.77	−0.46
3	Diglycine amide [30]	7.91	5.05	5.10	7.29		4.92	≈7.4	−0.13
4	Triglycine [30] [b]	7.96	5.24	5.22	6.60		4.87	8.17	−0.37
5	Tetraglycine [30] [c]	7.97	5.08	5.50	6.89	9.29	4.86	≈8.5	−0.22
6	Glycyl-L-leucine [48b, 65] [d]	8.28	5.89	4.76			5.75	8.58	−0.14
7	L-Leucylglycine [48b, 65] [e]	8.10	4.8	3.3			4.13	6.33	−0.7

[a] $pK^{H}_{H2L}=3.11$; [b] $pK^{H}_{H2L}=3.27$; [c] $pK^{H}_{H2L}=3.24$; [d] $pK^{H}_{H2L}=3.13$; [e] $pK^{H}_{H2L}=3.05$.

By way of contrast the initial complex formation between Cu^{2+}, the terminal amino residue and the oxygen of the neighboring amide group is independent of the potential binding sites in the side chain (*e.g.*, R = H or R = glycylglycylglycyl), because for steric reasons these sites are prevented from coordination. In agreement herewith are the observed $\Delta\log K$ values (Table 4) in the order expected for N/O-ligands (cf. Fig. 1). For completeness, it must be mentioned that a bulky group, as present in the leucyl moiety (cf. systems 6 and 7), imposes steric strains on the peptide which lead to a considerable influence on the initial complex formation and on the deprotonation of the amide group. Needless to say, all the described effects have large influences on the distribution of the several complex species (cf. the figures in Refs. [8] and [30]).

The structural changes imposed by mixed-ligand complex formation are also evident from the following examples. In $Cu(ATP)^{2-}$ the metal ion coordinates to N-7 of the adenine moiety and to the β- and γ-phosphate groups forming a macrochelate[66, 67]. By the formation of the mixed complex, Cu(Bipy)(ATP)$^{2-}$, the adenine moiety is pushed out of the coordination sphere[27, 68]. The same holds for the ternary 2,2'-bipyridyl-Cu^{2+}-nucleotide complexes with ITP, GTP, UTP, and TTP, as can be concluded from the deprotonation behavior of the base moieties[69]: free nucleotides, $pK_A \approx 9.5$; Cu^{2+} complexes, $pK_A \approx 7.7$; and ternary Cu^{2+} complexes, $pK_A \approx 9.0$. If coordination of the bases is prevented their deprotonation occurs at about the same pH as in the uncomplexed nucleotides, while in the binary complexes, where the purine and

certain protonated species that cannot be formed in either of the corresponding binary systems [8].

3.2. Charge-Transfer Interaction between the Two Ligands within a Ternary Complex

The adenine moiety of adenosine, AMP or ATP forms with 2,2'-bipyridyl or Cu(2,2'-bipyridyl)$^{2+}$ charge-transfer adducts which exhibit an absorption that may be used to determine the stability constants, K_{CT}, for Eqs. (26) and (27)[70].

$$\text{Bipy} + \text{Ad} \rightleftharpoons (\text{Bipy})(\text{Ad}) \quad (26)$$

$$\text{Cu(Bipy)}^{2+} + \text{Ad} \rightleftharpoons \text{Cu(Bipy)(Ad)}^{\pm n} \quad (27)$$

Ad = adenosine, AMP^{2-}, or ATP^{4-}

The data of Table 5 indicate that the binary charge-transfer adducts and that of Cu(Bipy)(adenosine)$^{2+}$ are of comparable stability, while the adducts formed between $Cu(Bipy)^{2+}$ and AMP^{2-} or ATP^{4-} are considerably more stable.

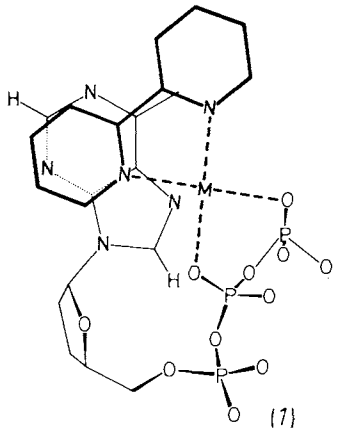
Table 5. Stability constants of charge-transfer adducts ($\log K_{CT}$) [70] between 2,2'-bipyridyl and Cu(2,2'-bipyridyl)$^{2+}$ and the purine moieties of adenosine or its nucleotides [a].

System	$\log K_{CT}$	$\log K^{Cu(Bipy)}_{Cu(Bipy)(NP)}$	$\log K^{Cu}_{Cu(NP)}$	$\Delta\log K$
Bipy + Adenosine	1.36 ± 0.06			
Bipy + AMP^{2-}	1.41 ± 0.09			
Bipy + ATP^{4-}	0.91 ± 0.22			
$Cu(Bipy)^{2+}$ + Adenosine	1.52 ± 0.04			
$Cu(Bipy)^{2+}$ + AMP^{2-}	3.78 ± 0.27	3.72 [b]	3.22 [b]	+0.50
$Cu(Bipy)^{2+}$ + ATP^{4-}	6.96 ± 0.25	6.91	6.38	+0.53

[a] The stability constants of the potentiometrically determined corresponding ternary ($\log K^{Cu(Bipy)}_{Cu(Bipy)(NP)}$) and binary ($\log K^{Cu}_{Cu(NP)}$) complexes are given for comparison [27]. If not otherwise stated the data refer to aqueous solutions and 25 °C. NP = AMP^{2-} or ATP^{4-}.
[b] Solvent: water containing 10 percent dioxane.

Comparison with the potentiometrically determined stability constants for these ternary complexes shows that $\log K_{CT} \approx \log K^{Cu(Bipy)}_{Cu(Bipy)(NP)}$ (cf. Table 5). Cu(Bipy)(AMP) and Cu(Bipy)(ATP)$^{2-}$ must exist in a conformation[70] which facilitates a charge-transfer interaction between 2,2'-bipyridyl and the adenine moiety; hence, we are studying metal ion-bridged charge-transfer adducts having the tentatively assigned structure (*1*)[68, 70].

It should be noted that the positive values obtained for $\Delta\log K$ (cf. Table 5) are most probably not a result of direct



(1)

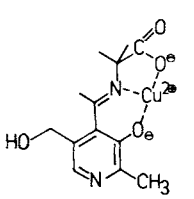
interaction between the two ligands within these ternary complexes. These data are of the order one would expect on the basis of results of Section 2.4 and Fig. 1. Finally, similar charge-transfer interactions have also been observed with inosine[68, 70] and guanosine[71] and their nucleotides, as well as in tryptophan-M^{2+}-ATP systems[72]; the biological implications are obvious.

Aside from the problems of major interest here it is worth noting that the stability constant of the binary Cu(adenosine)$^{2+}$ complex is $\log K^{Cu}_{Cu(ad)} = 0.70$[73] (or = 0.84)[67], *i.e.* smaller than that observed for the charge-transfer adduct between Cu(Bipy)$^{2+}$ and adenosine (Table 5). Even though in the latter formed species Cu^{2+} does not directly interact with the adenine residue, it is a ternary complex with the unique feature that an unsaturated metal ion is held in a distinct position. Such effects of "specificity" are certainly of importance in nature.

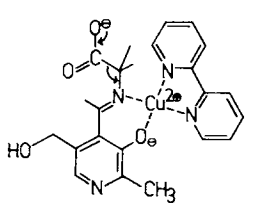
4. Reactivity of Ternary Cu^{2+} Complexes

4.1. Alteration of the Reactivity by Structural Effects

That structural effects will manifest themselves in the rate and specificity of reactions is to be expected. For example, the reactive species for the decarboxylation of pyridoxylidenealanine is created by the formation of a ternary complex[5, 74]. The Cu^{2+} 1:1 chelate of pyridoxylidenealanine (Structure *(2)*) is not readily decarboxylated since the required electron



(2)



(3)

shift in the carboxylate group is opposed by the electronic effect of the coordinated metal ion. When, however, the available coordination sites on Cu^{2+} are restricted to two donor groups by prior combination with 2,2'-bipyridyl, decarboxylation occurs in the now bivalently coordinated Schiff base. The electron-withdrawal effect of the metal ion assists the decarboxylation as indicated in Structure *(3)*.

On the contrary, the following example demonstrates the inhibition of a reaction by preventing the creation of the active species through mixed-ligand complex formation. The results of Fig. 4 show that the dephosphorylation of ATP in the ternary complex, Cu(Bipy)(ATP)$^{2-}$, is insignificant compared with that of the binary complex, Cu(ATP)$^{2-}$. Moreover, in the pH range <7 even free ATP is somewhat more sensitive toward hydrolysis than is ATP in the mixed-ligand complex[75]. In the latter species the adenine moiety, *i. e.* N-7[66, 67], is unable to participate in complex formation (cf. Sections 3.1 and 3.2)[27, 68, 70], while in Cu(ATP)$^{2-}$ the reactive species is created by formation of a macrochelate[75, 76]. In accord with this interpretation is the relative stability of Cu(CTP)$^{2-}$ where the base-metal ion interaction is insignificant. The same holds for Cu(CDP)$^{-}$, while ADP, ITP, IDP, GTP and GDP may also be stabilized by mixed-ligand complex formation[75, 77], a result of interest with regard to the transport of hydrolysis-sensitive phosphates in biological systems.

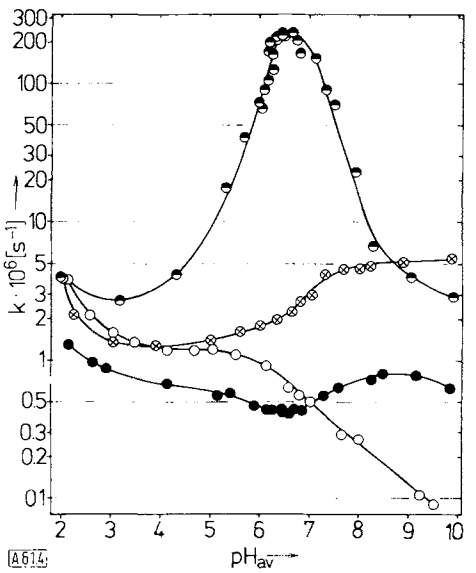


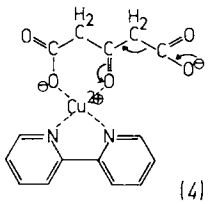
Fig. 4. Dephosphorylation of ATP under various conditions as a function of pH, characterized as the first order rate constant, k: ATP alone (○), ATP in the presence of Cu^{2+} (⊜) and of Cu^{2+} and 2,2'-bipyridyl (●). For comparison, the hydrolysis of CTP in the presence of Cu^{2+} is also shown (⊗). The concentration of all reagents was 10^{-3} M; $I = 0.1$, $NaClO_4$; 50 °C [75].

By mixed-ligand complex formation one may also influence the kind of reaction products formed. The oxidation of ascorbic acid to dehydroascorbic acid by O_2 with Cu^{2+} as catalyst leads to hydrogen peroxide, whereas in the presence of Cu^{2+} chelates water is formed. Both reactions proceed *via* higher order complexes[5, 78]. Similarly, there is some selectivity in the hydrolysis of amino acid esters, arising from the stereoselective interaction of optically active amino acids with Cu(L-valine-*N*-monoacetate). The rate of hydrolysis of leucine and phenylalanine methyl ester in the ternary complexes, L-valine-*N*-monoacetate-Cu^{2+}-ester, is higher for the D-amino acid ester than for the L-isomer[79].

4.2. Alteration of the Reactivity by Electronic Effects

This kind of influence is also to be expected, for example, by an increased tendency toward the formation of a reactive intermediate. Thus, the rate of the metal-ion catalyzed decarboxylation of acetonedicarboxylate, oxaloacetate, or dimethyloxaloacetate is increased by coordination of the metal ion

to an aromatic amine[80], while no enhancement or even lowering of the catalysis is observed with aliphatic amines[81] or anionic O donor ligands[82]. In the light of Section 2.4 this is understandable. For example, the rate constants, k_{cat}, obtained for the Cu^{2+}-catalyzed decarboxylation of acetonedicarboxylate with and without 2,2'-bipyridyl are 48 and 24 M^{-1} min^{-1}, respectively[80], *i.e.* by mixed-ligand complex formation the rate is increased by a factor of two. This corresponds exactly to the stability increase observed in the 2,2'-bipyridyl-Cu^{2+}-malonate system: $\Delta \log K = \log K^{Cu(Bipy)}_{Cu(Bipy)(Mal)} - \log K^{Cu}_{Cu(Mal)} = 5.37 - 5.10 = +0.27$[23], *i.e.* also a factor of about two. The connection between these two results is evident: the transition state *(4)* resembles malonate[*].



(4)

Similarly, the hydrolysis of diisopropyl fluorophosphate or of isopropyl methyl phosphonofluoride is catalyzed by Cu^{2+} complexes among which $Cu(Bipy)^{2+}$ is especially effective, while $Cu(Bipy)_2^{2+}$ is inactive. That $Cu(Bipy)^{2+}$ is an especially good catalyst, compared for example with $Cu(glycinate)^{+}$[85], appears very reasonable in terms of mixed-ligand complex formation and in the light of Section 2.4. Additionally, the complexes of L-histidine, 1,10-phenanthroline, and imidazole are also better catalysts than that of glycinate[85].

Another example is the Cu^{2+}-catalyzed disproportionation of hydrogen peroxide which is not only dependent upon the degree of saturation of the coordination sphere of the metal ion—*i.e.*, *e.g.* the activity decreases within the series of Cu^{2+} chelates formed with ethylenediamine > diethylenetriamine > triethylenetetramine—but also upon the kind of ligand bound to Cu^{2+}: *e.g.* within the following series of bidentate ligands the activity decreases (at a given pH), 2,2'-bipyridyl > ethylenediamine > glycinate > diphosphate[17]. Also, for Cu^{2+} and $Cu(Bipy)^{2+}$ ($=C$) the same rate law holds, *i.e.* $d[O_2]/dt = k[C][H_2O_2]^2/[H^+]$, indicating use of the same reaction path. However, $Cu(Bipy)^{2+}$ is 50 times more efficient as catalyst than is Cu^{2+}: $k_{Cu} = 1.15 \times 10^{-6}$ M s^{-1} and $k_{Cu(Bipy)} = 5.44 \times 10^{-5}$ M s^{-1}[86]. This observation can certainly not be explained solely by an increased tendency toward formation of Cu^{2+}-peroxo complexes in the presence of 2,2'-bipyridyl; in this case also a facilitated electron transfer in the intermediate 2,2'-bipyridyl-Cu^{2+}-peroxo species must be assumed.

5. General Conclusions

The driving forces leading to the formation of mixed-ligand Cu^{2+} complexes are *(i)* statistical reasons, *(ii)* neutralization of charge in the mixed-ligand complexes, *(iii)* steric factors and *(iv)* electronic effects, *i.e.* formation of π bonds (Sections 2.1—2.4). The same factors certainly apply to a large extent also to higher order complexes formed by other transition metal ions, like Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, and Zn^{2+}, while for those formed with ions like Mg^{2+} or Ca^{2+}, probably only points *(i)* to *(iii)* are important[8, 58]. A direct interaction between two ligands within a mixed-ligand complex, and thus a possible stability enhancement (Section 2.5), can occur with all metal ions forming such species. The indications given in Sections 2.6 and 2.7 may also help in estimating the stability of ternary complexes for any kind of metal ion.

That two different ligands in the coordination sphere of the same metal ion influence each other is quite obvious from the studies on the stability of ternary complexes. This influence may lead to distinct structural qualities (Section 3) as well as to pronounced effects on the reactivity (Section 4) of such systems; very subtle alterations can in this way be obtained. It is certainly not by chance that nature uses such higher order complexes for achieving specific conditions and reactions, as known for example from enzyme-metal ion-substrate complexes.

The support of this research by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung is gratefully acknowledged.

Received: August 8, 1974 [A 61 IE]
German version: Angew. Chem. *87*, 391 (1975)

[*] The linear relationship between the stability of binary divalent metal ion-malonate 1:1 complexes ($\log K^{Me}_{Mal}$) and the rate of decarboxylation ($\log k$) of acetonedicarboxylate has already been known for a long time [83]. An analogous relation exists for oxalate and oxaloacetate [84].

[1] *Y. Marcus* and *I. Eliezer*, Coord. Chem. Rev. *4*, 273 (1969).
[2] *H. Sigel*, Chimia *21*, 489 (1967).
[3] *A. T. Pilipenko* and *M. M. Tananaiko*, Zh. Anal. Khim. *28*, 745 (1973); cf. Chem. Abstr. *79*, 26723u (1973), contains 502 ref.: *V. P. R. Rao* and *Y. Anjaneyulu*, Mikrochim. Acta *1973*, 481 (1973); *R. F. Sieck* and *C. V. Banks*, Anal. Chem. *44*, 2307 (1972); *J. E. Chester*, *R. M. Dagnall*, and *T. S. West*, Talanta *17*, 13 (1970); *A. K. Babko*, *ibid. 15*, 721, 735 (1968).
[4] *D. S. Sigman* and *C. T. Jorgensen*, J. Amer. Chem. Soc. *94*, 1724 (1972); *R. Breslow* and *M. Schmir*, *ibid. 93*, 4960 (1971); *R. Breslow*, Advan. Chem. Ser. *100*, 21 (1971).
[5] *A. E. Martell:* Artificial Enzymes. Vol. 2 (1973) of Ref. [6], p. 207.
[6] *H. Sigel:* Metal Ions in Biological Systems. Marcel Dekker, New York.
[7] *D. D. Perrin* and *R. P. Agarwal:* Multimetal-Multiligand Equilibria: A Model for Biological Systems, Vol. 2 (1973) of Ref. [6], p. 167.
[8] *H. Sigel:* Structural Aspects of Mixed-Ligand Complex Formation in Solution, Vol. 2 (1973) of Ref. [6], p. 63.
[9] *H. Sigel* in *M. T. Beck:* Proc. 3rd Symp. Coord. Chem., Vol. I (1970), p. 191; Vol. II (1971), p. 241.
[10] *H. Sigel* and *D. B. McCormick*, Accounts Chem. Res. *3*, 201 (1970).
[11] *H. J. Kolb* and *H. Kolb*, Hoppe-Seyler's Z. Physiol. Chem. *354*, 331 (1973); *T. Nowak*, *A. S. Mildvan*, and *G. L. Kenyon*, Biochemistry *12*, 1690 (1973); *K. J. Schray* and *A. S. Mildvan*, J. Biol. Chem. *247*, 2034 (1972); *A. S. Mildvan* in *P. D. Boyer:* The Enzymes, Kinetics and Mechanisms, 3rd Edit., Vol. 2. Academic Press, New York 1970, p. 445.
[12] Cf. [6], Vol. 2 (1973).
[13] *V. S. Sharma* and *D. L. Leussing:* Kinetic Study of the Formation of Mixed-Ligand Complexes of Biological Interest, in [6], Vol. 2 (1973), p. 127.
[14] The distance of the axial ligands depends on the donor abilities of the atoms bound to the square plane; cf. *H. C. Freeman* in *J. Peisach*, *P. Aisen*, and *W. E. Blumberg:* The Biochemistry of Copper. Academic Press, New York 1966, p. 77; *H. C. Freeman*, Advan. Protein Chem. *22*, 257 (1967).
[15] *L. G. Sillén* and *A. E. Martell:* Stability Constants of Metal Ion Complexes. Spec. Publ. No. 17, The Chemical Society, London 1964; Suppl. No. 1, London 1971.
[16] *D. D. Perrin*, *I. G. Sayce*, and *V. S. Sharma*, J. Chem. Soc. *A 1967*, 1755; *1968*, 446; *1969*, 2060.
[17] *H. Sigel*, Angew. Chem. *81*, 161 (1969); Angew. Chem. internat. Edit. *8*, 167 (1969).
[18] The only exceptions to this rule are the octahedral 1:3 Cu^{2+} complexes formed with bidentate aromatic amines [15], like 2,2'-bipyridyl. However, ternary Cu^{2+} complexes containing 2,2'-bipyridyl are square planar [19—21].

[19] *F. A. Walker, H. Sigel,* and *D. B. McCormick,* Inorg. Chem. *11*, 2756 (1972).
[20] *I. M. Procter, B. J. Hathaway,* and *P. G. Hodgson,* J. Inorg. Nucl. Chem. *34*, 3689 (1972).
[21] *R. B. Martin* and *R. Prados,* J. Inorg. Nucl. Chem. *36*, 1665 (1974).
[22] *V. Romano* and *J. Bjerrum,* Acta Chem. Scand. *24*, 1551 (1970).
[23] *R. Griesser* and *H. Sigel,* Inorg. Chem. *9*, 1238 (1970).
[24] *R. DeWitt* and *J. I. Watters,* J. Amer. Chem. Soc. *76*, 3810 (1954).
[25] *S. Kida, Bull. Chem. Soc. Jap. 29*, 805 (1956).
[26] *V. S. Sharma* and *J. Schubert,* J. Chem. Educ. *46*, 506 (1969).
[27] *H. Sigel, K. Becker,* and *D. B. McCormick,* Biochim. Biophys. Acta *148*, 655 (1967).
[28] *R. F. Pasternack* and *H. Sigel,* J. Amer. Chem. Soc. *92*, 6146 (1970).
[29] *D. B. Moss, C.-T. Lin,* and *D. B. Rorabacker,* J. Amer. Chem. Soc. *95*, 5179 (1973).
[30] *H. Sigel, R. Griesser,* and *B. Prijs,* Z. Naturforsch. *27b*, 353 (1972).
[31] *H. Sigel, R. Caraco,* and *B. Prijs,* Inorg. Chem. *13*, 462 (1974).
[32] Under somewhat different conditions $\log X$ has been determined as 1.4 [33], 1.3 [34], 1.1 [25], and 1.0 [24].
[33] *J. I. Watters,* J. Amer. Chem. Soc. *81*, 1560 (1959).
[34] *W. B. Schaap* and *D. L. McMasters,* J. Amer. Chem. Soc. *83*, 4699 (1961).
[35] *J. I. Watters* and *E. D. Loughran,* J. Amer. Chem. Soc. *75*, 4819 (1953).
[36] *G. A. L'Heureux* and *A. E. Martell,* J. Inorg. Nucl. Chem. *28*, 481 (1966).
[37] *R. Näsänen* and *M. Koskinen,* Suom. Kemistilehti *B40*, 108 (1967).
[38] *W. E. Bennett,* J. Amer. Chem. Soc. *79*, 1290 (1957).
[39] *H. Sigel, P. R. Huber,* and *R. F. Pasternack,* Inorg. Chem. *10*, 2226 (1971).
[40] *P. R. Huber, R. Griesser,* and *H. Sigel,* Inorg. Chem. *10*, 945 (1971).
[41] *P. R. Huber* and *H. Sigel,* Z. Naturforsch. *27b*, 1319 (1972).
[42] *R. Griesser, B. Prijs,* and *H. Sigel,* Inorg. Nucl. Chem. Lett. *4*, 443 (1968).
[43] *H. Sigel, P. R. Huber, R. Griesser,* and *B. Prijs,* Inorg. Chem. *12*, 1198 (1973).
[44] *S. G. Schulman, W. P. Kilroy,* and *H. Gershon,* J. Phys. Chem. *72*, 3372 (1968); *S. G. Schulman* and *H. Gershon,* J. Inorg. Nucl. Chem. *31*, 2467 (1969).
[45] *R. Griesser, B. Prijs, H. Sigel,* and *D. B. McCormick,* Inorg. Nucl. Chem. Lett. *5*, 951 (1969).
[46] *H. Sigel, D. B. McCormick, R. Griesser, B. Prijs,* and *L. D. Wright,* Biochemistry *8*, 2687 (1969).
[47] *H. Sigel, R. Griesser,* and *D. B. McCormick,* Inorg. Chim. Acta *6*, 559 (1972).
[48] a) *H. Sigel* and *B. Prijs,* Chimia *29*, 134 (1975); b) *H. Sigel,* Inorg. Chem. *14* (1975), in press.
[49] *H. Sigel* and *B. Prijs,* Helv. Chim. Acta *50*, 2357 (1967).
[50] *H. Sigel,* Angew. Chem. *80*, 124 (1968); Angew. Chem. internat. Edit. *7*, 137 (1968).
[51] *M. Noack* and *G. Gordon,* J. Chem. Phys. *48*, 2689 (1968); *F. A. Walker* and *H. Sigel,* Inorg. Chem. *11*, 1162 (1972).
[52] Recently, it was concluded that this *cis* configuration is mainly due to electronic effects rather than a steric repulsion between the 6,6'-H atoms in a *trans* arrangement; *H. Sigel,* Inorg. Chim. Acta *6*, 195 (1972).
[53] *D. L. Leussing* and *D. C. Shultz,* J. Amer. Chem. Soc. *86*, 4847 (1964); *D. L. Leussing* and *E. M. Hanna, ibid. 88*, 693, 696 (1966); *D. L. Leussing* and *K. S. Bai,* Analyt. Chem. *40*, 575 (1968).
[54] *M. Calvin* and *K. W. Wilson,* J. Amer. Chem. Soc. *67*, 2003 (1945); *J. Bjerrum,* Chem. Rev. *46*, 381 (1950); *A. E. Martell* and *M. Calvin:* Chemistry of the Metal Chelate Compounds. Prentice-Hall, Englewood Cliffs, N. J. 1952; *H. Irving* and *H. Rossotti,* Acta Chem. Scand. *10*, 72 (1956).
[55] *H. Sigel* and *Th. Kaden,* Helv. Chim. Acta *49*, 1617 (1966).
[56] *R. Griesser, B. Prijs, H. Sigel, W. Föry, L. D. Wright,* and *D. B. McCormick,* Biochemistry *9*, 3285 (1970).
[57] *H. Sigel,* J. Inorg. Nucl. Chem. *37*, 507 (1975).
[58] *R. Griesser* and *H. Sigel,* Inorg. Chem. *10*, 2229 (1971).
[59] *R. P. Martin, M. M. Petit-Ramel,* and *J. P. Scharff:* Mixed-Ligand Metal Ion Complexes of Amino Acids and Peptides, in [6], Vol. 2 (1973), p. 1.
[60] Cf. Fig. 3 in [8], and Fig. 5 in [56].
[61] *E. W. Wilson, Jr., M. H. Kasperian,* and *R. B. Martin,* J. Amer. Chem. Soc. *92*, 5365 (1970); *H. Sigel* and *D. B. McCormick, ibid. 93*, 2041 (1971).
[62] *D. B. McCormick, H. Sigel,* and *L. D. Wright,* Biochim. Biophys. Acta *184*, 318 (1969); *G. Rotilio* and *L. Calabrese,* Arch. Biochem. Biophys. *143*, 218 (1971).
[63] *R. F. Pasternack, P. R. Huber, U. M. Huber,* and *H. Sigel,* Inorg. Chem. *11*, 276 (1972).
[64] The kinetics of mixed-ligand complex formation has recently been reviewed [13].
[65] *R. F. Pasternack, L. Gipp,* and *H. Sigel,* J. Amer. Chem. Soc. *94*, 8031 (1972).
[66] *M. Cohn* and *T. R. Hughes,* J. Biol. Chem. *237*, 176 (1962).
[67] *P. W. Schneider, H. Brintzinger,* and *H. Erlenmeyer,* Helv. Chim. Acta *47*, 992 (1964).
[68] *Ch. F. Naumann, B. Prijs,* and *H. Sigel,* Eur. J. Biochem. *41*, 209 (1974).
[69] *H. Sigel,* Eur. J. Biochem. *3*, 530 (1968); *H. Sigel,* J. Amer. Chem. Soc. *97* (1975), in press.
[70] *Ch. F. Naumann* and *H. Sigel,* J. Amer. Chem. Soc. *96*, 2750 (1974).
[71] *H. Sigel, Ch. F. Naumann,* and *B. Prijs,* Eur. J. Biochem. *46*, 589 (1974).
[72] *Ch. F. Naumann* and *H. Sigel,* FEBS Lett. *47*, 122 (1974); to be published.
[73] *A. M. Fiskin* and *M. Beer,* Biochemistry *4*, 1289 (1965).
[74] *A. E. Martell* in *M. T. Beck:* Proc. 3rd Symp. Coord. Chem., Vol. II (1971), p. 125.
[75] *D. H. Buisson* and *H. Sigel,* Biochim. Biophys. Acta *343*, 45 (1974); Angew. Chem. *84*, 1103 (1972); Angew. Chem. internat. Edit. *11*, 1025 (1972).
[76] *P. W. Schneider* and *H. Brintzinger,* Helv. Chim. Acta *47*, 1717 (1964).
[77] *H. Sigel, D. H. Buisson,* and *B. Prijs,* Bioinorg. Chem. (1975), in press.
[78] *M. M. Taqui Khan* and *A. E. Martell,* J. Amer. Chem. Soc. *89*, 4176, 7104 (1967); *90*, 6011 (1968).
[79] *B. E. Leach* and *R. J. Angelici,* J. Amer. Chem. Soc. *91*, 6296 (1969); cf. also *J. R. Blackburn* and *M. M. Jones,* J. Inorg. Nucl. Chem. *35*, 1597, 1605 (1973).
[80] *R. W. Hay* and *K. N. Leong,* Chem. Commun. *1967*, 800; J. Chem. Soc. *A 1971*, 3639.
[81] *J. V. Rund* and *K. G. Claus,* Inorg. Chem. *7*, 860 (1968).
[82] *J. V. Rund* and *R. A. Plane,* J. Amer. Chem. Soc. *86*, 367 (1964).
[83] *J. E. Prue,* J. Chem. Soc. *1952*, 2331; *R. J. P. Williams,* Endeavour *26*, 96 (1967).
[84] *E. Gelles* and *A. Salama,* J. Chem. Soc. *1958*, 3689.
[85] *T. Wagner-Jauregg, B. E. Hackley, Jr., T. A. Lies, O. O. Owens,* and *R. Proper,* J. Amer. Chem. Soc. *77*, 922 (1955); *R. L. Gustafson* and *A. E. Martell, ibid. 84*, 2309 (1962).
[86] *H. Sigel* and *K. Wyss,* unpublished results.

Field Desorption Mass Spectrometry

By H. D. Beckey and H.-R. Schulten[*]

Field desorption (FD) enables mass-spectrometric investigation of large organic molecules without their vaporization. The present state of our theoretical understanding of the ionization of these molecules in the adsorbed state on organic emitters is described. The special problems of the technique and prospective developments in the apparatus for future analytical problems are outlined. The present progress report concentrates on analytical studies of biochemical model compounds and degradation products from environmental chemicals and drugs. The method is particularly suitable for the detection and identification of submicrogram quantities of underivatized polar substances present in complex mixtures or pre-purified extracts from biological materials.

1. Introduction

In mid-1969 there appeared in this journal a review article on the qualitative and quantitative analysis of organic molecules by means of a field ionization mass spectrometer (FI-MS)[1]. The report mentioned field desorption (FD) of organic molecules[2] as a technique that had at that time been very recently introduced into mass spectrometry. Since then the FD technique has undergone rapid development. This new branch of mass spectroscopy is applied to the analysis of thermally labile and biologically important substances. Since the samples need not be vaporized for analysis, the mass of the molecular ion can in almost all cases be accurately determined, and the elemental composition of the compound can thus be established. In the following sections the physicochemical principles, the analytical possibilities and the problems of the FD method are summarized for the first time.

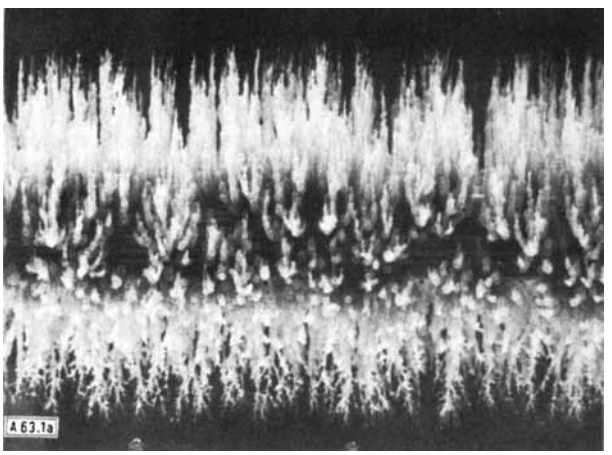
2. Principle of FD Mass Spectrometry

The "field desorption" concept has been known for a long time, especially through the fundamental work of *Müller*[3] and *Gomer*[4]. In their work atoms or small molecules such as H_2, O_2, or N_2 were desorbed from metallic tips into a field ion microscope by high electric fields of the order of 1×10^8 to 5×10^8 V/cm.

By "field desorption mass spectrometry" the mass spectroscopist today understands a special technique involving deposition of solid organic compounds on an "activated" field anode (emitter), subsequent field desorption of the compounds in an ionized state, and mass spectrometric analysis of these ions. A field anode is referred to as "activated" when it is covered with a very large number of carbonaceous microneedles.

In this technique the solid organic samples are not vaporized into the ion source[5]. They are dissolved or suspended in a suitable medium[21], usually at room temperature, and an activated field anode (preferably a 10-μm tungsten wire with a dense covering of microneedles) is then dipped into as concentrated as possible a solution of the sample ("emitter dipping technique"). When the field anode is subsequently removed some of the solution adheres to the microneedles or remains in the spaces between them. With a mean needle length of 30 μm this amounts to about 10^{-2} μl.

In another method[6] a droplet of the solution is dispensed onto the field anode from a microsyringe fitted to a micromanipulator. The advantages of this method are (i) that measured



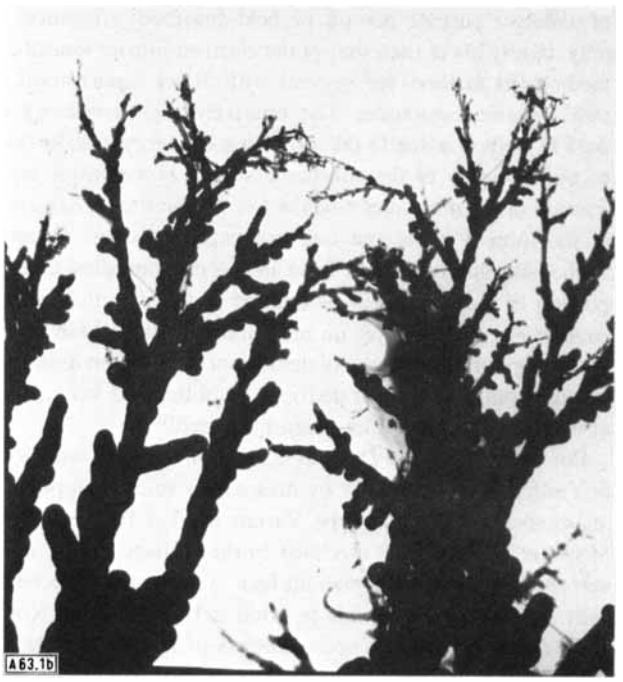


Fig. 1. a) Scanning electron microscope photograph of a tungsten wire 10 μm in diameter activated with benzonitrile vapor at 1200 °C. Length of microneedles ≈ 20 μm; b) Photograph of microneedles by a transmission electron microscope. On and between the microneedles there is a thin deposit (slighter darkening) of D-glucose which separated from a 0.01 M aqueous solution. The ends of the fine needles are brought closer together by some of the glucose threads (formed after evaporation of the water and are thereby somewhat bent).

[*] Prof. Dr. H. D. Beckey and Dr. H.-R. Schulten
Institut für Physikalische Chemie der Universität
53 Bonn, Wegelerstrasse 12 (Germany)

volumes of the solution can be deposited onto the anode (*e.g.* for a sensitivity test), (ii) that extremely small amounts of solution suffice, and (iii) that droplets of the sample solutions can be placed accurately on the center of the field anode.

The loaded field anode is then introduced through a vacuum lock into the ion source of a mass spectrometer. The solvent evaporates and the substance to be analyzed remains behind on or between the microneedles.

Fig. 1a is a photograph of a clean activated tungsten wire, taken by means of a scanning electron microscope. Fig. 1b is a transmission electronmicroscopic photograph of microneedles on and between which D-glucose has been deposited from 0.01 M solution. Although only about 10^{-8} g of D-glucose was deposited, an FD mass spectrum suitable for interpretation could be obtained. The detection limit of adenosine solution for analysis by the emitter dipping technique is about 10^{-5} M; this means that about 10^{-11} g is the smallest amount of an organic substance that can be detected by FD-MS when using a modified Varian MAT-CH4 mass spectrometer. This limit depends, on the one hand, on the nature of the substance, the solvent and its pH, and the morphological structure of the microneedles, and on the other, on the transmission of the mass spectrometer (see Section 8.1) and the sensitivity of the ion-detection system. If substances present in concentrations smaller than 10^{-5} M are to be analyzed then larger volumes of solution must be transferred to the field anode; for example, the field anode can be gently heated so as to evaporate the solvent. If the heating current just compensates the heat of evaporation of the solvent, no thermal decomposition of the sample will occur[7]. Since volumes of the order of 10^3 greater than by the "dipping technique" can be loaded in this way, solutions down to about 10^{-8} M can be investigated.

The sensitivity of the FD method (expressed in coulombs of collector current per µg of field-desorbed substance) is only slightly lower than that of the electron-impact ionization method (EI method) for systems with direct vaporization of solid organic substances. The relatively high sensitivity of the FD method is due to the ionization efficiency and, further, to the efficiency of the substance supply processes. A large fraction of the molecules adsorbed on the emitter is desorbed in the form of ions, and one can expect that, as a result of the field distribution in front of the microneedles, a large portion of these ions will be emitted in the direction of the counter electrode. As yet no measurements have been made of the angular distribution of field-desorbed ions on *activated* emitters; only the angular distribution of the field ion current at individual *metal* tips has been measured[8, 9].

For recording an FD mass spectrum the field anode is first adjusted mechanically by means of a micromanipulator (mass spectrometers of Type Varian MAT CH4/CH5, AEI MS9, and CEC21-110B modified by the authors) or alternatively brought through a vacuum lock system into a mechanically fixed and reproducible position in the ion source (commercially available mass spectrometers of Type Varian MAT CH5, 711, 731). The ion beam is then focused electrically, which involves loading the field anode at room temperature (so that no solid substance is field-desorbed), and admission of acetone vapor into the ion source which is used in the FI mode. The admission of acetone is stopped after optimization of the field ion current. The field anode is normally brought to a positive potential of 3—10 kV with respect to ground and the counter electrode, at a few mm distance, is brought to a negative potential of a few kV, so that the total potential difference between the field anode and the counter electrode amounts to 10—12 kV. The current due to ionization of the solvent (*e.g.* acetone, ether, benzene, water) soon ceases on gentle heating of the field anode. A small residual current of solvent ions does not interfere with the subsequent measurements. Characteristic FD mass spectra of relatively volatile organic substances can be obtained with the field anode at room temperature or slightly above. However, in the case of most polar organic solids the production of a sufficiently intense FD mass spectrum requires stronger heating of the field anode (heating currents of the order of 10—40 mA for activated 10 µm tungsten wires).

It should now be explained qualitatively why organic samples suffer less thermal stress in the FD technique than in field ionization (FI), electron-impact ionization (EI), or chemical ionization (CI). In the last three techniques the solid samples must be vaporized; this requires that energy equivalent to the total sublimation energy of the samples must be supplied. In the FD method, on the other hand, ionization of the adsorbed molecules and desorption of these ions from the field anode demands only the field desorption energy Q_{des}, which is small at high field strengths. This is shown schematically in Fig. 2 for an adsorbed atom (for molecules the situation is considerably more complicated). Fig. 2a shows the potential curves for the interaction of an adsorbed atom or atomic ion, respectively, with a pure metal surface M[4]. It is assumed here that the ionization energy I of the atom A is appreciably greater than the work function of the metal. For the conversion of the adsorbed atom into the ion A^+ an energy $E_{des} = Q_{des} + I - \Phi$ (normally of the order of several eV) must be supplied. When a strong electric field is applied (≈ 1 V/Å) the distorted potential curves shown in Fig. 2b are obtained: an appreciably lower energy Q'_{des} is required for the formation of the ion A^+. At extremely high field strengths the atom can thus be desorbed into the ionized state without the application of thermal energy. The theory of field desorption of *atoms* from pure metal surfaces has been treated, *inter alia*, by *Müller* and *Tsong*[10].

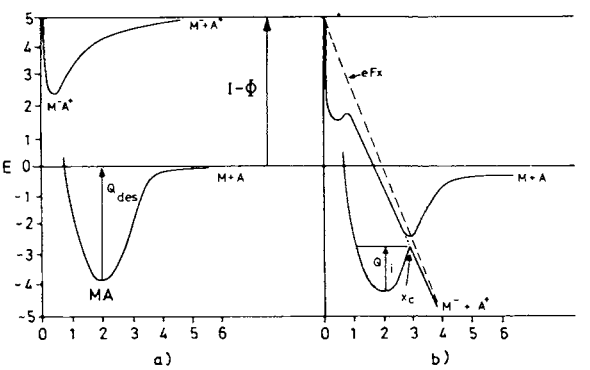


Fig. 2. a) Potential curves for the interaction of an atom (A) or an atom-ion (A^+) with a solid metal surface (M) in the absence of an external electric field (Φ = work function of the metallic emitter); b) Potential curves in the presence of a strong electric field. Smaller polarization terms have been neglected. eFx = potential of external field, F. Abscissa: x = distance of atoms from the metal surface in Å. For other designations see text.

There is as yet no quantitative theory for the field desorption of large organic molecules from microneedles of carbonaceous organic polymers with structured and graphitized regions[11].

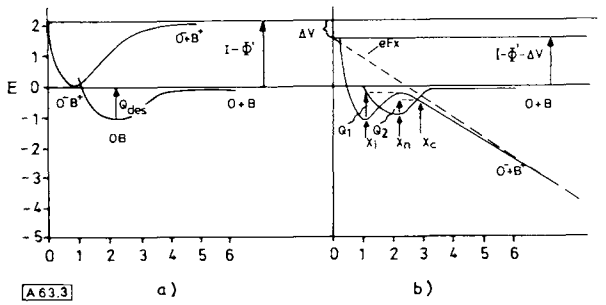


Fig. 3. a) Potential curves for the interaction of a molecule (B) or a molecular ion (B^+) with the surface (O) of a solid organic material in the absence of an external electric field (Φ' = work function of the organic emitter); b) Potential curves in the presence of a strong electric field. Field desorption energy Q_1 must be supplied for the desorption of an ion adsorbed at x_i, and energy Q_2 for the desorption of a neutral molecule adsorbed at x_n (x_c is the point of intersection of the curves for the neutral and ionized states of the molecule). Repulsion of the potential curves on the basis of the noncrossing rule, in contrast to Fig. 2b, has not been taken into account in Fig. 3b.

The observed complicated phenomena can be explained only qualitatively on the basis of Figs. 3a and 3b. The following effects, *inter alia*, should be pointed out:

1. Only some of the organic molecules are chemisorbed on the surface of the field anode. The other molecules which are bound to the surface by van der Waals and dipole forces are more easily field desorbed. The potential trough for these neutral molecules (Fig. 3a) is thus considerably shallower than that shown in Fig. 2a.

2. In a strong electric field the potential curve for the ionic adsorption state is shifted by an amount ΔV to lower potentials. Most of ΔV can probably be attributed to the potential drop in the microneedles, a further part to the penetration of the electric field into the microneedles.

3. Because of the low-lying localized energy levels, the electron work function of organic emitters can be greater by a few eV than that of metallic emitters[12].

Owing to these three effects the potential curves for the neutral and ionized states of the molecule may intersect one or more times (Fig. 3b).

3. Field Anodes for FD Mass Spectrometry

The best results in FD mass spectrometry have been obtained with microneedles 20—40 µm in length (cf. [13]). On the one hand microneedles as long as possible favor the deposition of the sample to be analyzed, since a large surface area is then available for adsorption; on the other hand, increasing needle length is accompanied by a decrease in the field strength in the emission centers and thus in the intensity of the ion currents produced. The needle length mentioned above has proven to be the best compromise.

Several activation methods for the preparation of microneedles have been developed by the research group at the University of Bonn[14].

Needles produced from benzonitrile at room temperature are often destroyed by chemically aggressive substances, particularly at high temperatures[15]. Field anodes activated at higher temperatures are chemically more stable[16]. *Schulten et al.* developed a high-temperature (HT) activation technique that produces microneedles which are extremely resistant both chemically and thermally[15,17][*]. Such microneedles make it possible, *inter alia*, to calibrate the mass scale by means of perhalogenated compounds such as perfluorokerosene or perfluorotributylamine, which destroy needles produced at room temperature.

It should be emphasized that FD mass spectrometry of organic substances stands or falls on the quality of the ion emitter.

4. Optimal Field Anode Temperature for Field Desorption

Finding the optimal field anode temperature T^* (often called also "best anode temperature" (BAT) in the literature) is very important in FD mass spectrometry. Because of the temperature gradients between the anode wire and the needle tips, T^* is not identical with the temperature of the carrier wire. In the case of direct electrical heating of the anode T^* is usually characterized by quoting the heating current.

With certain substances greater absolute and relative molecular ion currents can be achieved by heating the microneedles by thermal radiation[19]. This indirect heating of the field anode also has the advantage that after calibration with NTC resistances the mean temperature of the emitter surface can be determined to within *ca.* ± 2 °C[20]. At the optimal temperature T^* of the field anode the intensity of the molecular ion current is maximal and fragmentations minimal. To obtain thermally-/field-induced fragmentation the work is carried out at temperatures above T^*[23].

Determination of T^* will first be discussed for the case in which the FD spectrum is determined with electrical recording and a slow mass scan without use of the multiscaling technique (see Section 5). When the molecular weight of a sample is to be determined, the optimal anode temperature is the result of a compromise: if the field anode is heated too strongly, the sample vaporizes far too fast for a complete mass spectrum to be recorded; if the heating is too weak the field desorption of the sample is insufficient for the production of an ion current that would give rise to signals that can be clearly distinguished from the background noise of the ion detector.

T^* (expressed in mA of heating current) depends on the wire diameter, the effective field strength, the nature of the substance, the solvent and its pH, the layer thickness of the substance deposited on the field anode, and particularly on the length and structure of the microneedles. If the substance is insoluble it can be transferred onto the emitter from a suspension in readily volatilizable liquid[21].

T^* is determined by first setting the mass range of the molecular ion group (which is almost always dominant in field desorption) on the mass spectrometer. Several mass scans are then made through this region while slowly raising the temperature of the field anode. An intense and relatively well reproducible FD mass spectrum is often obtained only within a narrow temperature range. For some substances T^* is equal to room temperature (*e. g.* for naphthalene, phenanthrene and Endrin, *i. e.* substances having relatively high vapor pressures);

[*] Reproducible HT activation of field anode wires is described in Ref. [17]. An oxidation-reduction procedure [18] for the tungsten wire before activation becomes unnecessary if the parameters cited in Ref. [17] are all strictly observed.

for others T^* may be several hundred degrees centigrade, *i.e.* the field anode must then be heated with an emitter heating current of 10—40 mA.

5. Detection of Ions on Photographic Plates or by Rapid Electrical Recording

The disadvantages of the FD technique (small absolute ion current intensities, unknown optimal temperature T^* with samples of unknown composition; see also Section 7) can be overcome by integrating ion detection with photographic plates or by rapid electrical recording using the multiscaling technique.

When photographic plates are used in a double-focusing mass spectrometer, the optimal emitter temperature can be determined by heating the field anode until the ion current at the counter electrode amounts to about 5×10^{-8} A (for 8 kV acceleration potential and $d = 2$ mm)[22]. Because of the simultaneous recording of all types of ions on the photographic plate, no significance attaches to the variations in and the general decrease of the ion current due to consumption of the substance. This fact is even more important for the FD than for the electron-impact method. Furthermore, with photographic plates one can record an FD mass spectrum at temperatures somewhat above T^*; not only the molecular ion group but also numerous fragment ions then appear[23] and enable conclusions to be drawn about the functional groups or branching sites in an unknown organic molecule. An important application of FD mass spectrometry with photographic recording of the ions lies in a range well above T^* where pyrolytic products are detected *e.g.* in the pyrolysis of polymers (see Section 8.2).

Alternatively, rapid electrical recording of the ions may be undertaken instead of detection with photographic plates. In the multiscaling technique the scan through the mass spectrum is so fast that the intensities of the various ions do not change appreciably during a single scanning period. Since only a few ions per second reach the ion detector, use must be made of counting techniques *e.g.* with a multichannel analyzer. It is more advantageous to use a process computer which controls the mass scan through the magnetic field, stores the ion types, and programs the time/temperature profile of the field anode. In our laboratories we use a PDP 8/E process computer (Digital Equipment)[*].

6. Application of Field Desorption Mass Spectrometry

Mass spectrometry has found ever increasing use in the field of biochemistry over the last four years. Especially strict requirements must be met for analytical investigations in this field and in environmental research and medicine:

1. The detection limit should lie within or below the nanogram region.

2. The selectivity of the method should permit unambiguous detection of substances in only partly purified crude extracts of biological material in the presence of unavoidable impurities.

3. The mass spectra should not only show the characteristic fragment ions but also the molecular ions at the greatest possible intensity, since in many cases determination of the molecular weight and the empirical formula of an unknown compound are the main aims of MS investigations.

4. The procedures for qualitative and quantitative analysis must be reliable even if the samples are thermally unstable.

6.1. Analysis of Pesticides

In recent years mass spectrometry has proved its value in the qualitative and quantitative detection of toxic substances occurring in the environment. It has proved particularly valuable when used in combination with gas chromatography and with rapid electronic data recording and data processing by computer (libraries of spectra, teaching machines).

6.1.1. Chlorinated Polycyclic Hydrocarbons

Fig. 4a shows the electron-impact ionization (EI) mass spectrum of Endrin (a widely used insecticide, acaricide, and rodenticide)[25]. The molecular ion at m/e 378 is recorded with about 1 % relative intensity. In the FI mass spectra determined by *Damico et al.*[24] for a series of chlorinated polycyclic hydrocarbons the molecular ions of these compounds made up a major portion of the ion current produced. Endrin is sufficiently volatile for a field ionization mass spectrum to be obtained at 30 °C; in addition to the intense molecular ion group (base peak) a signal at m/e 342 was observed with about 10 % relative intensity. The corresponding mass lines for the metastable ions provide evidence of loss of HCl from the molecule. Fig. 4b shows a field desorption mass spectrum recorded at room temperature with electrical detection and at low resolution (modified Varian MAT-CH4 mass spectrometer)[26]; it consists exclusively of the molecular ion group, no fragments being detectable. Under the quoted experimental conditions FD spectra containing only the molecular ions are also obtained from other pesticides of the *dimethanonaphthalene* type, such as Dieldrin, Aldrin, and Isodrin[27].

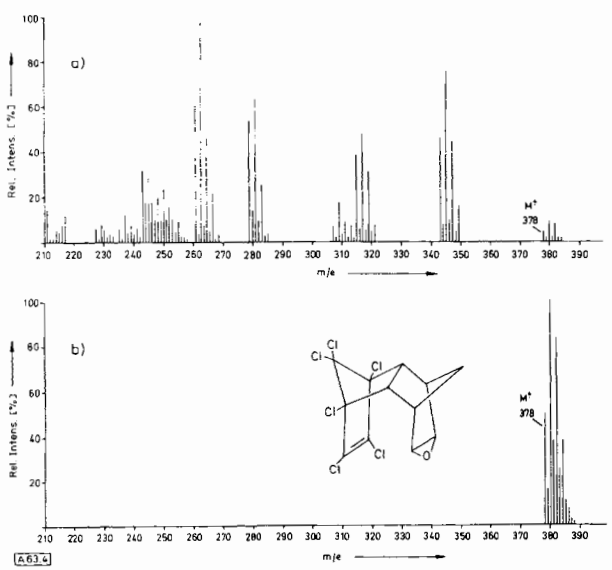


Fig. 4. a) EI mass spectrum of Endrin; sample temperature 55 °C [25]; b) FD mass spectrum of Endrin; 0 mA emitter heating current ≈ 30 °C. Both spectra were recorded electrically.

The only FD mass spectra so far published for insecticides of the *dimethanoindene* type are those of Chlorden, Heptachlor,

[*] The programs for carrying out these operations were compiled by *H. U. Winkler*, Bonn (Germany).

Endosulfan, Kelevan, and Kepone[27, 39]. A comparison of the EI and FD spectra of Chlorden shows that, under identical experimental conditions, there is again the typical picture of the fragment-free spectrum with FD and of intense fragmentation with EI. However, unlike Endrin, Chlorden is not desorbed optimally at room temperature, T^* being at slightly elevated emitter temperatures (8 mA emitter heating current ≈ 50 °C). The lower volatility of Chlorden is also shown in the EI spectrum, as above *m/e* 66 there are only two peaks, at *m/e* 101 and *m/e* 237, with more than 3% relative intensity[25].

6.1.2. Chlorinated Diphenylmethanes

The widespread, and extensively used insecticides of the chlorodiphenylmethane type may be mentioned as examples that illustrate the behavior of leading pesticides under the conditions of field desorption. On using photographic detection at a resolution of *ca.* 15000 (10% valley definition) the parent substance *p,p'*-DDT gives the FD spectrum shown in Fig. 5[28]. With the aim of producing thermally-/field-induced fragmentation this FD spectrum was obtained with an elevated emitter temperature (5 mA emitter heating current). If the FD mass spectrum of *p,p'*-DDT is produced at room temperature then almost only the molecular ion group is recorded with either electrical or photographic detection. In the EI spectrum this group appears with a relative intensity of less than 5%, as do the peaks at *m/e* 317 and *m/e* 282 $(M-Cl;\ M-2Cl)^+$[29]. The loss of one or two chlorine atoms from the DDT molecule is shown more clearly on FD, but the direct bond fission between C^1 and C^2 is still more marked at *m/e* 235 (base peak in the EI spectrum)[29]. Since a relatively intense peak is also observed at *m/e* 117 for $(CCl_3)^+$, a typical feature of many FD spectra becomes recognizable, namely the frequent fission of the investigated molecule into two complementary, charged particles. This direct bond cleavage appreciably simplifies interpretation of the spectrum.

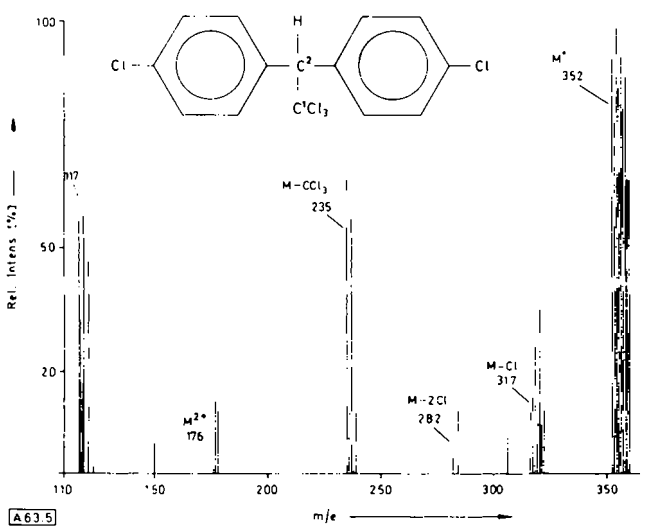


Fig. 5. FD mass spectrum of *p,p'*-DDT [28].

Doubly charged ions such as M^{2+} at *m/e* 176 and $(M-CCl_3)^{2+}$ at *m/e* 117.5 are of special interest with regard to the theoretical aspects of their formation in a high field. *Röllgen* and *Beckey*[30–32] have shown that in FI mass spectrometry intermediate surface bonding of singly charged ions is always a characteristic of the formation of doubly charged ions. The corresponding FD processes are complicated by the solid adsorbate layer. For the doubly charged ions that are formed by bond cleavage and/or elimination of neutral particles from the initial molecule one often finds an intense peak at a mass that is higher by one mass unit. Accurate mass measurements on sultam derivatives[23] have shown that protonation in the adsorbed layer must be responsible for the appearance of the second charge. Very recent FD measurements by *Games et al.*[33, 34] on alkali metal salts of bile acids (*e.g.* sodium glycocholate) showed doubly charged ions of composition $(M+2Na)^{2+}$. In field desorption of organic molecules it is thus generally better to speak of the transfer of a cation – *i.e.* "cationization" – instead of protonation[15, 35]. This process is particularly important from an analytical point of view, since the addition of *e.g.* an alkali metal cation to a large organic molecule containing nucleophilic groups produces stable even-electron ions, whereby the possibility of ionization and of detection of the intact molecule is increased[170].

6.1.3. Organic Phosphorus Compounds

The potentialities of the FD method become particularly apparent when we compare the EI, CI, FI, and FD spectra of some pesticides such as Delnav, Phosphamidon, and Temik. *Fales et al.*[36] were able to show that in fact the decisive advantage of field desorption lies in the comparatively mild thermal treatment. The EI, CI, FI, and FD spectra of Delnav are shown alongside one another in Fig. 6[36]. It will be seen at a glance that with all the ionization methods a signal is recorded in the high mass region at *m/e* 270 (271 for CI) [for the process $(M-(EtO)PS_2H)^+$]; the molecular ion is shown *only* in the FD mass spectrum—and as the base peak of the spectrum.

6.2. Analysis of Pesticide Decomposition Products

Why is FD mass spectrometry so particularly suitable for the investigation of metabolites?

1. Experience has shown that the starting compounds, whether pesticides or drugs, are metabolized into more polar substances (*e.g.* in higher organisms so as to increase their solubility in water); their volatility (*i.e.* the readiness with which the intact molecule can be vaporized) is thereby decreased. As metabolism progresses the original substance thus becomes increasingly unsuitable for direct investigation by a simple combination of gas chromatography and mass spectrometry. A coupling or combination of liquid chromatography and FD mass spectrometry, however, has proven positively ideal for such investigations.

Degradation products of pesticides containing carboxyl groups, *e.g.* hexachloro-5-norbornene-2,3-dicarboxylic acid[27] (from Isodrin), kelevanic acid[39] (from Kelevan), photoaldrindicarboxylic acid[28] (from Aldrin) and 2,2-bis(*p*-chlorophenyl)acetic acid[28] (from *p,p'*-DDT) have been subjected to a comparative study by EI and FD mass spectrometry. Similarly, metabolites containing hydroxyl groups have been analyzed, *e.g.* 2,2-bis(*p*-chlorophenyl)ethanol[28], 1-hydroxychlorden[39], aldrin-4,5-*cis*-*trans*-diol[27], and the isodrin-4,5-*cis*-diol shown in Fig. 7. The FD spectrum of the last-named compound illustrates particularly clearly the small effect of the heat treatment in field desorption; thus, in spite of the

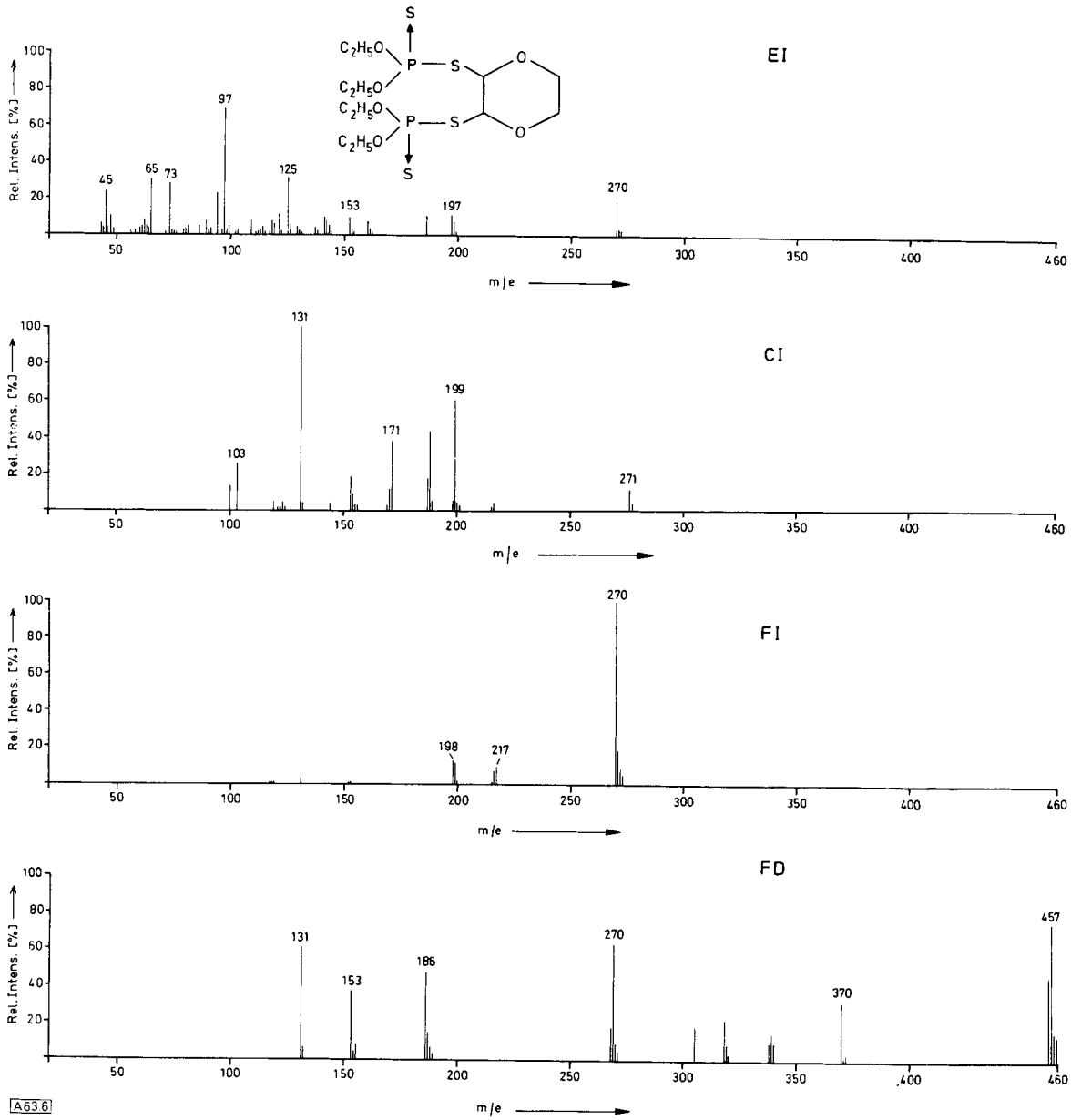


Fig. 6. EI, CI, FI, and FD mass spectra of Delnav (Dioxathione) [36].

relatively high intensity of the ion current that is necessary for the high resolution of 28500 (10% valley definition), the loss of water that might be expected in the thermal process

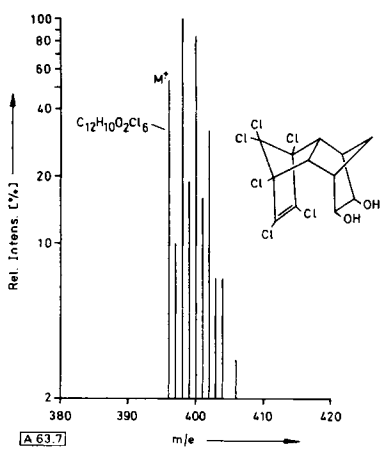


Fig. 7. FD mass spectrum of isodrin-4,5-*cis*-diol [27].

is not observed. In addition, it is important to point out that field desorption with photographic recording provides a resolving power comparable in order of magnitude with that obtainable by other methods: for EI with the commercial ion source the CEC21-110B mass spectrometer used affords a resolution of *ca.* 32000 and for FI with a special ion source one of *ca.* 30000[7].

2. Since the degradation products of living organisms are always produced in very small quantities, the sensitivity of the detection methods assumes decisive importance. The limit of detection by FD mass spectrometry lies in the region of 10^{-6} to 10^{-11} g. However, it must be expressly emphasized that these data refer to the amounts of substance adsorbed on the surface of the FD emitter. It is true that the quantities referred to suffice also for other mass-spectrometric methods, but with field desorption there is no need for derivatization. (For the sensitivity of the analysis see Section 2.)

3. The analytical samples available in metabolic studies are almost without exception mixtures. For the analysis of mixtures field ionization is recognized as being particularly

well suited[1, 37, 38] Field desorption, however, can also be used for the qualitative analysis of mixtures.

Pesticides used in practice often consist of several active constituents. For example, the acaricide Tetradifon is used together with the insecticide Carbaryl[*]. Fig. 8a shows the FD spectrum of Tetradifon. This relatively volatile substance affords only the molecular ion group and a peak at *m/e* 177 for M^{2+}. The FD spectrum of Carbaryl (Fig. 8b) also shows the molecular ion as the base peak, but together with several significant fragments at *m/e* 143, 101, 58, and 45[41]. For comparison it may be mentioned that the M^{+} ion in the EI spectrum appears with a relative intensity of less than 5%, and in the FI spectrum (source temperature 40 °C) with 50% relative intensity[24]. If one records the FD spectrum of the above mentioned mixture of active substances on a photographic plate with an emitter heating current of between 0 and 30 mA and 12 min exposure time, then the spectrum shown in Fig. 8c, with a resolution of 10000 is obtained. It can be recognized at once that this spectrum is composed approximately additively of the FD spectra of the individual components. Admittedly one must take into account reactions of the individual components with one another and with the emitter surface, as has been shown in more recent investigations on mixtures of organic[41] and inorganic salts[71]. After calibration of the FD spectra with standard concentrations of Carbaryl and Tetradifon the composition of the mixture can be estimated (here 4:1)[41]. Qualitative agreement of the FD spectra with the composition of mixtures has been confirmed by *Rinehart et al.*[42] for antibiotics of complex composition, by *Adlercreutz et al.*[43] for steroid conjugates, *Games et al.*[34] for bile acids, and recently *Schulten* and *Schurath* for the complex compositions of aerosols[72].

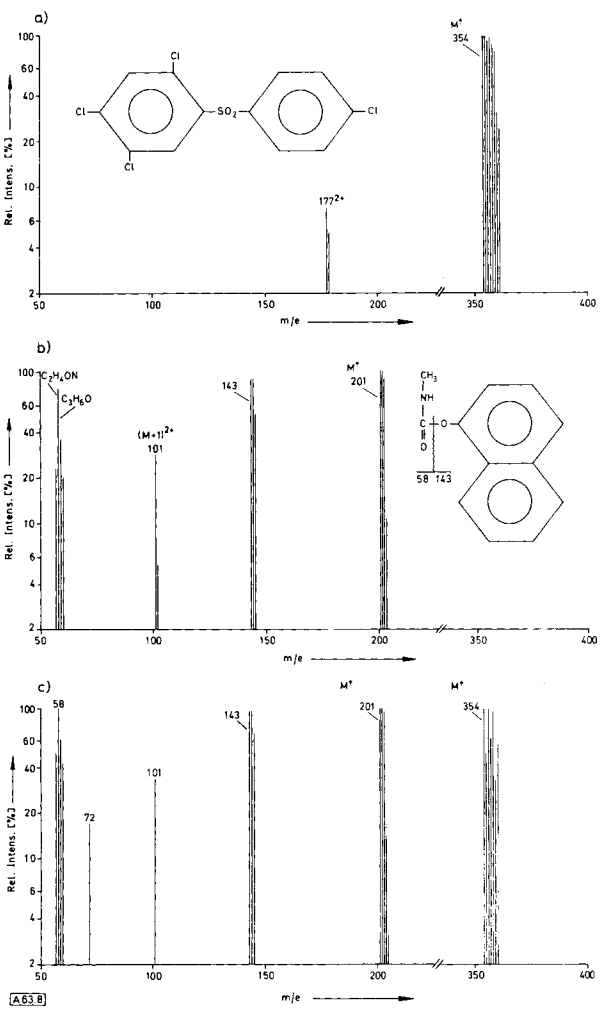


Fig. 8. a) FD mass spectrum of Tetradifon [41]; b) FD mass spectrum of Carbaryl [41]; c) FD mass spectrum of a mixture of active constituents containing 14% of Tetradifon and 50% of Carbaryl; solvent acetone; photographic recording, exposure time 10 min, optimal emitter heating current 14 mA [41].

[*] We are indebted to Dr. *Schinkel* of the Biologische Bundesanstalt, Braunschweig (Germany) for supplying this mixture of active substances.

4. Pesticides and drugs are often excreted as conjugates with amino acids, peptides, sugars and sugar derivatives, organic and inorganic acids, *etc.* By using model compounds it has been shown that FD mass spectrometry is particularly suitable for the analysis of such conjugates. The most extensive FD investigations carried out to date have been concerned with this aspect (see Sections 6.3 to 6.6)[44].

6.3. Analysis of Sugars and Sugar Derivatives

6.3.1. Oligosaccharides

The first substance measured by FD mass spectrometry was the monosaccharide D-glucose[2]; *Krone* and *Beckey* have reported the FD spectrum of the disaccharide cellobiose[45]. The FD spectrum of a triaminotrisaccharide is shown in Fig. 9[7]; although this compound contains seven free hydroxy and three free amino groups, the cationized (protonated) molecule provides the base peak; the peak with the second-highest relative intensity, at *m/e* 324, can again be ascribed to direct bond fission. Structurally related oligosaccharides with antibiotic activity, such as gentamycin and tobramycin, also provide high molecular ion intensities and undergo bond fission at the glycosidic oxygen. *Rinehart et al.*[42] have obtained the FD spectra of a series of antibiotics. Neomycin, streptolydigin, and novobiocin, which afforded no molecular ions in the EI or CI spectrum and showed the molecular weight as the base peak in the FD spectrum at *T**. Furthermore, field desorption provides qualitative indications on the composition of complex antibiotics such as streptovaricin, filipin, and dermostatin.

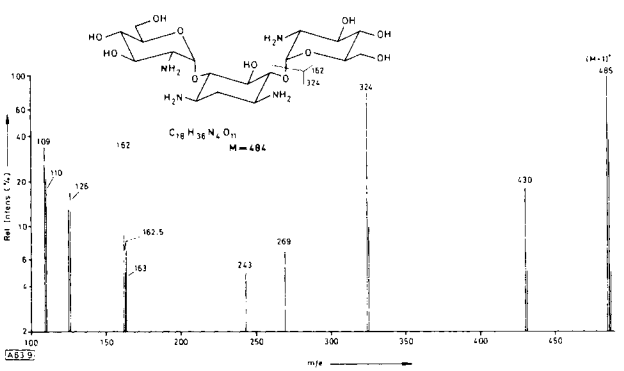


Fig. 9. FD mass spectrum of a triaminotrisaccharide.

Fig. 10a reproduces the 70 eV EI and Fig. 10b the 18 eV EI spectrum of underivatized neomycin B. The spectra terminate in the higher-mass region at *m/e* 446/447; astonishingly, no ion of this mass appears in the FD spectrum (Fig. 10c), but only relatively weak fragments at *m/e* 206, 307, and 455, while the $(M+H)^{+}$ ion (*m/e* 615) makes up 75% of the total ion current. To obtain a mass spectrum of this compound

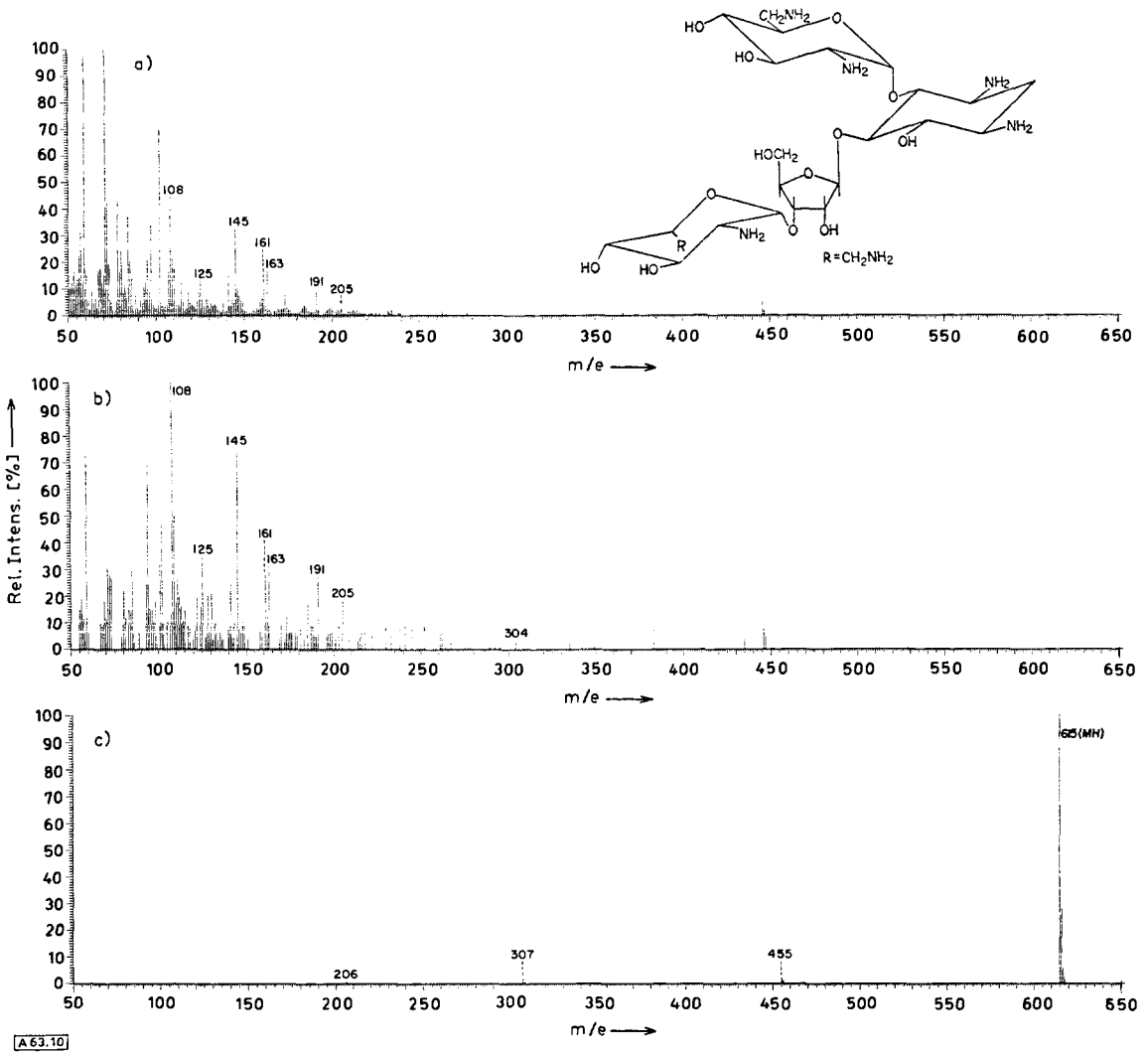


Fig. 10. a) EI mass spectrum of neomycin B, electron energy 70 eV; b) EI mass spectrum of neomycin B, electron energy 18 eV; c) FD mass spectrum of neomycin B [42].

with EI and using the direct insertion system it was necessary to prepare the hexa-*N*-acetylheptakis(*O*-trimethylsilyl) derivative[46]; this is difficult, and furthermore the protecting groups make the derivatized substance more than twice as heavy and thus bring it close to the limit for analysis with conventional mass spectrometers.

6.3.2. Glycosides

For all spectroscopic methods there is an approximately reciprocal relationship between the signal intensity and the resolution. Because of the relatively small ion currents in field desorption, high-resolution mass measurements make severe demands on the transmission of the mass spectrometer and on the quality of the emitter (see Section 3). The advantages of high resolution are as follows: accurate determination of the molecular weight and thus of the empirical formula, as well as important indications for the interpretation of fragments. High-resolution data for some aryl glycosides and for glycosides of the coumarin and flavone series have recently been published[47]. Fig. 11 shows the high-resolution FD spectrum of hesperidin; this also makes it clear how the molecular ion is stabilized by cationization; $M^{\ddagger}$ is certainly recognizable at *m/e* 610, but, unusually for FD, with less than 20% relative intensity. In contrast, addition of Na^+ appears to provide the base peak. The sodium ions arise from unavoidable impurities in extracts of the natural product (*e.g.* after column chromatography), and with higher emitter-heating currents also

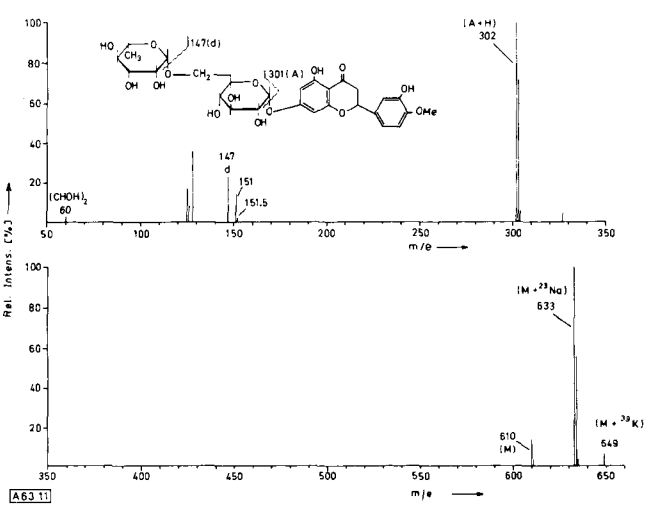


Fig. 11. FD mass spectrum of hesperidin [47].

from impurities in the emitter. The usefulness of these $(M+Na)^+$ and $(M+K)^+$ peaks for differentiation of $M^{\ddagger}$ from $(M+H)^+$ ions should be noted[48]. Since high resolution affords the elemental composition of the fragments, *m/e* 302.079 can be interpreted as $(A+H)^+$ and *m/e* 147.066 as due to

direct bond fission at the glycosidic oxygen of the terminal sugar unit. The aglycone also appears as a doubly charged ion at *m/e* 151.040. The EI spectrum of free hesperidin affords a peak for the aglycone (*m/e* 302) with 76% relative intensity, and the base peak lies at *m/e* 137; the molecular ion at *m/e* 610 is not detectable.

Clearly different FD spectra were obtained for α- and β-linked glycosides containing an aromatic aglycone, used as test substances for enzyme determination (substrate for glucosidases). Comparison with EI and FI spectra showed that the FD spectra are the simplest and provide the greatest differences between the stereoisomers[49].

6.3.3. Glucuronides

Steroid glucuronides are extremely important for hormone excretion. Fig. 12 shows a high-resolution spectrum of testosterone glucuronide (sodium salt). Investigations by *Adlercreutz et al.*[43] have gone beyond studies with model substances and have placed field desorption in the service of clinical

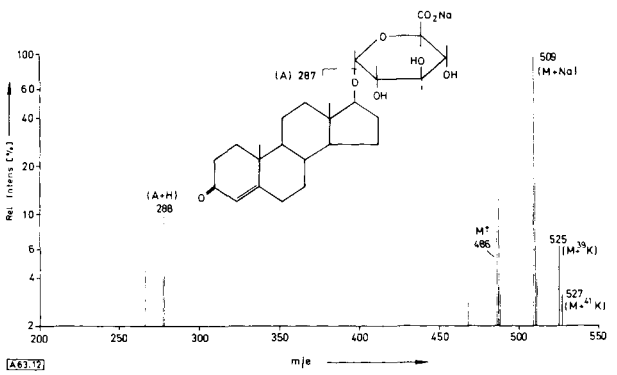


Fig. 12. FD mass spectrum of testosterone glucuronide (sodium salt) [47].

chemistry and medicine. Thus, estriol 16-glucuronide isolated from pregnancy urine could be detected with high molecular ion intensity by FD mass spectrometry. This detection was effected without derivatization at low resolution ($m/\Delta m$ 500—600), and was supported by FD measurements on synthetic reference compounds.

6.3.4. Nucleosides and Nucleotides

These compounds come into consideration, firstly since they form conjugates or take part in metabolic processes, and are therefore of interest for use underivatized in FD analysis, and secondly because a large number of modified, biologically active nucleosides have been synthesized[50] whose FD spectra could simplify structural determination. The most important nucleosides that occur as constituents of RNA and DNA have been measured as model compounds by FI[51] and FD[22] spectrometry. Except for guanosine, the molecular ion intensities in the FI spectra suffice to identify the underivatized compounds. The temperature given[51] for the direct introduction system (250 °C) clearly leads to thermal decomposition of the guanosine molecule before it is brought into the gas phase [m.p. 240 °C (dec.)]. The FD spectrum[22] of guanosine was determined above T^* at 18—20 mA with the intention of obtaining the complementary fragments—important for the determination of structure—for the sugar portion (S) and the base portion (B); the molecular ion then appeared with *ca.* 20% relative intensity. The marked influence of the solvent in FD was also discussed in the same paper.

Fig. 13 shows the high-resolution FD spectrum of adenosine. The peaks for $(B+H)^+$ at *m/e* 135.055 and for (S) at *m/e* 133.050 are characteristic, along with the base peaks for M^+

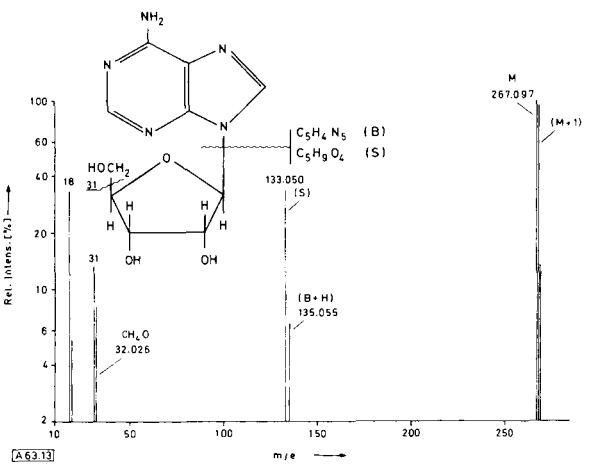


Fig. 13. FD mass spectrum of adenosine [22].

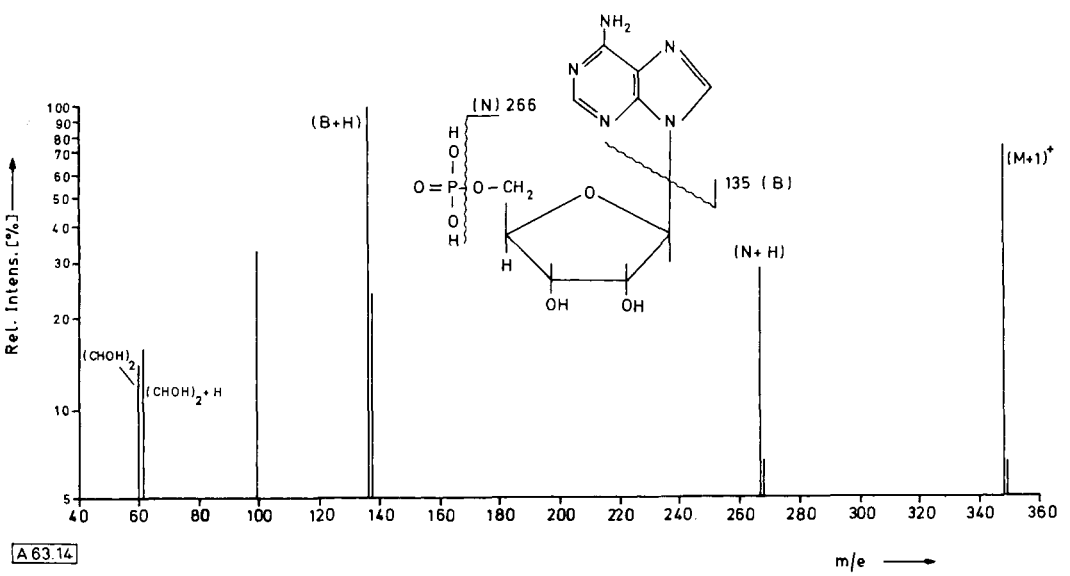


Fig. 14. FD mass spectrum of adenosine monophosphate [22].

and $(M+H)^+$ (emitter heating current 20 mA). The first free nucleotide detected by FD mass spectrometry was adenosine 5'-monophosphate as the intact protonated molecule ion $(M+H)^+$ (73% rel. intens.)[22] (Fig. 14). Bond fission between the phosphoric acid moiety and the nucleoside (N) adenosine was recorded with 29% relative intensity at *m/e* 267.097. The remaining fragments yielded intense mass lines for $(S)^+$ and $(B+H)^+$, as in the case of the nucleoside. Relatively weak signals at *m/e* 60.021 $(CHOH)_2^+$ and 61.029 $[(CHOH)_2+H]^+$ provided evidence that the compound was a riboside. With emitter heating currents well above T^*, *e.g.* up to 50 mA, protonated orthophosphoric acid was detected at *m/e* 98.985. Other free nucleotides such as the 5'-monophosphates of thymidine, deoxycytidine, and deoxyguanosine gave similar FD spectra.

6.3.5. Vitamins

The 70 eV and 12 eV EI and the high-resolution FD spectrum of vitamin C (ascorbic acid) were measured in connection with the problems of determining mutagenic compounds[28]. In this investigation the intensity of the M^+ ion in the EI spectrum had a relative intensity of 10%. The base peak in the FD spectrum was formed by the molecular ion group $M^+/(M+H)^+$ when the spectrum was determined at T^*. The characterization of several B vitamins has recently been reported[52].

6.3.6. Sodium Salts of Deoxyfluoro-D-glucose 6-Phosphates

At the end of this listing of compounds in increasing polarity come the alkali salts of the sugar phosphates. The high-resolution FD spectra of these substances[53] contain $(M+H)^+$ as the base peak but disclose also other products that are formed by replacement of H^+ by Na^+, elimination of water, and pyrolytic processes. Since these salts are desorbed within narrow time and heating current intervals, they can only be recorded photographically. Tarry residues deposited on the FD emitter (0—50 mA heating current, 10 min exposure time) strongly reduce the emission properties of the emitter.

6.4. Analysis of Amino Acids

A series of biologically important α-amino acids has been studied by FD mass spectroscopy by *Winkler* and *Becker*[54]. The FD spectra usually show the molecular ion or the quasi-molecular ion with relatively high intensity. This is also the case for arginine and cystine, whereas these ions are not detectable by EI, CI, or FI methods. The FD spectrum of arginine is shown in Fig. 15: the $(M+H)^+$ ion appears with 30% relative intensity, and the base peak of the spectrum

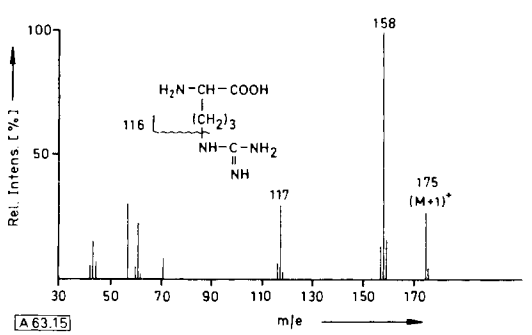


Fig. 15. FD mass spectrum of arginine [54].

at *m/e* 158 is characterized by loss of ammonia from the protonated molecule $[(M+H)-NH_3]^+$. In addition, the bond between the guanidino residue and C^5 is broken, leading to *m/e* 116 and *m/e* 117. With α-amino acids (*e.g.* Glu, Val, Pro, Ser, and Cys) a peak is generally obtained at (M−45), which can be interpreted as $[(M+H)-COOH_2]^+$.

6.5. Analysis of Peptides

It was first shown for the simplest dipeptide, glycylglycine[55], that application of field desorption to underivatized peptides affords complete mass spectra in which, with an emitter heating current of 18—24 mA, the molecular ions provide the base peak. In a subsequent FD investigation *Winkler* and *Becker*[56] were able to record spectra from partially protected and free oligopeptides containing three to nine amino-acid residues (including for example arginine and histidine), not only with high molecular ion intensities but also with some information about the amino-acid sequence. The FD spectrum of Ac-Gly-Arg-Arg-Gly-OMe is reproduced in Fig. 16 as example. Although the *N*-terminal group of

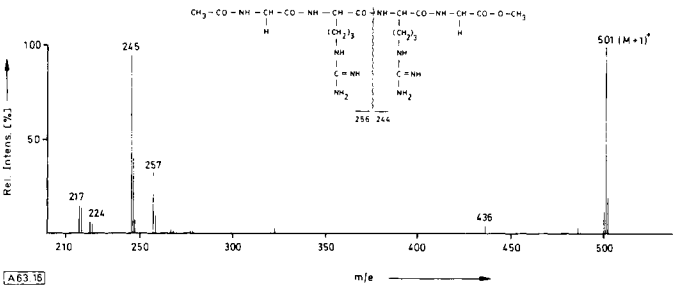


Fig. 16. FD mass spectrum of Ac-Gly-Arg-Arg-Gly-OMe [56].

the tetrapeptide is acetylated and the *C*-terminal carboxyl group is methylated, the base intensity of the $(M+H)^+$ ion at *m/e* 501 is an outstanding characteristic of the spectrum, for the peptide contains, *inter alia*, two unprotected Arg units which strongly reduce the volatility. Direct bond fission (with hydrogen transfer) in the middle of the molecule leads to two sequence-specific fragments. As already explained in Section 6.1.2, the molecular ion and the complementary peaks at *m/e* 256 and *m/e* 244 provide relatively easily interpretable information about the structure. It must, however, be added that in this case it is only the additional data from the EI spectra that enable the identities of the amino acids and their sequence to be recognized. Thus, if the complete sequence is to be determined a combination of EI, CI, and FD spectroscopy would have the greatest chance of success. Nevertheless, it was very recently possible to fragment the peptide skeleton so strongly that the complete sequence of an unprotected tripeptide and a nonapeptide could be discussed on the basis of FD spectra alone[57]. However, an attempt to use higher emitter heating currents to produce temperatures considerably above T^*, and thus to obtain thermally-/field-induced fragments, easily leads to pyrolysis products and not to sequence fragments.

6.6. Analysis of Drugs and Drug Metabolites

Since 1971 the FD investigations of anti-cancer drugs have played a major role in exploring the scope of FD mass spectroscopy[58]. EI and FD spectra of propane- and butanesultams (some of which show an antitumor effect against Ehrlich ascites

tumors) were obtained; the FD spectra exhibit the following five general phenomena:

1) High intensity of the molecular ions,
2) formation of most of the fragments in "one step",
3) elimination of neutral particles (H_2O, NH_3, HCOOH) from the protonated molecule,
4) formation of fragments by direct bond fission, and
5) production of doubly charged ions.

The extension of studies on model compounds, such as *e.g.* medicinal carbamates[40], to the investigation of cyclophosphamide *(1)* (Endoxan) and its metabolites[59] represents an important advance in the direction of solving "real" analytical problems by field desorption. According to these investigations, individual components can be identified by means of high-resolution FD spectra not only in mixtures of the parent compounds themselves (as in Section 6.2) but also in mixtures of parent compounds with metabolites. Fig. 17 shows a part of the FD spectrum of a mixture of cyclophosphamide *(1)* with three of its most important metabolites *(2)*, *(3)*, and *(4)*; although the polarities of these compounds extend over a wide range—*(4)* was stabilized as its cyclohexylammonium salt—the molecular ions of all the components appear with high relative intensities. The degradation products of cyclophosphamide could also be demonstrated (after thin-layer chromatography) in extracts of body fluids. However, the FD spectra were "electron-impact-like" and rich in lines because of the impurities carried over, and interpretation of these spectra is very difficult without additional information about the compounds looked for.

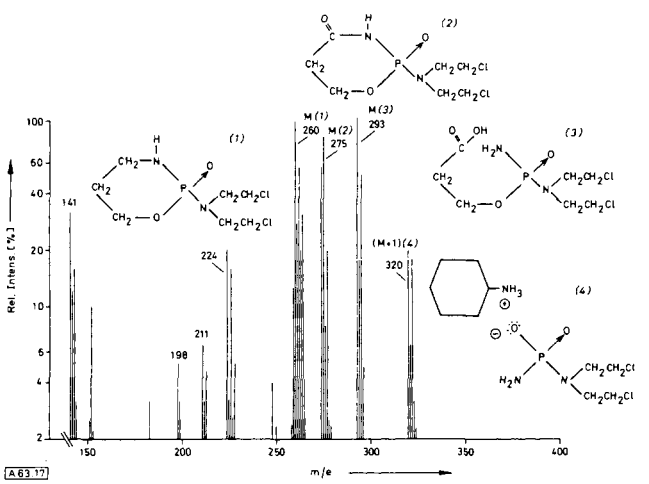


Fig. 17. FD mass spectrum of a mixture of cyclophosphamide *(1)* and three of its important metabolites *(2)*, *(3)*, and *(4)* [59].

Azathioprine (Imuran) is a widely used immunosuppressive drug. The EI spectrum of this compound is shown in Fig. 18a[60]; the relative intensity of the molecular ion is less than 1%. The FD spectrum at T^* (22 mA) shows exclusively the (M + 1) ion. The use of heating currents above T^* yields the FD spectrum shown in Fig. 18b; it is clear that the signals in the higher-mass range of the EI and of the FD (at 25 mA) spectrum are due to the same fragments (*e.g. m/e* 231, 152, 119). Apparently here the predominant thermal decomposition of the azathioprine molecule in EI is simulated by the thermally-/field-induced fragmentation in FD; the same elemental composition of these ions is found in high-resolution

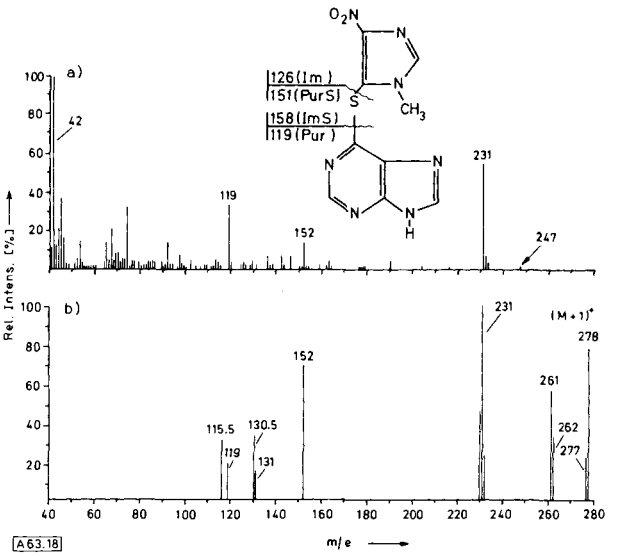


Fig. 18. a) EI mass spectrum of azathioprine (Imuran), electron energy 70 eV; b) FD mass spectrum of azathioprine, emitter heating current $T^* = 25$ mA [60].

measurements by EI and by FD. Greater importance in this connection attaches to a metabolite of azathioprine, namely a glutathionyl conjugate; the EI spectrum in Fig. 19a is characterized predominantly by pyrolytic decomposition of the molecule. At T^* (24 mA) the FD spectrum once again yields exclusively the (M + 1) ion. Above T^* fragmentation can be induced within a very narrow range of emitter heating currents (Fig. 19b).

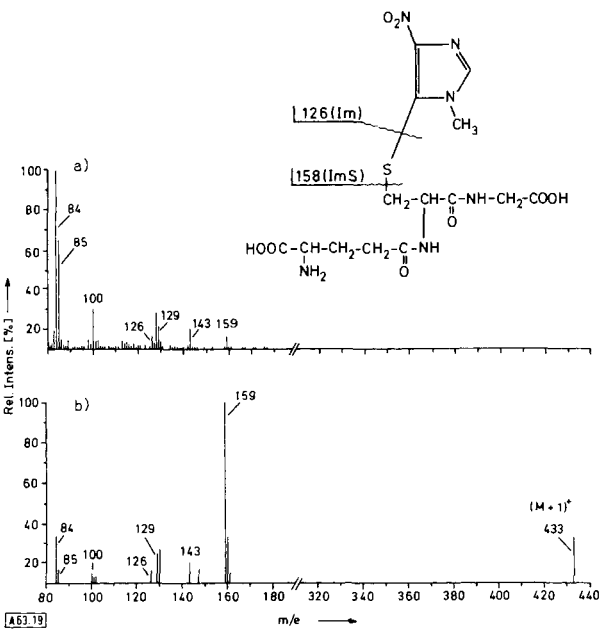


Fig. 19. a) EI mass spectrum of 1-methyl-5-nitro-5-(*S*-glutathionyl)imidazole, electron energy 70 eV [60]; b) FD mass spectrum of the same compound at 27 mA emitter heating current ($> T^*$) [60].

To explore the possibilities of field desorption in the detection of metabolites, a sample was isolated from the urine of a rat to which azathioprine had been administered orally. After column chromatography and purification by paper chromatography a cysteinyl conjugate could be identified in the FD spectrum[60].

7. Advantages and Disadvantages of the FD Method in Comparison with Other Ionization Methods

Let us compare the FD method with other ionization methods that are also regarded as "mild", *e.g.* CI, FI, and EI at low electron energies. The FD method is very suitable for *qualitative* analysis of complex mixtures, but currently still less suitable for *quantitative* analysis of such mixtures. As has already been explained in Section 4, there is an optimal T^* of the field anode for each component of the mixture. At a constant anode temperature the FD signals are certainly not proportional to the molar fractions of the components of a mixture of substances in solution. Moreover, it is hardly likely that it will be possible to obtain such proportionality by introducing a variable temperature program. The intensities of the ions from any one substance depend in a complicated manner on the structure and the chemical properties of the organic microneedles grown on the emitter surface, on the concentrations of the individual components in the mixture, on the thickness of the sample layer deposited on the microneedles, on the solvent, and on other parameters such as the residence time of the sample on the field anode during field desorption.

The potential of the FD method lies undoubtedly in the field of qualitative analysis of substances that are thermally labile on evaporation. Nevertheless, it must be emphasized that the FD spectrum of a substance is, in the present state of the technique, less reproducible than a CI or FI spectrum. This aspect is, however, of minor importance since the FD method is used in those cases where, as a result of their low volatility, the samples do not afford unambiguously identifiable molecular ions in the CI and FI or the EI methods. Under these circumstances combination of FD with EI and/or CI is optimal. A great advantage of the FD method is that the substances, which are often available only in picogram amounts, do not need to be treated chemically in order to increase their volatility. The major application of the FD method is thus in the *analysis of very small quantities of strongly polar, underivatized substances.*

An advantage of the electron-impact method is the wealth of structurally specific fragments that are observed in the mass spectrum. In the 30 or so years since the EI method gained importance as an analytical tool experience has been gained with a great number of substances, which has resulted in extensive catalogs of spectra and many empirical rules concerning fragmentation.

The method of chemical ionization introduced by *Munson* and *Field*[61] has been used for only about four years in a rather large number of laboratories; the FD method has been tested and further developed systematically for only about three years, mainly by the Bonn group. Nevertheless, it is already recognized that there are many specific applications for which FD will prove invaluable.

8. Prospects

8.1. The FD Quadrupole Mass Spectrometer

While FD quadrupole mass spectrometry is still in its infancy, it could become important in special areas of FD mass spectrometry. The significance of a rapid mass scan has already been mentioned in Section 5 for the case where electrical ion recording is used.

The quadrupole mass spectrometer (QMS) can be used for the FD technique at low resolution (<500) because of the following reasons[62]:

1. The mass scan rate can reach the order of 1000 mass units per second.

2. The intensity of the ion current and the resolving power are almost independent of the energy of ions entering the QMS (the maximal energy for EI is about 5—10 eV).

3. The product of the transmission *(T)* and the resolving power *(A)* is almost constant in the lower-mass region[63] (transmission is defined as the ratio of the current measured at the first dynode of the SEV ion detector to the total ion current emitted from the field anode). The ratio T/A can be set electronically on the QMS; thus, when desired, a large mass range at large transmission and low resolving power can be arranged, providing a rapid survey of the FD mass spectrum, or the resolving power can be raised so that, for instance, the molecular ion group can be analyzed more accurately.

The high recording rate with the QMS makes it possible to adapt the processing of the FD mass spectrum to the specific desorption behavior of the substance under analysis. This is important for studies on the fundamental phenomena of field desorption and also for the application of FD in analysis. As an example we may mention the rapid determination of certain components in a mixture of substances such as may be obtained in chemical synthesis of compounds or by extraction methods in biochemistry[64].

8.2. Pyrolysis-Mass Spectrometry

Some of the biologically most important active compounds (polysaccharides, polynucleotides, and polypeptides) have very high molecular weight (>20000). Controlled thermal degradation and identification of the structural units by mass-spectrometric methods holds out good prospects in two directions: 1. Rapid, accurate, and reproducible analysis of the pyrolysis products, *e.g.* with a combination of Curie point pyrolyzer, quadrupole MS, and data system, leads to fingerprint spectra[65]. The use of this system, with comparison of the spectra, can provide unambiguous identification of known polymers. 2. Identification of ionized primary fragments, which should be as large as possible, in the mass spectrum provides indications of the composition and structure of known and still unknown polymers. Pyrolysis field desorption is suitable for investigations on biopolymers[21, 66] and industrial polymerization products, because of the very small consumption of the sample material ($\approx 10^{-8}$ g), the very close sequence, both in time and space, of pyrolysis and ionization, as well as the mild ionization.

It must be emphasized that this promising and very recently developed technique of combining pyrolysis and field desorption can be applied only when two fundamental prerequisites are satisfied. In the first place, very high demands are made on the resolving power of the mass spectrometer employed. Without excellent values for the resolving power (>30000) unequivocal assignment of the peaks runs into increasing difficulties with increasing mass number. Secondly, the extremely complicated spectra of the multicomponent mixtures encountered can be evaluated only if electronic data processing is available.

8.3. Liquid Chromatography-Field Desorption

The coupling of a gas chromatograph to the mass spectrometer is regarded as the most successful mass-spectrometric combination. However, compounds are amenable to this system only if they themselves are sufficiently volatile or if this volatility can be produced by chemical pretreatment, *i.e.* by the preparation of derivatives. In view of the rapid progress in both high-pressure liquid chromatography and field desorption, and in order to avoid vaporization of the analytical sample, a combination of the two methods appears promising. The first experiments in this direction were made by an off-line technique[67]. The eluate from the liquid chromatograph was collected, concentrated on the emitter, and analyzed by FD spectrometry. In this sequence the FD mass spectrometer serves as a (second) molecule-specific detector[68]. It remains to be seen whether the great efforts devoted to the on-line technique[69] will lead to the solution of the enormous technical problems, especially as regards the analysis of highly polar substances, and whether the analytical information obtained by this direct coupling will be justified in view of the effort and expense involved.

We thank the Deutsche Forschungsgemeinschaft, the Landesamt für Forschung des Landes Nordrhein-Westfalen and the Fonds der Chemischen Industrie for generous financial support of our work.

Received: November 25, 1975 [A 63 IE]
German version: Angew. Chem. 87, 425 (1975)

[1] *H. D. Beckey*, Angew. Chem. *81*, 662 (1969); Angew. Chem. internat. Edit. *8*, 623 (1969).
[2] *H. D. Beckey*, Int. J. Mass Spectrom. Ion Phys. *2*, 500 (1969).
[3] *E. W. Müller*, Phys. Rev. *102*, 618 (1956).
[4] *R. Gomer*, J. Chem. Phys. *31*, 341 (1959).
[5] *H. D. Beckey*: Field Ionization Mass Spectrometry. Pergamon, Oxford 1971.
[6] *H. D. Beckey, A. Heindrichs*, and *H. U. Winkler*, Int. J. Mass Spectrom. Ion Phys. *3*, App. 9—11 (1970).
[7] *H.-R. Schulten*, unpublished results.
[8] *H. D. Beckey, J. Dahmen*, and *H. Knöppel*, Z. Naturforsch. *21a*, 142 (1966).
[9] *I. V. Goldenfeld* and *V. A. Nazarenko*, Int. J. Mass Spectrom. Ion Phys. *5*, 197 (1970).
[10] *E. W. Müller* and *T. T. Tsong*: Field Ion Microscopy. Elsevier, New York 1969.
[11] *R. Ajeian, H. D. Beckey, A. Maas*, and *U. Nitschke*, Appl. Phys. *6*, 111 (1975).
[12] *F. W. Röllgen*, Bonn, personal communication.
[13] *H. D. Beckey, S. Bloching, M. D. Migahed, E. Ochterbeck*, and *H.-R. Schulten*, Int. J. Mass Spectrom. Ion Phys. *8*, 1969 (1972).
[14] *H. D. Beckey, A. Heindrichs, E. Hilt, M. D. Migahed, H.-R. Schulten*, and *H. U. Winkler*, Messtechnik *78*, 196 (1971).
[15] *H.-R. Schulten* and *H. D. Beckey*, Org. Mass Spectrom. *6*, 895 (1972); Messtechnik *81*, 121 (1973).
[16] *M. D. Migahed*, Dissertation, Universität Bonn 1970; *M. D. Migahed* and *H. D. Beckey*, Int. J. Mass Spectrom. Ion Phys. *7*, 1 (1971).
[17] *H. D. Beckey, E. Hilt*, and *H.-R. Schulten*, J. Sci. Instrum. *6*, 1043 (1973).
[18] *D. G. Barofsky* and *E. Barofsky*, Int. J. Mass Spectrom. Ion Phys. *14*, 3 (1974).
[19] *H. U. Winkler* and *H. D. Beckey*, Org. Mass Spectrom. *7*, 1007 (1973).
[20] *H. U. Winkler* and *B. Linden*, Bonn, unpublished results.
[21] *H.-R. Schulten, H. D. Beckey, A. J. H. Boerboom*, and *H. L. C. Meuzelaar*, Anal. Chem. *45*, 2358 (1973).
[22] *H.-R. Schulten* and *H. D. Beckey*, Org. Mass Spectrom. *7*, 861 (1973).
[23] *H.-R. Schulten, H. D. Beckey, G. Eckhardt*, and *S. H. Doss*, Tetrahedron *29*, 3861 (1973).
[24] *J. N. Damico, R. P. Barron*, and *J. A. Sphon*, Int. J. Mass Spectrom. Ion Phys. *2*, 161 (1969).
[25] *J. N. Damico, R. P. Barron*, and *J. M. Ruth*, Org. Mass Spectrom. *1*, 331 (1968).
[26] *H.-R. Schulten*, Research Conference on Pesticide Metabolites—Enzymology, Isolation and Characterization. Fargo, N. Dak. (USA), June 1972.
[27] *H.-R. Schulten* and *H. D. Beckey*, J. Agr. Food Chem. *21*, 372 (1973).
[28] *H.-R. Schulten*, Research Conference on New Methodology in Ecological Chemistry. Susono City (Japan), Nov. 1973; see also *F. Coulston, F. Korte*, and *M. Goto*: New Methods in Environmental Chemistry and Toxicology. International Academic Printing Co., Tokyo 1973, p. 31ff.
[29] *J. A. Sphon* and *J. N. Damico*, Org. Mass. Spectrom. *3*, 51 (1970).
[30] *F. W. Röllgen* and *H. D. Beckey*, Surface Sci. *23*, 69 (1970).
[31] *F. W. Röllgen* and *H. D. Beckey*, Ber. Bunsenges. Phys. Chem. *75*, 988 (1971).
[32] *R. W. Röllgen* and *H. D. Beckey*, Z. Naturforsch. *29a*, 230 (1974).
[33] *D. E. Games, M. P. Games, A. H. Jackson, A. H. Olavesen, M. Rossiter*, and *P. J. Winterburn*, Tetrahedron Lett. *1974*, 2377.
[34] *D. E. Games, A. H. Jackson*, and *M. Rossiter*, Biomed. Mass Spectrom., in press.
[35] *H.-R. Schulten* and *H. D. Beckey*, Advan. Mass Spectrom. *6*, 499 (1974).
[36] *H. M. Fales, G. W. A. Milne, H. U. Winkler, H. D. Beckey, J. N. Damico*, and *R. Barron*, Anal. Chem. *47*, 207 (1975).
[37] *J. B. Forehand* and *W. F. Kuhn*, Anal. Chem. *42*, 1839 (1970).
[38] *H.-R. Schulten, H. D. Beckey, A. J. H. Boerboom*, and *H. L. C. Meuzelaar*, Anal. Chem. *45*, 191 (1973).
[39] *H.-R. Schulten, H. Prinz, H. D. Beckey, W. Tomberg, W. Klein*, and *F. Korte*, Chemosphere *2*, 23 (1973).
[40] *D. J. Rouse* and *D. A. Brent*, Biomed. Mass Spectrom. *1*, 256 (1974).
[41] *H.-R. Schulten*, J. Agr. Food. Chem., in press.
[42] *K. L. Rinehart, Jr., J. C. Cook, Jr., K. H. Maurer*, and *U. Rapp*, J. Antibiot. *27*, 1 (1974).
[43] *H. Adlercreutz, B. Soltmann*, and *M. J. Tikkanen*, J. Steroid Biochem. *5*, 163 (1974).
[44] *H.-R. Schulten*, Proc. 2nd International Symposium on Mass Spectrometry in Biochemistry and Medicine. Milan, Italy, June 24—26, 1974, in press.
[45] *H. Krone* and *H. D. Beckey*, Org. Mass. Spectrom. *2*, 427 (1969).
[46] *W. T. Shier, K. L. Rinehart, Jr.*, and *D. Gottlieb*, Proc. Nat. Acad. Sci. USA *63*, 198 (1969).
[47] *H.-R. Schulten* and *D. E. Games*, Biomed. Mass Spectrom. *1*, 120 (1974).
[48] *H.-R. Schulten* and *H. D. Beckey*, Org. Mass Spectrom. *9*, 1154 (1974).
[49] *W. D. Lehmann, H.-R. Schulten*, and *H. D. Beckey*, Org. Mass Spectrom. *7*, 1103 (1973).
[50] *A. Bloch* in *E. J. Ariens*: Medicinal Chemistry. Academic Press, New York 1973, Vol. IV, 286.
[51] *P. Brown, G. R. Pettit*, and *R. K. Robins*, Org. Mass Spectrom. *2*, 521 (1969).
[52] *M. C. Sammons, M. M. Bursey*, and *D. A. Brent*, Biomed. Mass Spectrom. *1*, 169 (1974).
[53] *H.-R. Schulten, H. D. Beckey, E. M. Bessel, A. B. Foster, M. Jarman*, and *J. H. Westwood*, J. C. S. Chem. Comm. *13*, 416 (1973).
[54] *H. U. Winkler* and *H. D. Beckey*, Org. Mass Spectrom. *6*, 655 (1972).
[55] *H. D. Beckey, G. Hoffmann, K. H. Maurer*, and *H. U. Winkler*, Advan. Mass Spectrom. *5*, 626 (1971).
[56] *H. U. Winkler* and *H. D. Beckey*, Biochem. Biophys. Res. Commun. *46*, 391 (1972).
[57] *S. Asante-Poku, G. W. Wood*, and *D. E. Schmidt, Jr.*, Biomed. Mass Spectrom., in press.
[58] *H. D. Beckey, H.-R. Schulten*, and *H. U. Winkler*, Proc. 18th Field Emission Symposium. Eindhoven, Aug. 1971, p. 81ff.
[59] *H.-R. Schulten*, Biomed. Mass Spectrom. *1*, 223 (1974).
[60] *D. A. Brent, P. de Miranda*, and *H.-R. Schulten*, J. Pharm. Sci. *63*, 1370 (1974).
[61] *M. S. B. Munson* and *F. H. Field*, J. Amer. Chem. Soc. *88*, 2621 (1966).
[62] *H. J. Heinen, Ch. Hotzel*, and *H. D. Beckey*, Int. J. Mass Spectrom. Ion Phys. *13*, 55 (1974).
[63] *W. Paul, H. P. Reinhard*, and *U. v. Zahn*, Z. Phys. *152*, 143 (1958).
[64] *H. H. Gierlich, H. J. Heinen*, and *H. D. Beckey*, Biomed. Mass. Spectrom. *2*, 31 (1975).
[65] *H. L. C. Meuzelaar* and *P. G. Kistemaker*, Anal. Chem. *45*, 587 (1973); *H. L. C. Meuzelaar, M. A. Posthumus, P. G. Kistemaker*, and *J. Kistemaker*, *ibid. 45*, 1546 (1973).
[66] *H.-R. Schulten* in *C. G. Heden* and *T. Illeni*: New Approaches to the Identification of Microorganisms. Wiley, New York 1974, p. 117.
[67] *H.-R. Schulten* and *H. D. Beckey*, J. Chromatogr. *83*, 315 (1973).
[68] *H. D. Beckey* and *H.-R. Schulten*, Z. Anal. Chem. *273*, 345 (1975).
[69] *P. Arpino, M. A. Baldwin*, and *F. W. McLafferty*, Biomed. Mass Spectrom. *1*, 80 (1974), and literature cited therein.
[70] *F. W. Rollgen* and *H.-R. Schulten*, Org. Mass Spectrom., in press.
[71] *H.-R. Schulten* and *U. Schurath*, Atmos. Env., in press.
[72] *H.-R. Schulten* and *U. Schurath*, J. Phys. Chem. *79*, 51 (1975).

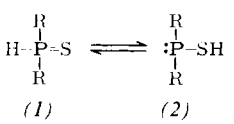
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying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

Isomerization of Dimethylphosphane Sulfide on Transition Metals[**]

By *Ekkehard Lindner* and *Hans Dreher*[*]

Dedicated to Professor Eugen Müller on the occasion of his 70th birthday

In principle secondary phosphane sulfides *(1)* and thiophosphinic acids *(2)*, R_2HPS and R_2PSH, can be assumed to exist in a tautomeric equilibrium[1]:

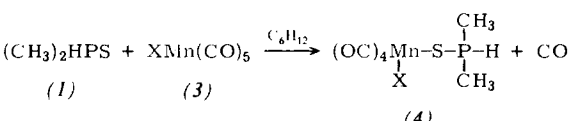


(1) *(2)*

At room temperature, however, the system lies completely on the side of *(1)*[2].

Temperature-dependent ^{1}H-NMR studies have shown that the P—H bond in $(CH_3)_2HPS$ *(1)* is cleaved only above 180 °C, and it appears rather unlikely that the thiophosphinic acid $(CH_3)_2PSH$ *(2)* can exist under these conditions.

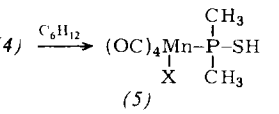
Accordingly[2], compound *(1)* initially coordinates *via* sulfur[3] to carbonylmetal systems such as $XMn(CO)_5$ *(3a—b)* with replacement of one CO ligand to form the *S*-isomeric complexes *(4a—b)*, which are sparingly soluble in cyclohexane:



(1) *(3)* *(4)*

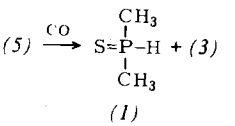
X		T [°C]
Cl	*(a)*	40
Br	*(b)*	50

If the temperature is raised by about 5 °C in each case, then quantitative isomerization to the cyclohexane-soluble *P*-bonded complexes *(5a—b)* occurs in which the ligand is now bonded as thiophosphinic acid.



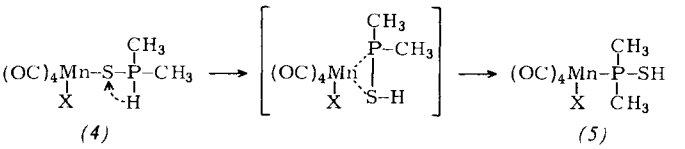
(4) *(5)*

Thus the conversion of *(1)* into *(2)* proceeds under relatively mild conditions on a metal. Thiophosphinic acid *(2)* is apparently only stable in the complexed state since *(1)* is immediately regenerated from the free ligand.



(5) *(1)*

On reaction of *(1)* with $IMn(CO)_5$ *(3c)* the temperatures for CO substitution and isomerization of *(4c)* to *(5c)* are almost identical (70 °C) and $(OC)_4IMnP(CH_3)_2SH$ *(5c)* is therefore formed directly.



(4) *(5)*

Available evidence suggests that the isomerization of *(4)* to *(5)* proceeds *via* an intramolecular mechanism. The compositions and structures of the yellowish brown and orange monomeric diamagnetic linkage isomers *(4a—b)* and *(5a—c)* follow from elemental analysis and mass, IR, ^{1}H-NMR, and ^{31}P-NMR spectra (see Table 1).

Table 1. ^{1}H-NMR spectra of $(CH_3)_2HPS$ *(1)* and the bromotetracarbonylmanganese complexes *(4b)* and *(5b)* (solution in $CDCl_3$, TMS as standard, recorded at 60 MHz).

Cpd.	Coupling constants J [Hz]				Chemical shifts δ [ppm]		
	J_{PCH}	J_{PH} [a]	J_{HPCH}	J_{PSH}	CH_3	PH	SH
(1)	14	448	4.5	—	1.9	7.4	—
(4b)	14	490	4.5	—	1.9	7.0	—
(5b)	8	—	—	4.5	2.0	—	3.7

[a] The large coupling constant of 450—500 Hz is characteristic of all protons bonded directly to phosphorus [4].

Procedure:

$(CH_3)_2HPS$ *(1)* (4 mmol) and *(3a)* or *(3b)* (4 mmol) are heated together to 40 or 50 °C, respectively, in cyclohexane (30 ml) until evolution of gas has ceased; the mixture is filtered and the precipitate is washed with cold light petroleum. Recrystallization from CH_2Cl_2/light petroleum affords analytically pure *(4a)* or *(4b)*. To prepare *(5a—b)* a suspension of *(4a—b)* in cyclohexane is heated to 45 or 55 °C, respectively, until dissolution is complete. The mixture is filtered, the solvent removed under vacuum, and the product recrystallized from light petroleum.

Received: December 6, 1974 [Z 185 IE]
German version: Angew. Chem. *87*, 447 (1975)
Publication delayed at authors' request

[*] Prof. Dr. E. Lindner and Dipl.-Chem. H. Dreher
Lehrstuhl für Anorganische Chemie II der Universität
74 Tübingen 1, Auf der Morgenstelle (Germany)

[**] The Behavior of Mono- and Diorganylphosphane Sulfides towards Metal Carbonyl Systems, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: ref. [3].

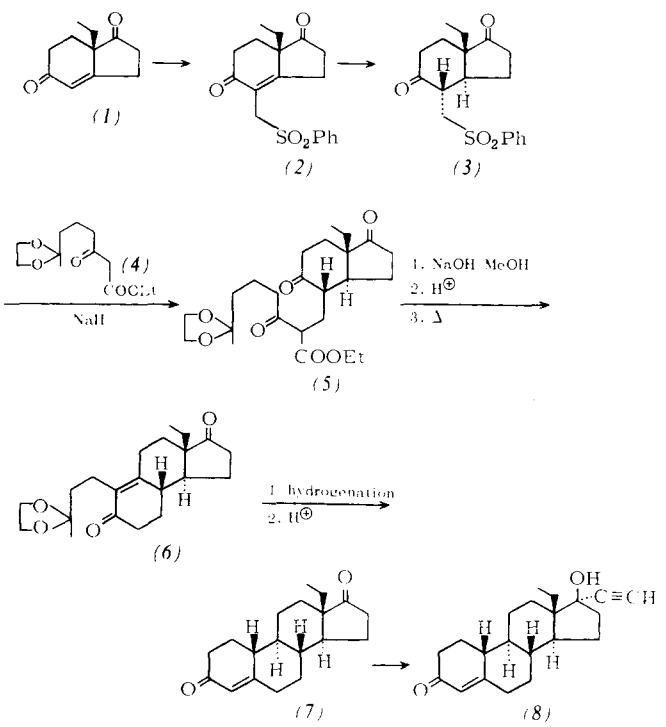
CAS Registry numbers:
(1), 6591-05-5; *(3a)*, 14100-30-2; *(3b)*, 14516-54-2; *(3c)*, 14879-42-6; *(4a)*, 54751-04-1; *(4b)*, 54751-05-2; *(4c)*, 54751-06-3; *(5a)*, 54751-03-0; *(5b)*, 42593-43-1; *(5c)*, 54751-07-4

[1] *K. Sasse* in: Methoden der organischen Chemie (Houben-Weyl-Müller), 4th Edit., Vol. XII/1. Thieme, Stuttgart 1955, p. 212.
[2] *L. Maier*, Helv. Chim. Acta *49*, 1249 (1966); references cited therein.
[3] *E. Lindner* and *W.-P. Meier*, J. Organometal. Chem. *67*, 277 (1974).
[4] *L. Maier*, Top. Phosphorus Chem. *2*, 43 (1965).

Synthesis of D-Norgestrel[1]

By *Gerhard Sauer*, *Ulrich Eder*, *Gregor Haffer*, *Günter Neef*, and *Rudolf Wiechert*[*]

D-Norgestrel[2, 3] (17α-ethynyl-18-methyl-19-nortestosterone *(8)* is a clinically proven, extraordinarily strong progestational and ovulation inhibiting steroid. The regioselective sulfonylmethylation of optically active 7a β-ethyl-6*H*-7,7a-dihydroindan-1,5-dione *(1)*[4] opens the possibility of a new, technically simpler synthesis of D-norgestrel.

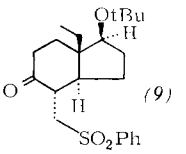


Me = CH_3, Et = C_2H_5, tBu = $C(CH_3)_3$, Ph = C_6H_5

Reaction of the (+)-enedione *(1)* with paraformaldehyde and benzenesulfinic acid in a mixture of nitrilotriethanol (triethanolamine)[5] and acetic acid[6] at 50°C affords the sulfone *(2)* in 85% yield (Table 1). Other bifunctional bases such as *N,N,N',N'*-tetramethylethylenediamine can be used; essential, however, is that base and acetic acid are used in a volume ratio of about 3:1. Presence of a larger amount of acetic acid accelerates the reaction, but the regioselectivity is thereby reduced, and considerable amounts of doubly alkylated products of varying structure are formed.

In acid solution (ethanol with 1% aqueous 1 N hydrochloric acid) with 6% palladium on charcoal (10%) as catalyst, the sulfone *(2)* is hydrogenated to the *trans*-fused sulfone *(3)* (Table 1). The yield of crystalline product is 75%. Some hydrogenolysis of the 5-carbonyl group takes place as side reaction.

The quoted ring coupling in the hydrogenated sulfone *(3)* is proven by chemical correlation with the hydrogenated sulfone *(9)*[7], whose structure is confirmed by the chemical shift and coupling constant of the proton at C-1 ($\delta = 3.48$, broad triplet, $J = 8$ Hz) (Table 1). From the positive Cotton effect ($\Delta\varepsilon_{289} = +1.64$) it would appear that the phenylsulfonylmethyl group is α, *i.e.* in an equatorial position.



(9)

Table 1. Prepared compounds *(2)*, *(3)*, and *(9)*.

(2), m.p. 124—125°C (CCl_4); $[\alpha]_D = +198°$ (1% in $CHCl_3$); IR (KBr): 1750 (5-ring ketone), 1675 (unsat. ketone), 1140 and 1300/1310 cm^{-1} (SO_2); UV (CH_3OH): $\varepsilon_{218} = 11700$, $\varepsilon_{252} = 10400$; CD (dioxane): $\Delta\varepsilon_{253} = -34.9$, $\Delta\varepsilon_{302} = +11.8$, $\Delta\varepsilon_{311} = +12.5$; ^{1}H-NMR ($CDCl_3$): $\delta = 0.98$ (3H, t, $J = 7.5$ Hz, CH_3—CH_2), 4.09 and 4.36 (2H, AB, $J = 13$ Hz, CH_2—SO_2), 7.82 (2H, dd, $J = 8$ Hz, $J = 2$ Hz, arom. H), 7.4—7.7 (3H, m, arom. H).

(3), m.p. 160—161 °C (ethyl acetate); $[\alpha]_D = +82$ (1% in $CHCl_3$); IR (KBr): 1732 (5-ring ketone), 1715 (6-ring ketone), 1310/1315 and 1145/1155 cm^{-1} (SO_2); CD (dioxane): $\Delta\varepsilon_{296} = +4.19$; ^{1}H-NMR ($CDCl_3$): $\delta = 0.94$ (3H, t, $J = 7.2$ Hz, CH_3—CH_2), 2.98 (1H, AB—X, $J = 4$ Hz, $J = 16$ Hz, CH—CH_2—SO_2), 3.23 (1H, m, $W_{1/2} = 23$ Hz, CH—CH_2—SO_2), 4.06 (1H, AB—X, $J = 4.6$ Hz, $J = 16$ Hz, CH—CH_2—SO_2), 7.55—7.59 (3H, m, arom. H), 7.88—7.98 (2H, m, arom. H).

(9), m.p. 138—139°C (ethyl acetate/diisopropyl ether); $[\alpha]_D = +41°$ (1% in $CHCl_3$); IR (KBr): 1715 (6-ring ketone), 1140 and 1300 cm^{-1} (SO_2); CD (dioxane): $\Delta\varepsilon_{289} = 1.64$; ^{1}H-NMR ($CDCl_3$): $\delta = 1.12$ (3H, t, $J = 7$ Hz, CH_3—CH_2), 1.12 (9H, s, $(CH_3)_3C$), 2.89 (1H, AB—X, $J = 2.8$ Hz, $J = 14$ Hz, CH_2SO_2), 3.10 (1H, m, $W_{1/2} = 24$ Hz, CH—CH_2—SO_2), 3.48 (1H, t, $J = 8$ Hz, CH—O—$C(CH_3)_3$), 3.96 (1H, AB—X, $J = 5.8$ Hz, $J = 14$ Hz, CH_2—SO_2), 7.48—7.62 (3H, m, arom. H), 7.82—7.97 (2H, m, arom. H).

In non-polar solvents (pentane/benzene) *(3)* reacts with the anion prepared from ethyl 7,7-ethylenedioxy-3-oxooctanoate *(4)*[8] and sodium hydride to give high yields of the ester *(5)*. This crude product is then cyclized, hydrolyzed, and decarboxylated. The tricyclic compound *(7)* (cf. *Hajos et al.*[8]) was isolated as an oil and for this reason a more detailed characterization was not carried out. Subsequent hydrogenation, ketal cleavage, and cyclization afford 18-methyl-19-norandrostenedione *(7)* in an overall yield of 35% (from *(1)*).

D-Norgestrel *(8)*[2] can be obtained from *(7)* by ethynylation; its structure, like that of *(7)*, is confirmed by comparison with authentic material.

Received: February 5, 1975 [Z 195 IE]
German version: Angew. Chem. *87*, 413 (1975)

CAS Registry numbers:
(1), 33878-95-4; *(2)*, 54832-84-7; *(3)*, 54832-85-8; *(4)*, 27428-41-7; *(5)*, 54851-83-1; *(6)*, 24894-31-3; *(7)*, 21800-83-9; *(8)*, 797-63-7; *(9)*, 54832-86-9

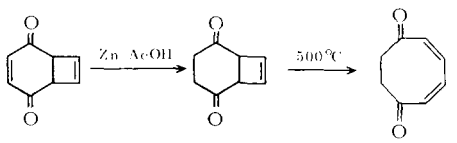
[*] Dr. G. Sauer, Dr. U. Eder, Dr. G. Haffer, Dr. G. Neef, and Prof. Dr. R. Wiechert
Schering AG, Berlin/Bergkamen
1 Berlin 65, Müllerstrasse 170—178 (Germany)

[1] Total Synthesis of Optically Active Steroids, Part 12.—Part 11: *U. Eder, G. Sauer, J. Ruppert, G. Haffer*, and *R. Wiechert*, Chem. Ber., in press.
[2] *H. Smith, G. A. Hughes, G. H. Douglas, G. R. Wendt, G. C. Buzby, jun., R. A. Edgren, J. Fisher, T. Foell, B. Gadsby, D. Hartley, D. Herbst, A. B. A. Jansen, K. Ledig, B. J. McLoughlin, J. McMenamin, T. W. Pattison, P. C. Phillips, R. Rees, J. Siddall, J. Siuda, L. L. Smith, J. Tokolics*, and *D. H. P. Watson*, J. Chem. Soc. *1964*, 4472.
[3] *C. Rufer, H. Kosmol, E. Schröder, K. Kieslich*, and *H. Gibian*, Liebigs Ann. Chem. *702*, 141 (1967).
[4] a) *U. Eder, G. Sauer*, and *R. Wiechert*, Angew. Chem. *83*, 492 (1971); Angew. Chem. internat. Edit. *10*, 496 (1971); b) *Z. G. Hajos* and *D. R. Parrish*, J. Org. Chem. *39*, 1615 (1974).
[5] *D. H. Kirk* and *V. Petrow*, J. Chem. Soc. *1962*, 1091.
[6] *H. Hellmann* and *K. Müller*, Chem. Ber. *98*, 638 (1965).
[7] Preparation of *(9)*: *G. Sauer et al.*, to be published.
[8] *Z. G. Hajos* and *D. R. Parrish*, J. Org. Chem. *38*, 3239, 3244 (1973).

2,5,7-Cyclooctatriene-1,4-dione

By *Masaji Oda, Yasutaka Kayama, Hideo Miyazaki*, and *Yoshio Kitahara*[*]

Recently, there has been considerable interest in the synthesis of cyclooctatrienediones[1] and their valence bond isomers[2]. In the thermolysis of bicyclo[4.2.0]octa-3,7-diene-2,5-dione *(1)* which gives tropone, we have suggested the intermediacy of *cis,cis,cis*-2,5,7-cyclooctatriene-1,4-dione *(6)* or its *cis,cis,trans* isomer[2c]. Quite recently, *Chaloner et al.* have reported the synthesis of the bis(ethyleneketal) of *(6)*[3]. We here report the synthesis of *(6)*.

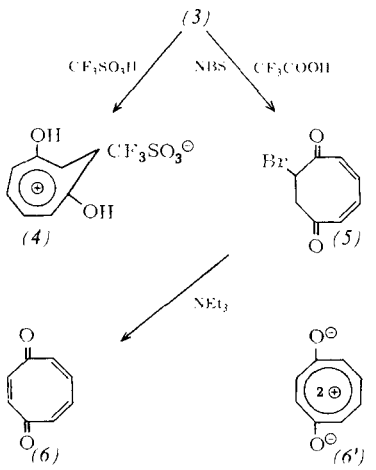


(1) *(2)* *(3)*

Reduction of *(1)*[2b] with zinc in acetic acid at 90 °C gave bicyclo[4.2.0]octa-7-ene-2,5-dione *(2)* (yield 65 %) whose synthesis by an independent and different method has recently been described[4]. Flash thermolysis of *(2)* in vacuum at 500 °C afforded the 5,7-cyclooctadiene-1,4-dione *(3)* (yield 91 %) as a pale yellow liquid; IR: $\nu = 1660, 1615\ cm^{-1}$; UV ($C_2H_5OH$): $\lambda_{max} = 256$ ($\log\varepsilon = 3.78$), 270 sh (3.74), 338 sh (2.71), 354 nm sh (2.62); ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 2.79$ (s, 4H), 6.02 (dt, $J = 13.2$, 2.0 Hz, 2H), 6.39 ppm (dt, 13.2, 2.0 Hz, 2H); ^{1}H-NMR (CF_3COOH, CH_2Cl_2 (5.30 ppm)): $\delta = 3.00$ (s, 4H), 6.39 (dt, 2H), 6.88 ppm (dt, 2H).

Attempts to dehydrogenate *(3)* with benzoquinone compounds and selenium dioxide or to brominate with *N*-bromosuccinimide (NBS) in refluxing carbon tetrachloride have been unsuccessful, giving starting material or complex mixtures[5].

The conditions for successful bromination were found as a result of the following observation: The ^{1}H-NMR spectrum of *(3)* in CF_3COOH—CF_3SO_3H (2:1) exhibits signals at $\delta = 1.50$ (dd, $J = 11$, 9 Hz, 1H), 4.17 (dd, 11, 9 Hz, 1H), 5.32 (t, 9 Hz, 1H), 7.5 (m, 3H), and 8.04 ppm (dd, 12, 7 Hz, 1H), thus indicating that the species in this solution is 1,6-dihydroxyhomotropylium ion *(4)*. Therefore, the appreciable downfield shift of olefin protons of *(3)* in CF_3COOH compared with those in $CDCl_3$ seems to reflect fast equilibrium between *(3)* and *(4)*. Bromonium ions would be expected to react at C-7 of *(4)*.



Actually, treatment of *(3)* with NBS in CF_3COOH—CH_2Cl_2 (1:2) at room temperature gave the unstable 2-bromo-5,7-cyclooctadiene-1,4-dione *(5)*. Dehydrobromination of *(5)*, without isolation, with triethylamine afforded, after chromatography on silica-gel (CH_2Cl_2-ethyl acetate, 95:5), 2,5,7-cyclooctatriene-1,4-dione *(6)* in 28% yield as a yellow liquid; MS: *m/e* 134 (M^+), 106 (M−CO), 78 (M−2CO, 100 %); IR (liquid): $\nu = 3030$ w, 1650 br. s, 1610 s, 1125 s, 840 m, 805 m, 784 m, 710 m cm^{-1}; UV (cyclohexane): $\lambda_{max} = 224$ ($\log\varepsilon = 4.01$), 277 sh (3.22), 370 nm (2.15); ^{1}H-NMR (CCl_4): $\delta = 6.00$ (dt, $J = 13.5$, 2.0 Hz, 2H), 6.40 (dt, 13.5, 2.0 Hz), 6.61 ppm (s, 2H).

The ^{1}H-NMR signals of the diene protons of *(6)* and of *(3)* are almost the same, thus indicating that contribution of the polar form *(6')* can be neglected, *i.e. (6)* is not aromatic.

(6) can be hydrogenated with PtO_2 to 1,4-cyclooctanedione[3, 6].

Compound *(6)* is stable in aprotic solvents; however, it is unstable in protonic, particularly in acidic, solvents, giving complex mixtures (thin layer chromatography). Dissolution in CF_3COOH at room temperature led to complete decomposition of *(6)*.

Although the mass spectrum of *(6)* is very similar to that of *(1)*, thermal decomposition of *(6)* at 500 °C is only slight. This result rules out the intermediacy of *(6)* in the thermolytic conversion of *(1)* into tropone. The *cis,cis,trans*-isomer of *(6)*, which, according to *Woodward-Hoffmann*[8], is expected as the initial product of thermal ring-opening of *(1)* still, however, remains as a possible intermediate.

Received: February 19, 1975 [Z 196 IE]
German version: Angew. Chem. 87, 414 (1975)

CAS Registry numbers:
(1), 54251-47-7; *(2)*, 54832-87-0; *(3)*, 54832-88-1; *(5)*, 54832-89-2; *(6)*, 54832-90-5

[1] *M. P. Cava* and *K. W. Ratts*, J. Org. Chem. *27*, 752 (1962); *D. McIntyre, G. R. Proctor*, and *L. Rees*, J. Chem. Soc. *C 1966*, 985; *P. Yates, E. G. Lewars*, and *P. H. McCabe*, Can. J. Chem. *48*, 788 (1970); *50*, 1548 (1972); *J. Tsunetsugu, M. Sato*, and *S. Ebine*, J. C. S. Chem. Comm. *1973*, 363.

[2] a) *P. Yates* and *G. V. Nair*, Synthetic Commun. *3*, 337 (1973); b) *M. Oda, Y. Kayama*, and *Y. Kitahara*, Tetrahedron Lett. *1974*, 2019; c) *Y. Kayama, M. Oda*, and *Y. Kitahara*, ibid. *1974*, 3293.

[3] *P. A. Chaloner, A. B. Holmes, M. A. McKervey*, and *R. A. Raphael*, Tetrahedron Lett. *1975*, 265.

[4] *G. A. Russell, J. R. Dodd, T. Ku, C. Tanger*, and *C. S. C. Chung*, J. Amer. Chem. Soc. *96*, 7255 (1974). The IR and NMR data of our compound are in accordance with those reported in the literature.

[5] Under basic conditions, compound *(3)* is liable to cyclize, finally giving bicyclo[4.2.0]octa-3-ene-2,7-dione.

[6] Our authentic sample was prepared by hydrogenation of 2-cyclooctene-1,4-dione [Ref. 7].

[7] *Y. Kayama, M. Oda*, and *Y. Kitahara*, Chem. Lett. *1974*, 345.

[8] *R. B. Woodward* and *R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).

[*] Dr. M. Oda, Dipl.-Chem. Y. Kayama, Dipl.-Chem. H. Miyazaki, and Prof. Dr. Y. Kitahara [**]
Dept. of Chemistry
Faculty of Science
Tohoku University
Sendai 980 (Japan)

[**] To whom all correspondence should be addressed.

A Novel Simple Synthesis of Helicenes[**]

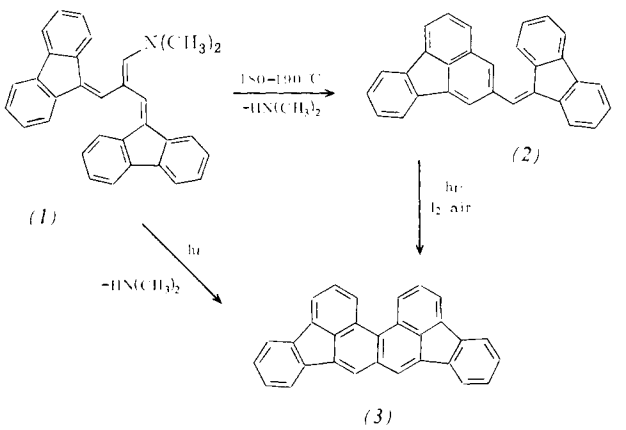
By *Christian Jutz* and *Hans-Georg Löbering*[*]

Dilute solutions of the orange-red 1-dimethylamino-2,2-bis(9-fluorenylidenemethyl)ethylene *(1)*[1] are slowly decolor-

[*] Prof. Dr. C. Jutz [+] and Dipl.-Chem. H.-G. Löbering
Organisch-Chemisches Laboratorium der Technischen Universität München 2, Arcisstrasse 21 (Germany)
[+] Author to whom correspondence should be addressed.

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

ized on exposure to sunlight with formation of a strongly fluorescing hydrocarbon[2]. After three hours' irradiation[3] of a solution of *(1)* in THF, we were able to isolate this hydrocarbon in 64% yield and to identify it as benzo[*e*]fluoreno[9,1-*kl*]acephenanthrylene *(3)*, light-yellow needles, m.p. 259—260 °C. The photo-dehydrocyclization of 2-(9-fluorenyli-



denemethyl)fluoranthene *(2)* in benzene in the presence of iodine and atmospheric oxygen likewise afforded *(3)* in 50% yield after 10 hours' irradiation. The required compound *(2)* (pale yellow crystals, m.p. 146 °C) was obtained by thermolysis of *(1)* in quinoline (10 h, 180—190 °C, 81% yield). The combination of thermal cyclization with dimethylamine elimination [*(1)* → *(2)*][4] and photo-dehydrocyclization [*(2)* → *(3)*][5] opens new synthetic aspects.

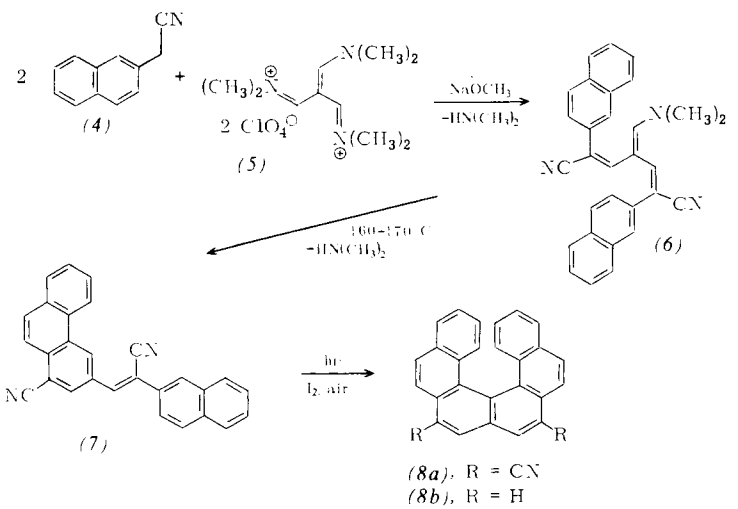
Phenanthro[3,4-c]phenanthrene (hexahelicene) (8b)

To the formylation mixture—prepared under cooling from dimethylformamide (36 g) and $POCl_3$ (46 g)—is added 10.4 g malonic acid with stirring. After strong evolution of CO_2 has subsided the mixture is heated to 90—95 °C for 3 hours, treated under cooling with 200 ml ethanol, and finally 35 g 70% $HClO_4$ in a little ethanol is added. The orange-yellow *(5)* is filtered off under suction, and then washed with cold ethanol and finally with ether. Twofold crystallization from acetonitrile/ether affords 25.5 g (67%) of *(5)* as colorless needles of m.p. 220—221 °C (dec).

To a stirred suspension of 4.20 g *(5)* in 30 ml ethanol is added 20 mequiv. $NaOCH_3$ solution (*ca.* 3 N in methanol). This is followed by addition of a solution of 3.50 g *(4)* in 10 ml ethanol/benzene (1 : 1). After heating for a short while the reaction mixture solidifies, and after cooling and filtration *(6)* is isolated as fine orange-yellow needles 3.33 g (78%), m.p. 180—191 °C (dec).

2.60 g *(6)* in 5 ml quinoline is heated in a slow current of N_2 to 160—180 °C for 2 h (termination of evolution of dimethylamine) and the contents of the flask then triturated with 2 N HCl. The filtered and dried product is then recrystallized from chlorobenzene/ethanol: 2.30 g (99%) *(7)*, fine, green-yellow matted needles, m.p. 216—218 °C; IR(KBr): $\nu_{CN} = 2225, 2215\ cm^{-1}$.

A solution of *(7)* (0.8 g) in benzene (800 ml) treated with a few grains of iodine is irradiated with cooling at 600 W[3]. After evaporation of the benzene in vacuum and chromatography of the residue in CH_2Cl_2 on aluminum oxide (Act. II, neutral) 8.0 g *(8a)* is isolated (after recrystallization from ben-



(8a), R = CN
(8b), R = H

Thus, we have obtained all-benzene hexahelicene-7,10-dicarbonitrile (phenanthro[3,4-*c*]phenanthrene-7,10-dicarbonitrile) *(8a)* in a total yield of 74% based on 2-naphthaleneacetonitrile. The condensation of 2-dimethylamino-1,1-bis(dimethyliminiomethyl)ethylene diperchlorate *(5)*[1, 6] with *(4)* in ethanol with addition of sodium methoxide afforded 4-(dimethylaminomethylene)-2,6-di(2-naphthyl)-2,5-heptadienedinitrile *(6)*, which on thermal cyclization at 160 to 170 °C for 2 hours gave 3-(1-cyano-3-phenanthryl)-2-(2-naphthyl)acrylonitrile *(7)* quantitatively. On irradiation of a benzene solution of *(7)* in the presence of iodine and atmospheric oxygen a quantitative photo-dehydrocyclization to *(8a)* took place within 3 hours. For proof of structure, *(8a)* was first hydrolyzed and then decarboxylated to the hexahelicene *(8b)*.—In an analogous reaction sequence with benzyl cyanide instead of *(4)* we obtained benzo[*c*]phenanthrene-5,8-dicarbonitrile, m.p. 331—332 °C.

zene/hexane 0.76 g (96%), lemon-yellow hexagonal druses, m.p. 305—307 °C, IR(KBr): $\nu_{CN} = 2230\ cm^{-1}$.

The hydrolysis of 1.0 g *(8a)* in 15 ml 2-methoxyethanol with KOH affords, after 6 hours' heating and acidification, 1.1 g yellow dicarboxylic acid (m.p. >350 °C, dec.) which is treated with 8 ml quinoline and 0.1 g Cu powder and heated for 7 h on a metal bath to 240 °C. After work-up and chromatography on aluminum oxide (Act. II, neutral) in benzene 0.64 g (74%) of *(8b)*[7] is obtained as pale yellow hexagonal leaflets, m.p. 229—231 °C from benzene/ethanol (m.p. 230.4 to 230.9 °C[8]).

Received: February 26, 1975 [Z 197 IE]
German version: Angew. Chem. 87, 415 (1975)

CAS Registry numbers:
(1), 2601-61-8; *(2)*, 54832-95-0; *(3)*, 54832-96-1; *(4)*, 7498-57-9;

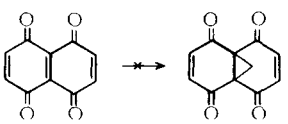
(5), 2009-81-6; (6), 54832-97-2; (7), 54852-58-3; (8a), 54832-98-3; (8b), 187-83-7

[1] C. Jutz and H. Amschler, Chem. Ber. 97, 3331 (1964).
[2] D. Rewicki, private communication.
[3] Photoreactor 9336 with Hg high-pressure vapor lamp TQ178 (Hanau, Quarzlampen GmbH) from Otto Fritz GmbH-Normschliff, Hofheim/Taunus (Germany).
[4] C. Jutz and R. M. Wagner, Angew. Chem. 84, 299 (1972); Angew. Chem. internat. Edit. 11, 315 (1972); C. Jutz and E. Schweiger, Chem. Ber. 107, 2383 (1974).
[5] F. R. Stermitz in O. L. Chapman: Organic Photochemistry. Marcel Dekker, New York 1967, Vol. 1, p. 247; C. S. Wood and F. B. Mallory, J. Org. Chem. 29, 3373 (1964); R. H. Martin, Angew. Chem. 86, 727 (1974); Angew. Chem. internat. Edit. 13, 649 (1974).
[6] Z. Arnold, Collect. Czech. Chem. Commun. 26, 3051 (1961).
[7] ^{1}H-NMR-Spectrum see R. H. Martin, N. Defay, H. P. Figeys, M. Flammang-Barbieux, J. P. Cosyn, M. Gelbcke, and J. J. Shurter, Tetrahedron 25, 4985 (1969).
[8] M. S. Newman and D. Lednicer, J. Amer. Chem. Soc. 78, 4765 (1956).

Electrochemical Entry to 9,10-Homonaphthodiquinone

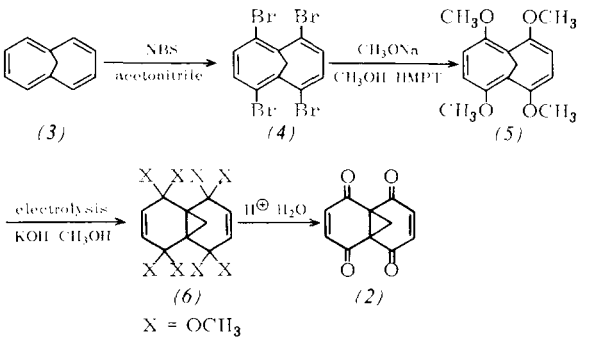
By *Wolfgang Bornatsch* and *Emanuel Vogel*[*]

In the course of planning a number of syntheses in the annulene field we came across the hitherto unknown 9,10-homonaphthodiquinone[1] (tricyclo[4.4.1.0^{1,6}]undeca-3,8-diene-2,5,7,10-tetrone) *(2)* as a potentially versatile synthon. The apparently obvious method of preparing *(2)* in one step from readily accessible 1,4,5,8-naphthodiquinone *(1)*[2] by cyclopropanation was unsuccessful. *(1)* failed to give the desired product on treatment with either diazomethane or methylene-transfer agents such as dimethyloxosulfonium methylide. Our search for other possible preparations of *(2)* has now revealed that 1,6-methano[10]annulene *(3)*[3] can be transformed into *(2)* in satisfactory overall yield *via* a pathway entailing an electrochemical reaction as essential step.



(1) *(2)*

On reaction with brominating agents, 1,6-methano[10]annulene *(3)* affords products whose composition is highly dependent upon the nature of the agent and the solvent and upon the reaction temperature[4]. Bromination of the hydrocarbon with *N*-bromosuccinimide (NBS) (5.5 mol) in acetonitrile, initially at 20—25 °C and then, after addition of half of the NBS, at 80 °C (duration of reaction 15 h), affords 2,5,7,10-tetrabromo-1,6-methano[10]annulene *(4)* as major product, which was isolated by chromatography over a short Al_2O_3 column (pentane) [yellow crystals, m.p. 128—129 °C (from ethanol); yield 42%; NMR (CCl_4): singlets at $\tau = 2.65$ and 9.93 (annulene and bridge protons, respectively); UV (cyclohexane): $\lambda_{max} = 224$ ($\varepsilon = 10500$), 291 (50000), 355 (11900), 453 (960, sh), 462 (1050), 473 nm (760, sh)]. The bromine atoms of *(4)* can be replaced remarkably easily by methoxy groups on treatment with sodium methoxide in methanol/hexamethylphosphoric triamide (1:2); 2,5,7,10-tetramethoxy-1,6-methano[10]annulene *(5)* is formed even at 0 °C in an exothermal reaction (cooling). Compound *(5)* was purified by chromatography over Al_2O_3 [pentane/ether (2:1)] and recrystallization from *n*-hexane [red needles, m.p. 79 °C; yield 73%; NMR (CCl_4): singlets at $\tau = 3.38$, 6.14, and 10.81 (annulene, methoxy, and bridge protons, respectively); UV (*n*-hexane): $\lambda_{max} = 268$ ($\varepsilon = 40200$), 290 (18900, sh), 343 (7400), 475 nm (3700)]. Since no rearranged products having β-methoxy groups were observed on bromine-methoxy exchange, the substitution probably proceeds *via* an addition-elimination mechanism[5].



As suggested by the electrochemical methoxylation of hydroquinone dimethyl ether to *p*-benzoquinone tetramethyl acetal[6], electrolysis of *(5)* at a platinum gauze anode (anodic current density: 20 mA/cm^2) in 1% methanolic potassium hydroxide solution at 0 °C leads cleanly to the octamethyl acetal *(6)*[7] of 9,10-homonaphthodiquinone [colorless crystals, m.p. 95—96 °C (from pentane); yield 55%; NMR (CCl_4): singlets at $\tau = 4.31$, 9.00 (olefinic and cyclopropane protons, resp.) and at 6.71, 6.78 (methoxy protons)]. The octamethyl acetal *(6)* is hydrolyzed relatively fast in a mixture of acetone and 3% hydrochloric acid (1:2) at room temperature; the stable compound *(2)* [yellow crystals (rhomboid) from acetonitrile, decomp. > 200 °C; yield 62%] was isolated as product.

The 9,10-homonaphthodiquinone structure *(2)* of the compound is confirmed by its spectra. The NMR spectrum (CD_3NO_2) consists solely of two singlets at $\tau = 3.46$ and 7.27 (olefinic and cyclopropane protons, respectively) and shows a ^{13}C—H coupling constant of 175 Hz for the CH_2 protons, thus unambiguously establishing the presence of a cyclopropane ring[8]. The presence of the enedione partial structure follows from the similarity of the UV spectrum [(acetonitrile) $\lambda_{max} = 218$ ($\varepsilon = 24100$), 265 (1800, sh), 365 nm (130)] to that of homo-*p*-benzoquinone[1a] and those of other related enediones[9]; moreover, the IR spectrum (KBr) contains CO and C=C bands at 1695 and 1605 cm^{-1}, respectively. The successive loss of 4CO units observed in the mass spectrum [*m/e* (rel. intensity): 202 (100%) M^+, 174 (7%) $M^+ - CO$, 146 (19%) $M^+ - 2CO$, 118 (25%) $M^+ - 3CO$, 90 (11%) $M^+ - 4CO$] is also in full accord with structure *(2)*.

The question whether *(2)* is to be regarded as a quinone should be answered by polarographic studies which are still in progress. Chemically, *(2)* exhibits quinone-type behavior in so far as it can be reductively acetylated to 2,5,7,10-tetraacetoxy-1,6-methano[10]annulene [yellow crystals, m.p. 157—158 °C (from ethanol); yield 62%; NMR ($CDCl_3$): singlets at $\tau = 3.07$, 7.76, and 10.27 (annulene, acetyl, and bridge protons, respectively); UV (methanol): $\lambda_{max} = 268$ ($\varepsilon = 63000$), 325 (7700), 433 nm (1100)] with zinc and acetic anhydride in the presence of pyridine.

Received: March 4, 1975 [Z 198 IE]
German version: Angew. Chem. 87, 412 (1975)

CAS Registry numbers:
(1), 23077-93-2; (2), 54832-91-6; (3), 2443-46-1; (4), 54832-93-8; (5), 54832-93-8; (6), 54832-94-9

[*] Prof. Dr. E. Vogel and Dipl.-Chem. W. Bornatsch
Institut für Organische Chemie der Universität
5 Köln 1, Zülpicher Strasse 47 (Germany)

[1] The homo derivatives of *p*-benzoquinone, which like *(2)* have hitherto resisted preparation by direct cyclopropanation, have very recently become available *via* original syntheses: a) homo-*p*-benzoquinone: C. B. Chapleo and A. S. Dreiding, Helv. Chim. Acta 57, 1259 (1974); G. A. Russell, J. R. Dodd, T. Ku, C. Tanger, and C. S. C. Chung, J. Amer.

Chem. Soc. 96, 7255 (1974); b) *syn*- and *anti*-bishomo-*p*-benzoquinone: *J. Heller, A. Yogev*, and *A. S. Dreiding*, Helv. Chim. Acta *55*, 1003 (1972); *G. L. Buchanan, R. A. Raphael*, and *R. Taylor*, J. C. S. Perkin I *1973*, 373; *J. E. Heller, A. S. Dreiding, B. R. O'Connor, H. E. Simmons, G. L. Buchanan, R. A. Raphael*, and *R. Taylor*, Helv. Chim. Acta *56*, 272 (1973); *C. B. Chapleo* and *A. S. Dreiding, ibid. 57*, 873 (1974).

[2] *K. Zahn* and *P. Ochwat*, Liebigs Ann. Chem. *462*, 72 (1928); *B. Schröder*, Dissertation, Universität München 1965. We thank Prof. *J. Sauer*, Universität Regensburg, for informing us of this work carried out under his supervision.

[3] *E. Vogel, W. Klug*, and *A. Breuer*, Org. Syn., in press.

[4] *E. Vogel* and *W. A. Böll*, Angew. Chem. *76*, 784 (1964); Angew. Chem. internat. Edit. *3*, 642 (1964); *E. Vogel, W. A. Böll*, and *M. Biskup*, Tetrahedron Lett. *1966*, 1569.

[5] *J. F. Bunnett*, Quart. Rev. Chem. Soc. *12*, 1 (1958); *F. Pietra, ibid. 23*, 504 (1969).

[6] *B. Belleau* and *N. L. Weinberg*, J. Amer. Chem. Soc. *85*, 2525 (1963); cf. also. electrochemical methoxylation of furans: *N. Elming*, Advan. Org. Chem. *2*, 67 (1960).

[7] For conversion of 1,6-bridged [10]annulenes into tricyclo[4.4.1.$0^{1,6}$]undecane derivatives ([4.4.1]propellanes) see *D. Ginsburg*: Propellanes. Verlag Chemie, Weinheim, in press.

[8] *H. Günther*: NMR-Spektroskopie. G. Thieme Verlag, Stuttgart 1973, pp. 365ff.

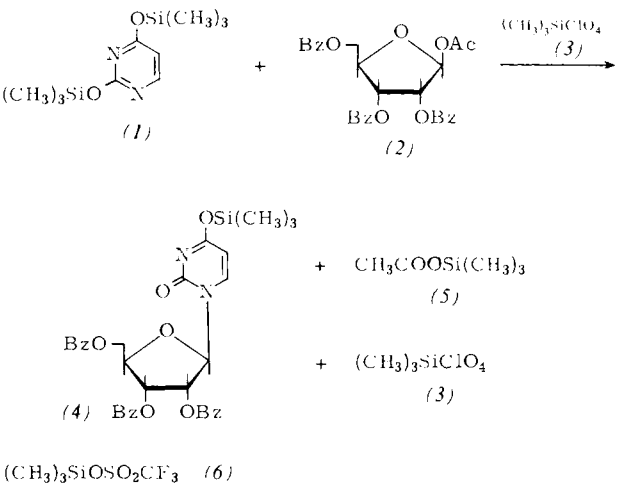
[9] *E. W. Garbisch, Jr.*, J. Amer. Chem. Soc. *87*, 4971 (1965).

New Catalysts for the Synthesis of Nucleosides[1]

By *Helmut Vorbrüggen* and *Konrad Krolikiewicz*[*]

Reaction of silylated heterocycles with protected 1-*O*-acyl or 1-*O*-alkyl sugars in the presence of Friedel-Crafts catalysts like $SnCl_4$ usually gives high yields of nucleosides[2, 3], but workup is often complicated by the formation of emulsions and colloids.

As we have recently observed[4], the easily prepared trimethylsilyl perchlorate *(3)*[5], which is formed as an intermediate in the $AgClO_4$ method[6], as well as trimethylsilyl trifluoromethanesulfonate *(6)*[7] show the properties of strong Lewis acids and are suitable as Friedel-Crafts catalysts. We have therefore reacted silylated uracil *(1)* as well as other silylated heterocycles with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose *(2)* in 1,2-dichloroethane with 0.1 equiv. of a solution of *(3)* or of *(6)* in benzene. On prolonged standing at 22 °C, or on boiling for *ca.* 4 h, in addition to trimethylsilyl acetate *(5)* 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl perchlorate (or trifluoromethanesulfonate) is probably formed, which reacts with *(1)* to give 4-*O*-silylated uridine-tri-*O*-benzoate *(4)*.



Since new *(3)* or *(6)* is generated during this reaction catalytic amounts of *(3)* or *(6)* are usually sufficient. The workup with $NaHCO_3/CH_2Cl_2$ with saponification of *(4)* is very simple and gives uridine-tri-*O*-benzoate in *ca.* 80% yield.

The analogous reactions, which are summarized in Table 1, demonstrate that this new modification of the silyl-Hilbert-Johnson reaction gives in analogy to the $SnCl_4$ method[2, 3] the desired natural β-nucleosides in high yields.

Table 1. Reaction of silylated heterocycles with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose *(2)* in 1,2-dichloroethane.

Heterocycles (silylated)	Catalyst	Conditions *T*/*t*	Product	Yield [%]	M.p. [°C]
uracil	0.1 equiv. *(3)*	82 °C/6 h	uridine-2',3',5'-tri-*O*-benzoate	80 [a]	138—140
uracil	0.25 equiv. *(3)*	22 °C/7 d	uridine-2',3',5'-tri-*O*-benzoate	76	138—140
cytosine	1 equiv. *(6)*	82 °C/1 h	cytidine-2',3',5'-tri-*O*-benzoate	90	amorphous
2-thio-6-azauracil [b]	0.1 equiv. *(3)*	82 °C/3 h	2-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-thio-2*H*-1,2,4-triazin-5-one	67	221—223 [2]
N-benzoyladenine	0.1 equiv. *(3)*	82 °C/7 h	adenosine [c]	81	230—232
2-pyridone	0.1 equiv. *(6)*	82 °C/2 h	1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-pyridone	86	136—138 [2]
lumazine	0.1 equiv. *(6)*	24 °C/24 h	lumazine-riboside [d] [8]	64	154—155

[a] The analogous reaction in acetonitrile gave the same yield.
[b] Reaction with 1,2,4,6-penta-*O*-acetyl-β-D-glucopyranose.
[c] After saponification with CH_3OH/NH_3 (22 °C/16 h) and recrystallization from CH_3OH/H_2 (2:1).
[d] After saponification with CH_3OH/NH_3 (24 °C/84 h) and recrystallization from C_2H_5OH/i-PrOH.

[*] Dr. H. Vorbrüggen [**] and K. Krolikiewicz
Research Laboratories of Schering A.G., Berlin/Bergkamen
1 Berlin 65, Postfach 650311 (Germany)
[**] Author to whom inquiries should be directed.

Procedure:

To 10 mmol of bissilylated lumazine[8] and 5.04 g (10 mmol) *(2)* in 50 ml 1,2-dichloroethane, 1 mmol *(6)*[7] (2 ml of a stan-

dard solution in benzene) was added and the reaction mixture stirred for 24 h at 24 °C under argon. After shaking with ice-cold $NaHCO_3$ solution, drying (Na_2SO_4) and evaporating, 6.5 g of amorphous homogeneous lumazine-tri-*O*-benzoyl-riboside was obtained, which was stirred with CH_3OH/NH_3 for 84 h at 24 °C. After evaporation, 100 ml H_2O was added and the aqueous solution extracted with ether. Evaporation of the aqueous phase afforded 3.2 g crude lumazine-riboside, which was extracted with 200 ml boiling ethanol. Concentration to 50 ml and addition of 150 ml isopropanol gave, in several crops, 1.9 g (64%) lumazine-riboside, m.p. 154—155 °C (Ref. [8]: 182—189 °C).

Received: March 10, 1975 [Z 200 IE]
German version: Angew. Chem. *87*, 417 (1975)

CAS Registry numbers:
(1), 10457-14-4; *(2)*, 6974-32-9; *(3)*, 18204-79-0; *(6)*, 27607-77-8; uracil, 66-22-8; cytosine, 71-30-7; 2-thio-6-azauracil, 626-08-4; *N*-benzoyladenine, 4005-49-6; 2-pyridone, 142-08-5; lumazine, 487-21-8; uridine-2',3',5'-tri-*O*-benzoate, 1748-04-5; cytidine-2',3',5'-tri-*O*-benzoate, 31652-74-1; 2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-thio-2*H*-1,2,4-triazin-5-one, 29725-44-8; adenosine, 58-61-7; 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-pyridone, 5116-31-4; lumazine-riboside, 34097-18-2; 1,2,3,4,6-penta-*O*-acetyl-β-glucopyranose, 604-69-3

[1] Synthesis of Nucleosides, Part 16; Reactions with Silyl Esters of Strong Acids, Part 1.—Part 15 cf. Ref. [4].
[2] *U. Niedballa* and *H. Vorbrüggen*, Angew. Chem. *82*, 449 (1970); J. Org. Chem. *39*, 3654, 3660, 3664, 3668, 3673 (1974).
[3] *F. W. Lichtenthaler*, *P. Voss*, and *A. Heerd*, Tetrahedron Lett. *1974*, 2141.
[4] *H. Vorbrüggen* and *K. Krolikiewicz*, Angew. Chem. *87*, 251 (1975); Angew. Chem. internat. Edit. *14*, 255 (1975).
[5] *C. Eaborn*, J. Chem. Soc. *1955*, 2517; *U. Wannagat* and *W. Liehr*, Angew. Chem. *69*, 783 (1957).
[6] *H. Vorbrüggen* and *P. Strehlke*, Chem. Ber. *106*, 3039 (1973).
[7] *H. C. Marsmann* and *H. G. Horn*, Z. Naturforsch. *27b*, 1448 (1972).
[8] *G. Ritzmann* and *W. Pfleiderer*, Chem. Ber. *106*, 1401 (1973).

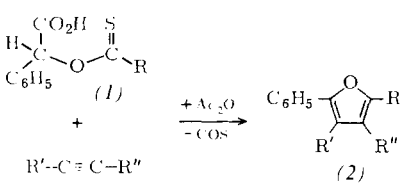
[3+2]-Cycloadditions of Mesoionic 1,3-Oxathio-4-ones to Alkynes. A New Entry to the Furan Series[**]

By *Hans Gotthardt*, *Michael C. Weisshuhn*, and *Karl Dörhöfer*[*]

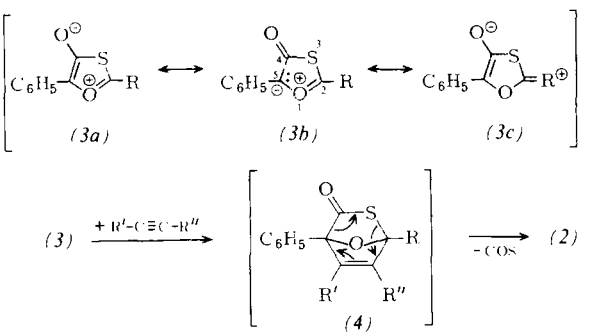
The 1,3-oxathiolylium-4-olate system of type *(3)*, a new mesoionic 6π arene[1], is presumably too unstable to be detected at room temperature. We have now been able to produce *(3) in situ* from thiocarbonyloxyacetic acids and to trap it by [3+2]-cycloaddition.

If a benzene solution of phenyl(piperidinothiocarbonyloxy)acetic acid (*(1)*, $R = C_5H_{10}N$)[2] is heated to 70—80 °C for 3 h with 5.9 equivalents of acetic anhydride in the presence of 1.2 equivalent of methyl propiolate, then COS is liberated with formation of methyl-5-phenyl-2-piperidinofuran-3-carboxylate *(2a)*[3], m.p. 74—76 °C (further examples are given in Table 1).

In the initial step of this new furan synthesis, the action of acetic anhydride or dicyclohexylcarbodiimide on *(1)*



appears to promote elimination of water to form the 1,3-oxathiolium-4-olate *(3)*. As symbolized by the resonance structure *(3b)*, the mesoionic 6π arene *(3)*, which can only be described in terms of zwitterionic resonance formulas, can be formally regarded as a carbonyl ylide.



The second reaction step involves cycloaddition of the mesoion *(3)* in positions 2,5 to activated alkynes, forming nonisolable primary adducts *(4)* which rearomatize to the furan derivatives *(2)* after elimination of COS. These reactions are comparable with, *e.g.*, 1,3-dipolar cycloadditions of sydnones[4], münchnones[5], 1,3-dithiolylium-4-olates[6], and 1,3,2-oxathiazolylium-5-olates[7] to alkynes.

Table 1. Furans *(2)* from *(1)* and alkynes (reaction temperature 60—80 °C).

Furan [a]	R	R'	R''	Time [h]	Yield [%]
(2a)	Piperidino	H	CO_2CH_3	3	34 [b]
(2b)		CO_2CH_3	CO_2CH_3	2	37 [b], 67 [c]
(2c)		C_6H_5	$COCH_3$	1	40 [c]
(2d)		$COCH_3$	C_6H_5		49 [c]
(2e)		C_6H_5CO	C_6H_5CO	0.5	51 [c]
(2f)	Morpholino	H	CO_2CH_3	5	52 [b]
(2g)		CO_2CH_3	CO_2CH_3	8	49 [b]
(2h)	Pyrrolidino	H	CO_2CH_3	0.5	55 [c]
(2i)		CO_2CH_3	CO_2CH_3	3.5	60 [b]
(2j)	SCH_3	CO_2CH_3	CO_2CH_3	1	80 [c]

[a] All furans were analyzed and characterized by spectroscopy.
[b] With acetic anhydride as cyclization agent.
[c] With dicyclohexylcarbodiimide as cyclization agent.

Received: March 11, 1975 [Z 201 IE]
German version: Angew. Chem. *87*, 416 (1975)

CAS Registry numbers:
(1), R = piperidino, 54932-50-2; *(1)*, R = morpholino, 54932-51-3; *(1)*, R = pyrrolidino, 54932-52-4; *(1)*, R = SCH_3, 54932-53-5; *(2a)*, 54932-54-6; *(2b)*, 54932-55-7; *(2c)*, 54932-56-8; *(2d)*, 54932-57-9; *(2e)*, 54932-58-0; *(2f)*, 54932-59-1; *(2g)*, 54932-60-4; *(2h)*, 54932-61-5; *(2i)*, 54932-62-6; *(2j)*, 54932-63-7; methyl propiolate, 922-67-8; dimethyl 2-butynedioate, 762-42-5; 4-phenyl-3-butyn-2-one, 1817-57-8; 1,4-diphenyl-2-butyne-1,4-dione, 1087-09-8

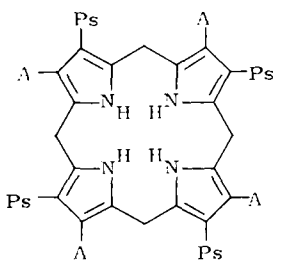
[1] Mesoionic arenes: *W. Baker* and *W. D. Ollis*, Quart. Rev. Chem. Soc. *11*, 15 (1957); *M. Ohta* and *H. Kato* in *J. P. Snyder*: Nonbenzenoid Aromatics. Academic Press, New York 1969, Vol. 1, p. 117.
[2] Preparation of *(1)* by analogy with: *M. Matell*, Acta Chem. Scand. *14*, 677 (1960).
[3] 60-MHz ^{1}H-NMR ($CDCl_3$): τ = 8.32 (br. s, 6H), 6.43 (mc, 4H), 6.29 (s, OCH_3), 3.21 (s, 4-H), 2.92—2.45 (m, C_6H_5).
[4] *R. Huisgen*, *H. Gotthardt*, and *R. Grashey*, Chem. Ber. *101*, 536 (1968); *R. Huisgen* and *H. Gotthardt*, *ibid. 101*, 1059 (1968).
[5] *R. Huisgen*, *H. Gotthardt*, *H. O. Bayer*, and *F. C. Schaefer*, Chem. Ber. *103*, 2611 (1970).
[6] *H. Gotthardt* and *B. Christl*, Tetrahedron Lett. *1968*, 4747; 1,3-dithiolylium-4-olates bearing nitrogen-, sulfur-, and oxygen-containing substituents on C-2 have already been subjected to 1,3-dipolar cycloaddition: *M. C. Weisshuhn* and *H. Gotthardt*, unpublished experiments.
[7] *H. Gotthardt*, Chem. Ber. *105*, 196 (1972).

[*] Priv.-Doz. Dr. H. Gotthardt [+], Dipl.-Chem. M. C. Weisshuhn, and K. Dörhöfer
Institut für Organische Chemie der Universität
8 München 2, Karlstrasse 23 (Germany)
[+] To whom correspondence should be addressed.
[**] This work was supported by the Fonds der Chemischen Industrie.

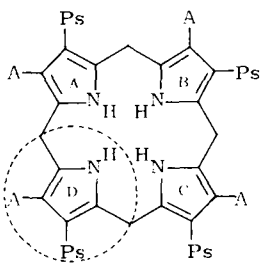
Synthesis of Linear Tri- and Tetrapyrroles of Biogenetic Significance[1][**]

By *Burchard Franck* and *Arend Rowold*[*]

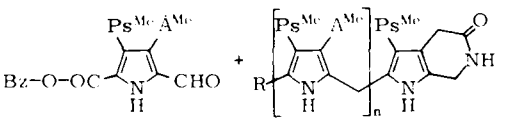
Since the recent demonstration that the blood pigment heme arises directly and without skeletal rearrangement from the cyclic tetrapyrrole uroporphyrinogen III *(2)* during metabolism[1], interest has been focused on the synthesis and reactivity of acyclic linear tetrapyrroles of similar structure. Tetrapyrroles such as *(6d)* and those having an isomeric arrangement of side chains are possible intermediates of porphyrin biosynthesis and the chemical biogenetic-type cyclotetramerization of the monopyrrole porphobilinogen *(6a)*[2]. We now report synthesis of the linear highly reactive tri- and tetrapyrroles *(6c)* and *(6d)* in protected form [*(5a)* and *(5b)*, respectively] and their release and condensation to give uroporphyrinogens *(1)*, *(2)*, *etc.*[3].



(1)

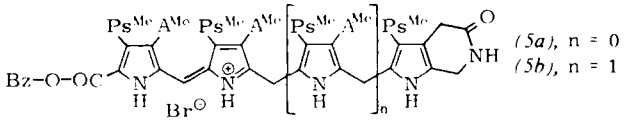


(2)

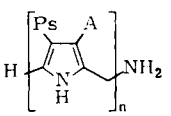


(3)

(4a), n = 1, R = H
(4b), n = 2, R = CO_2H
(4c), n = 2, R = H
(4d), n = 3, R = CO_2H



(5a), n = 0
(5b), n = 1



(6a), n = 1
(6b), n = 2
(6c), n = 3
(6d), n = 4

A = $-CH_2-CO_2H$, A^{Me} = $-CH_2-CO_2CH_3$
Ps = $-CH_2-CH_2-CO_2H$, Ps^{Me} = $-CH_2-CH_2-CO_2CH_3$
Bz = $-CH_2-C_6H_5$

Owing to the high reactivity and ease of condensation expected for the linear oligopyrroles *(6c)* and *(6d)*, their derivatives *(5a)* and *(5b)* were adopted as synthetic targets. Their terminal α position and the aminomethylene group are protected by a benzyloxycarbonyl group and by lactam ring closure, respectively, and a central pyrrole unit by dehydrogenation (cf. ref.[4]).

Condensation of the pyrrolecarbaldehyde *(3)* prepared by a modification of known procedures[4, 6] with the dipyrrylmethane *(4a)*, prepared therefrom by a simplified route, in methanol/HBr (6 h, 20 °C) gave a 44 % yield of the red crystalline tripyrrene *(5a)*: m.p. 148–151 °C; FD-MS (8 kV)[5]: *m/e* 828 (base peak, $M^{\oplus}-HBr$); UV (methanol): λ_{max} = 459, 279 nm. Renewed condensation with the pyrrolecarbaldehyde *(3)* was accomplished by hydrogenation of *(5a)*, with accompanying debenzylation, in methanol/NH_3 with palladium to give *(4b)* and brief treatment with trifluoroacetic acid (15 min, 20 °C), which led to decarboxylation to form the colorless tripyrrane *(4c)*. Condensation of *(4c)* with the pyrrolecarbaldehyde *(3)* (methanol/HBr, 24 h, 20 °C) afforded an 18 % yield of the protected tetrapyrrole *(5b)* as fine red crystals: m.p. 168–170 °C; FD-MS (6 kV)[5]: *m/e* 1665 (79 %, $M^{\oplus}-HBr$); UV (methanol): λ_{max} = 462, 279 nm. Hydrogenation of this product gave, in analogy to *(5a)* → *(4b)*, the tetrapyrrolecarboxylic acid *(4d)*: FD-MS (6 kV)[5]: 979 (28 %, $M^{\oplus}+2H$).

The protected tri- and tetrapyrrole derivatives *(5a)* and *(5b)* which have thus become available, can be converted into the free oligopyrroles in three steps: a) catalytic hydrogenation and debenzylation; b) alkaline hydrolysis of the lactam and ester groups; c) decarboxylation with trifluoroacetic acid. Since isolation of the free oligopyrroles *(6c)* and *(6d)* proved impossible, owing to their extremely high reactivity and sensitivity to oxidation (see also ref.[7]), they were condensed to form uroporphyrinogens (pH 7.4, phosphate buffer, 32 °C, 10–100 h) on liberation. Under these conditions which effectively rule out isomerization of the resulting uroporphyrinogens, the tetrapyrrole *(6d)* predominantly (80 %) afforded uroporphyrinogen I *(1)*, and the tripyrrole *(6c)* a 1 : 1 mixture of uroporphyrinogens I *(1)* and III *(2)*[8]. The result of condensation of *(6d)* is remarkable because it demonstrates that a linear tetrapyrrole of this kind can be cyclized *in vitro* almost without isomerization.

Received: February 18, 1975 [Z 202a IE]
German version: Angew. Chem. 87, 418 (1975)

CAS Registry numbers:
(3), 54932-10-4; *(4a)*, 32615-45-5; *(4b)*, 54932-11-5; *(4c)*, 54344-19-3; *(4d)*, 54932-12-6; *(5a)*, 54932-13-7; *(5b)*, 54932-14-8; *(6c)*, 51446-24-3; *(6d)*, 36459-84-4

[*] Prof. Dr. B. Franck [+] and Dr. A. Rowold
Organisch-Chemisches Institut der Universität
44 Münster, Orleans-Ring 23 (Germany)
[+] To whom correspondence should be addressed.

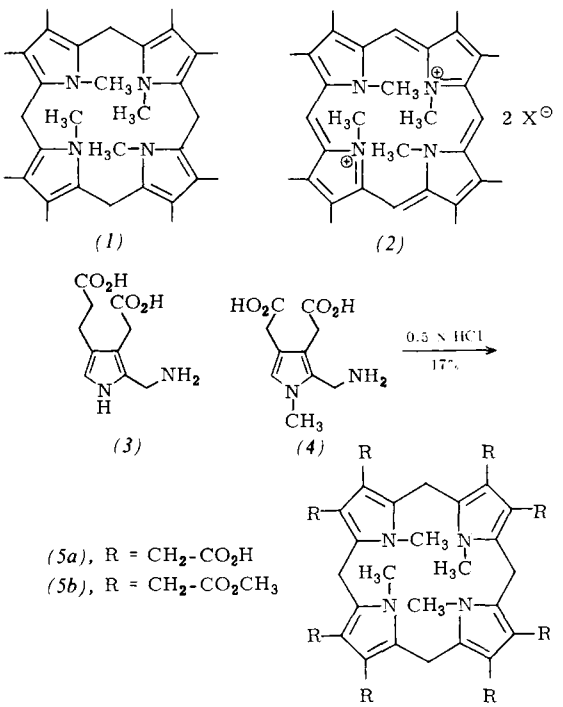
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] Tetrapyrrole Biosynthesis, Part 3. Part 2: *B. Franck, D. Gantz, F.-P. Montforts*, and *F. Schmidtchen*, Angew. Chem. *84*, 433 (1972); Angew. Chem. internat. Edit. *11*, 421 (1972).
[2] *G. H. Cookson* and *C. Rimington*, Biochem. J. *57*, 476 (1954).
[3] Synthesis of a partially protected, similar tripyrrole and condensation experiments have recently also been reported by other authors: *J. M. Osgerby, J. Pluscec, Y. C. Kim, F. Boyer, N. Stojanac, H. D. Mah*, and *S. F. MacDonald*, Can. J. Chem. *50*, 2652 (1972); *R. B. Frydman, A. Valasinas, S. Levy*, and *B. Frydman*, FEBS Lett. *38*, 134 (1974).
[4] *G. P. Arsenault* and *S. F. MacDonald*, Can. J. Chem. *39*, 2043 (1961); *B. Frydman, S. Reil, A. Valasinas, R. B. Frydman*, and *H. Rapoport*, J. Amer. Chem. Soc. *93*, 2738 (1971).
[5] We are are grateful to Dr. *U. Rapp*, Varian MAT, Bremen, for the field-desorption mass spectra (FD-MS).
[6] *G. W. Kenner, K. M. Smith*, and *J. F. Unsworth*, J. C. S. Chem. Comm. *1973*, 43.
[7] *R. Radmer* and *L. Bogorad*, Biochemistry *11*, 904 (1972).
[8] The resulting uroporphyrinogen mixtures were analyzed after dehydrogenation and decarboxylation to the coproporphyrins by *G. Ufer* (Diplomarbeit, Universität Münster 1974) by chromatography according to the method of *P. R. Edmondson* and *S. Schwartz*, J. Biol. Chem. *205*, 605 (1953).

A *N,N',N'',N'''*-Tetramethylporphyrinogen[1][**]

By *Burchard Franck* and *Christian Wegner*[*]

N,N',N'',N'''-Tetramethyl derivatives of porphyrinogens *(1)* and porphyrins *(2)* have long been viewed as a synthetic goal[2-4]. They should provide valuable information about deformability, aromaticity, complex formation, and structure-activity relations of these parents of biologically active natural products. Using a simple route based on porphyrin biosynthesis we have now achieved the synthesis of compound *(5a)* as the first *N,N',N'',N'''*-tetramethylporphyrinogen. It is structurally related to uroporphyrinogen III, the biosynthetic precursor of the blood pigment heme, from which it differs by virtue of the four *N*-methyl groups.

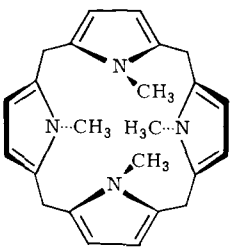


(1) *(2)* *(3)* *(4)*

(5a), R = CH_2-CO_2H
(5b), R = CH_2-CO_2CH_3

Of the two pathways deserving consideration for the preparation of *N*-methylated porphyrinogens—methylation of the completed parent skeleton[3] and cyclotetramerization of *N*-methylpyrroles[4]—only the former has so far permitted partial *N*-methylations. In order to exploit the latter synthetic pathway, *N*-methylnorporphobilinogen *(4)* was prepared and subjected to acid-catalyzed condensation (0.5 N HCl, 100 °C, 30 min), in analogy to the biogenetic-type synthesis of uroporphyrinogen from porphobilinogen *(3)*[5]. The *N,N',N'',N'''*-tetramethylporphyrinogen *(5a)*, m.p. 233 °C, which crystallizes in 17% yield on cooling of the reaction mixture, was converted by treatment with methanol/HCl into the crystalline octamethyl ester *(5b)*; m.p. 218 °C; Ehrlich reaction negative; FD-MS (8 kV)[6]: *m/e* 948 ± 1 (base peak, $M^{\oplus}$); UV (methyl acetate): $\lambda_{max} = 252$ nm; ^{1}H-NMR (D_6-acetone): $\delta = 3.80$ (s, 8 H, CH_2 bridges), 3.50 (s, 16 H, CH_2 of side chains), 3.57 (s, 24 H, 8 CH_3O), 2.60 (s, 12 H, 4 CH_3N). The octacarboxylic acid shows a base peak at *m/e* 484.3569 ($M^{\oplus} - 8\,CO_2$, calc. for $C_{32}H_{44}N_4$: 484.3566) in its high resolution mass spectrum; ^{13}C-NMR (NaOD): δ (multiplicity in off-resonance spectrum, assignment) 182.7 (s, CO_2H), 127.9 (s, pyrrole α-C), 114.6 (s, pyrrole β-C), 34.6 (t, CH_2 of side chains), 31.1 (q, CH_3N), 22.3 (t, CH_2 bridges).

Contrary to previous thinking[4], the colorless *N,N',N'',N'''*-tetramethylporphyrinogen *(5a)* and its ester *(5b)* have thus proved to be readily accessible, in spite of steric hindrance of the *N*-methyl groups. *(5b)* displays remarkable differences in reactivity compared to the non-methylated compound. For instance, while normal porphyrinogens [*(1)*, NH in place of N—CH_3] are rapidly dehydrogenated to dark red fully conjugated porphyrins by atmospheric oxygen or iodine, *(5b)* remains unchanged. The question whether it can be transformed into the aromatic bisquaternary porphyrin of type *(2)* under energetic conditions is currently under study. According to model considerations, which suggest that *(1)* has a conformation *(1a)* with pronounced twisting of adjacent pyrrole rings against each other, the completely dehydrogenated essentially planar molecule *(2)* should exhibit considerable strain.



(1a)

Received: February 18, 1975 [Z 202b IE]
German version: Angew. Chem. 87, 419 (1975)

CAS Registry numbers:
(3), 487-90-1; *(4)*, 54932-07-9; *(5a)*, 54932-08-0; *(5b)*, 54932-09-1

[1] Tetrapyrrole Biosynthesis, Part 4.—Part 3: *B. Franck* and *A. Rowold*, Angew. Chem. *87*, 418 (1975); Angew. Chem. internat. Edit. *14*, 423 (1975).
[2] *W. K. McEwen*, J. Amer. Chem. Soc. *68*, 711 (1946); *A. H. Corwin* and *W. M. Quattlebaum*, *ibid.* *58*, 1081 (1936); *R. C. Ellingson* and *A. H. Corwin*, *ibid.* *68*, 1112 (1946).
[3] *R. Grigg*, *A. Sweeney*, *G. R. Dearden*, *A. H. Jackson*, and *A. W. Johnson*, Chem. Commun. *1970*, 1273.
[4] *A. H. Jackson* and *G. R. Dearden*, Ann. N. Y. Acad. Sci. *206*, 151 (1973).
[5] *G. H. Cookson* and *C. Rimington*, Biochem. J. *57*, 476 (1954).
[6] We are grateful to Dr. *U. Rapp*, Varian MAT, Bremen, for the field desorption mass spectra (FD-MS).

[*] Prof. Dr. B. Franck [+] and Dipl.-Chem. Ch. Wegner
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)
[+] To whom correspondence should be addressed.

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

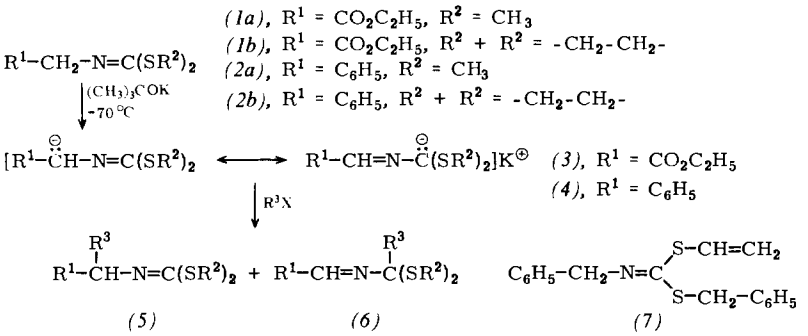
Metalated Dialkyl *N*-Alkyliminocarbonates: New Masked α-Amino and α-Thio Carbanions

By *Dieter Hoppe*[*]

Masked α-amino carbanions $\rangle\overset{\oplus}{\ddot{C}}-N\langle$ are becoming increasingly important for the nucleophilic introduction of α-aminoalkyl groups[1]. We suspected the bis(alkylthio)methyleneamino group $(RS)_2C{=}N$ in the open or cyclic[2] dialkyl *N*-alkyliminodithiocarbonates *(1)*, *(2)*, and *(8)* (representing a masked amino function) to be capable of stabilizing neighboring carbanionic centers by allylic resonance. The compounds *(1)*, *(2)*, and *(8)* are readily accessible in high yields by dithiocarboxylation of amines and subsequent bis- (or cyclo-) alkylation[3].

We found that only those compounds of type *(1)* and *(2)* which bear mesomeric electron-withdrawing groups in the α-position can be metalated with potassium *tert*-butoxide in tetrahydrofuran at −70 °C to the anions *(3)* and *(4)*, respectively, whereas *(8a)* and *(8c)*, for example, do not

[*] Dr. D. Hoppe
Organisch-Chemisches Institut der Universität
34 Göttingen, Tammannstrasse 2 (Germany)



react under these conditions. The ambidentate anions *(3)* react regiospecifically with alkyl iodides or benzyl bromides with chain-extension to form the carbonic acid derivatives *(5)*[4]; *(4)* also yields the isomeric orthocarboxylic acid derivatives *(6)* (IR: 1640 cm^{-1}) (see Table 1). Apart from the carbonic acid derivative *(5e)*, 2-benzylimino-1,3-dithiolane *(2b)* additionally gives the vinyl thioester *(7)* by base-induced ring opening to the dithiocarbamate anion and subsequent benzylation.

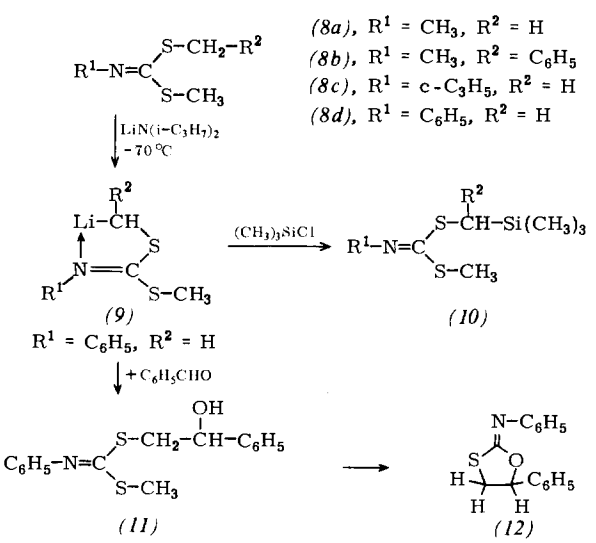
was trapped as *(10)* with trimethylchlorosilane (see Table 1). Metalation in this position is apparently favored by chelation of the lithium by the basic imino nitrogen.

The lithium derivatives *(9)* readily add aldehydes and ketones at −70 °C; for example, reaction of *(9d)* with benzaldehyde followed by neutralization at −70 °C affords an 80% yield of the β-hydroxyalkyl iminodithiocarbonate *(11)* [IR: 3380 (OH), 1570 cm^{-1} (C=N)] which cyclizes slowly at room temperature, and faster in boiling benzene, with elimination

Table 1. Metalation of dialkyl *N*-alkyliminodithiocarbonates *(1)*, *(2)*, and *(8)* and reaction with electrophiles R^3X.

Starting compound	Base [a]	R^3X	Products [b]	R^1	R^2	R^3	Yield [%]	B.p. [°C/torr]
(1a)	KOtBu	CH_3I	*(5a)*	$CO_2C_2H_5$	CH_3	CH_3	70	94/0.5
(1b)	KOtBu	CH_3I	*(5b)*	$CO_2C_2H_5$	CH_2—	CH_3	73 [c]	
(2a)	KOtBu	$C_6H_5CH_2Br$	*(5c)* + *(6c)* [e]	C_6H_5	CH_3	$C_6H_5CH_2$	81 [d]	
(2a)	KOtBu	C_2H_5I	*(5d)* + *(6d)* [f]	C_6H_5	CH_3	C_2H_5	95 [d]	
(2b)	KOtBu	$C_6H_5CH_2Br$	*(5e)* + *(7)* [g]	C_6H_5	CH_2—	$C_6H_5CH_2$	69 [c]	
(2a)	$LiN(iPr)_2$	$(CH_3)_3SiCl$	*(6f)* + *(9f)* [h]	C_6H_5	CH_3	$(CH_3)_3Si$	80 [d]	126—28/0.1
(8a)	$LiN(iPr)_2$	$(CH_3)_3SiCl$	*(10a)* [i]	CH_3	H	$(CH_3)_3Si$	75	78—84/1.3
(8c)	$LiN(iPr)_2$	$(CH_3)_3SiCl$	*(10b)* [i]	*c*-C_3H_5	H	$(CH_3)_3Si$	80	104—08/1.0

[a] KOtBu = potassium *tert*-butoxide (freshly sublimed); $LiN(iPr)_2$ = lithium diisopropylamide.
[b] ^{1}H-NMR spectra and IR spectra are in accord with the structures; the compounds gave correct CH analyses.
[c] Purification by chromatography over silica gel (neutral) with light petroleum (40—60 °C)/diethyl ether (1:2).
[d] Purification and separation by chromatography over silica gel (neutral) with light petroleum (40—60 °C)/benzene (2:1).
[e] *(5c)*:*(6c)* = 90:10 (NMR).
[f] *(5d)*:*(6d)* = 40:60 (NMR).
[g] *(5e)*:*(7)* = 65:35 (both products were isolated).
[h] *(6f)*:*(9f)* = 15:85 (both products were isolated).
[i] At room temperature *(7)* and *(10)* exist as stable (on NMR time scale) *E*/*Z* mixtures. *F. Vögtle, A. Mannschreck,* and *H. A. Staab,* Liebigs Ann. Chem. *708*, 51 (1967).



Lithium diisopropylamide (in tetrahydrofuran/*n*-hexane, 70 °C) preferentially abstracts an α-proton of the *S*-alkyl group from the iminocarbonic esters *(8)*—and also from *(2a)*—to give [alkylimino(alkylthio)methylthio]alkyllithium *(9)*, which

of methanethiol to form 5-phenyl-2-phenylimino-1,3-oxathiolane *(12)*[5] (IR: 1650 cm^{-1} (C=N); ^{1}H-NMR ($CDCl_3$): τ = 6.45, 6.65 (4-H), $^{1,3}J$ = 10 Hz; 4.4 (5-H), $^{1,4}J_{cis}$ = 6 Hz and $^{1,4}J_{trans}$ = 9 Hz). In similar manner, *(9b)* and acetone give 4-benzyl-5,5-dimethyl-2-methylimino-1,3-oxathiolane [78%, m.p. 91 °C; IR: 1655 cm^{-1} (C=N)].

Received: March 14, 1975 [Z 204a IE]
German version: Angew. Chem. *87*, 449 (1975)

CAS Registry numbers:
(1a), 54985-61-4; *(1b)*, 54985-62-5; *(2a)*, 54985-63-6; *(2b)*, 2080-48-0; *(5a)*, 54985-64-7; *(5b)*, 54985-65-8; *(5c)*, 54985-66-9; *(5d)*, 54985-67-0; *(5e)*, 54985-68-1; *(6c)*, 54985-69-2; *(6d)*, 54985-70-5; *(6f)*, 55012-66-3; *(7)*, 54985-71-6; *(8a)*, 18805-25-9; *(8c)*, 54985-72-7; *(9b)*, 54985-73-8; *(9d)*, 54985-74-9; *(9f)*, 54985-75-0; *(10a)*, 54985-76-1 *(10b)*, 55012-67-4; *(11)*, 54985-77-2; *(12)*, 54985-78-3; benzaldehyde, 100-52-7; 4-benzyl-5,5-dimethyl-2-methylimino-1,3-oxathiolane, 54985-79-4

[1] Review: *D. Seebach* and *D. Enders*, Angew. Chem. *87*, 1 (1975); Angew. Chem. internat. Edit. *14*, 15 (1975); for chemistry of metalated isocyanides, see: *U. Schöllkopf*, Angew. Chem. *82*, 795 (1970); Angew. Chem. internat. Edit. *9*, 763 (1970); *D. Hoppe*, Angew. Chem. *86*, 878 (1974); Angew. Chem. internat. Edit. *13*, 784 (1974); for reactions of lithio-2-azaallyl anions (metalated azomethines) see: *Th. Kauffmann*, Angew. Chem. *86*, 715 (1974); Angew. Chem. internat. Edit. *13*, 627 (1974).
[2] Systematic name: 2-Alkylimino-1,3-dithiolanes.

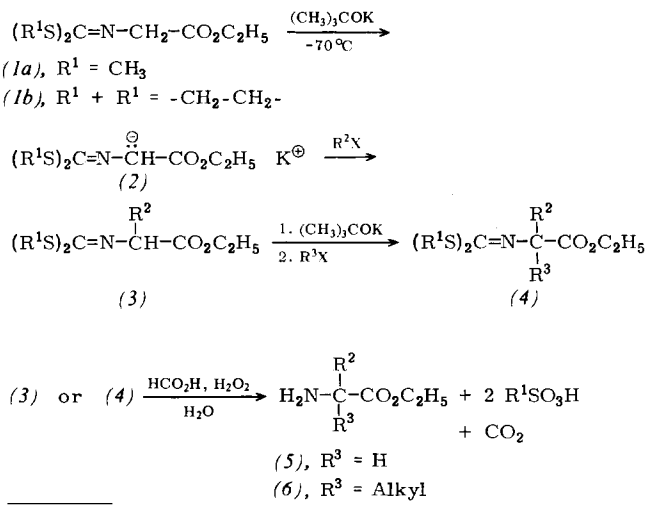
[3] Prepared by analogy with: *E. Fromm* and *M. Bloch*, Ber. Deut. Chem. Ges. *32*, 2212 (1899); *M. Delépine*, Bull. Soc. Chim. Fr. [3] *27*, 48, 57 (1902); *Y. Ueno*, *T. Nakai*, and *M. Okawara*, Bull. Chem. Soc. Jap. *43*, 162 (1970).
[4] Use in amino acid synthesis: *D. Hoppe*, Angew. Chem. *87*, 450 (1975); Angew. Chem. internat. Edit. *14*, 426 (1975).
[5] Compounds of type *(11)* and *(12)* decompose on work-up in the presence of bases to form episulfides.

Chain-Extended and α-Branched α-Amino Acids by Alkylation of Metalated α-[Bis(alkylthio)methyleneamino] Acid Esters

By *Dieter Hoppe*[*]

As esters of iminodithiocarbonic acid[1] *N*-[bis(methylthio)-methylene]- and *N*-(1,3-dithiolan-2-ylidene)glycine ethyl esters *(1a)* and *(1b)*, respectively, are conveniently obtainable from glycine ethyl ester hydrochloride. Their reaction with potassium *tert*-butoxide at −70 °C leads to the α-amino carbanions *(2)* which afford chain-extended esters *(3)* on treatment with alkyl iodides or benzyl bromides between −60 and 0 °C (see Table 1). The monoalkylated products *(3)* are formed almost exclusively (>97 %) with one equivalent of base and the alkylating agent; renewed metalation [without isolation of *(3)*] and alkylation permits introduction of a second alkyl group (which may differ from R^2) to form the α-branched α-amino acid derivatives *(4)*.

Selective monoalkylation of relatively stable carbanions generally runs into difficulties[2]. The reason behind the clear-cut course of our new synthesis is a topic for further study. On treatment at 5—20 °C with aqueous performic acid produced *in situ*, the esters *(3)* and *(4)* undergo oxidative-hydrolytic desulfuration to the amino acid esters *(5)* and *(6)*, respectively.



(1a), $R^1 = CH_3$
(1b), $R^1 + R^1 = -CH_2-CH_2-$

(2)

(3) *(4)*

(5), $R^3 = H$
(6), R^3 = Alkyl

Table 1. α-[Bis(alkylthio)methyleneamino] acid ethyl esters *(3)* and *(4)* prepared.

Starting compound	R^2X (+R^3X)	Product [a]	R^1	R^2	R^3	Yield [%]	B.p. [°C/torr]
(1a)	CD_3I	*(3a)*	CH_3	CD_3	—	74 [b]	94—5/0.5
(1a)	C_2H_5I	*(3b)*	CH_3	C_2H_5	—	83 [b]	90—1/0.2
(1b)	CH_3I	*(3c)*	CH_2—	CH_3	—	73 [c]	
(1b)	$(CH_3)_2CHI$	*(3d)*	CH_2—	$(CH_3)_2CH$	—	48 [c]	
(1b)	$C_6H_5CH_2Br$	*(3e)*	CH_2—	$C_6H_5CH_2$	—	73 [c]	
(1a)	*p*-$BrC_6H_4CH_2Br$ (+C_2H_5I)	*(4a)*	CH_3	*p*-$BrC_6H_4CH_2$	C_2H_6	84 [c]	
(1b)	$(CH_3)_2CHCH_2I$ (+CH_3I)	*(4b)*	CH_2—	$(CH_3)_2CHCH_2$	CH_3	74 [c]	

[a] The IR and ^{1}H-NMR spectra are in accord with the structures; the products gave correct CH analyses.
[b] Distillative work-up.
[c] Purified by chromatography over silica gel (neutral) with light petroleum (40—60 °C)/diethyl ether (1:2; 3:1 for *(4a)*).

Ethyl 2-[bis(methylthio)methylene]amino-2-(p-bromobenzyl)-butyrate (4a)

Compound *(1a)* (4.14 g, 20 mmol) in THF (10 ml) is added dropwise at −70 °C to freshly sublimed potassium *tert*-butoxide[3] (2.24 g, 20 mmol) in dry THF under N_2. Stirring is continued for 10 min, and a solution of *p*-bromobenzyl bromide (5.0 g, 20 mmol) in THF (20 ml) is then added. After warming up to room temperature, the mixture is stirred for another 15 min and recooled to −70 °C. Potassium *tert*-butoxide (2.36 g, 21 mmol) in THF (30 ml) is added from a dropping funnel cooled with dry ice/acetone, and ethyl iodide (3.4 g, 22 mmol) is squirted in after 15 min; the reaction mixture is then treated as above. After removal of solvent under vacuum, the residue is taken up in ether (50 ml) and water (30 ml), the organic phase washed with water and dried over sodium sulfate. The pale yellow oil (7.7 g) left on removal of the ether is chromatographed over silica gel (250 g, neutral) with light petroleum (40–60 °C)/diethyl ether (3:1) to give *(4a)* (6.80 g, 84 %) as a viscous colorless oil (R_f = 0.40).—IR (film): 1732 (C=O) and 1587 cm^{-1} (C=N). ^{1}H-NMR (CCl_4): τ = 2.7 (d) and 3.1 (d), aromatic H; 6.7 and 6.9 (AB part, J = 13 Hz, diastereotopic benzyl H; 8.1 (q) and 9.2 (t), ethyl H; 5.9 (q) and 8.8 (t), ester ethyl H; 7.6 (s) and 7.8 (s), S-methyl H broadened by slow inversion.

2-Ethyl-p-bromophenylalanine ethyl ester (6a)

30 % hydrogen peroxide (7.4 g, 65 mmol) and *p*-toluenesulfonic acid (0.05 g) are added with stirring to *(4a)* (4.05 g, 10 mmol) in 98—100 % formic acid (15 ml) at 0 °C. The temperature is maintained at 10 °C for 4 h by cooling (exothermic reaction, evolution of carbon dioxide) and then allowed to rise and kept at 20 °C for 20 h. The acid is drawn off under vacuum in a rotary evaporator (bath temperature <50 °C) and 50 % formic acid (10 ml) added to the residue; the mixture is then again evaporated to dryness[4]. The (cold) residue is covered with ether (30 ml), 2 N sodium hydroxide solution (10 ml, 20 mmol) cooled to 0 °C is added, and the mixture is stirred until dissolution is complete. After separation of the ethereal phase the process is repeated with 5 ml of 2 N sodium hydroxide. The united solutions are washed with a small volume of water, dried over sodium sulfate, and the ether drawn off under vacuum. *(6a)* (2.7 g, 90 %) is obtained as a viscous colorless oil.—IR (film): 3350 and 1590 (NH_2),

[*] Dr. D. Hoppe
Organisch-Chemisches Institut der Universität
34 Göttingen, Tammannstrasse 2 (Germany)

1725 cm^{-1} (C=O). ^{1}H-NMR (CCl_4): τ = 2.6 (d) and 3.0 (d); 7.0 and 7.4 (AB part, J = 13 Hz), benzyl H; 8.3 (m) and 9.15 (t), ethyl H; 5.9 (q) and 8.75 (t), ester ethyl H; 8.7 (br. s), amino H.

Received: March 14, 1975 [Z 204b IE]
German version: Angew. Chem. 87, 450 (1975)

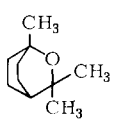
CAS Registry numbers:
(1a), 54985-61-4; *(1b)*, 54985-62-5; *(3a)*, 54985-80-7; *(3b)*, 54985-81-8; *(3c)*, 54985-65-8; *(3d)*, 54985-82-9; *(3e)*, 54985-83-0; *(4a)*, 54985-84-1; *(4b)*, 54985-85-2; *(6a)*, 54985-86-3

[1] Cf. *D. Hoppe*, Angew. Chem. *87*, 449 (1975); Angew. Chem. internat. Edit. *14*, 424 (1975).
[2] Alkylation of ethyl potassioisocyanoacetate under analogous conditions, for instance, affords mainly dialkylation products; cf. *U. Schöllkopf, D. Hoppe*, and *R. Jentsch*, Angew. Chem. *83*, 357 (1971); Angew. Chem. internat. Edit. *10*, 331 (1971); *U. Schöllkopf, D. Hoppe*, and *R. Jentsch*, Chem. Ber. *108*, in press.
[3] *D. E. Pearson* and *C. A. Buehler*, Chem. Rev. *74*, 45 (1974).
[4] The crude product (containing sulfonic acid) may be used for conversion into free amino acids by acid or alkaline hydrolysis.

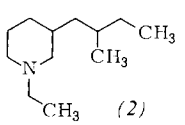
The Spreading Alkaloid Stenusin from the Staphylinid *Stenus comma* (Coleoptera: Staphylinidae)[**]

By *Hermann Schildknecht, Dietlinde Krauss, Jutta Connert, Hans Essenbreis*, and *Nicolas Orfanides*[*]

Stenus comma, a staphylinid weighing 2.5 mg and measuring only 5 mm, inhabits the sandy banks of stagnant and sluggishly flowing bodies of water. While hunting for springtail it sometimes falls into the water and would be doomed to drowning if it were not able to dash over the surface at about 40 to 75 cm/s—as if on water skis—to reach the safety of the bank. While doing so it makes no use of its legs but merely dips the tip of its abdomen for a brief moment into the water and releases a tiny drop of secretion from two paired pygidial defense glands.



(1)



(2)

From the little reservoir of the pygidial defense glands we have isolated, apart from 6-methyl-5-hepten-2-one and an isopiperitenol, eucalyptole *(1)* (also known as 1,8-cineole)[1]. At this stage we could have regarded the spreading phenomenon as solved—*(1)* has been known as a flotation agent for a very long time—if it had not been for the major gas chromatographic fraction of the spreading secretion: 6 mg of an oil, isolated from the collecting bladders (length 0.4 mm) of a thousand beetles, which we have called stenusin.

Structural elucidation of stenusin as an *N*-ethyl-3-(2-methylbutyl)piperidine *(2)* relied heavily on mass spectrometric analysis, especially the study of metastable transitions by the DADI technique[2]. We recognized the molecular ion at *m/e* 183 ($C_{12}H_{25}N$) and the key fragments *m/e* 30, 44, 58, 72, and 113. The 220 MHz ^{1}H-NMR spectrum showed absorption corresponding to an *N*-ethyl group at δ = 2.3 ppm (q, J = 7 Hz, CH_2) and at 1.05 ppm (t, J = 7 Hz, CH_3) as well as an absorption at 2.76 ppm due to two protons situated α to nitrogen. Of decisive importance for our structural proposal *(2)* was the exclusive appearance of the ion at *m/e* 113 with significant intensity in the mass spectrum of the natural product, in contrast to the spectra of synthetic piperidines and perhydroazepines of molecular formula $C_{12}H_{25}N$. This ion of odd mass number can arise directly from the molecular ion of *(2)* by loss of a pentenyl group from position 3 and a hydrogen migration. The pentyl side chain should also be branched such that a propyl fragment cannot be eliminated.

We have prepared *(2)* by total synthesis; the IR, ^{1}H-NMR, and MS spectra were practically identical with those of stenusin; the specific rotation $[\alpha]_{365}^{20}$ of the synthetic product[3] was 5.4 ± 0.3° (c = 3 mg/ml ethanol) and that of the natural product 5.8 ± 0.3° (c = 1.15 mg/ml ethanol). The absolute configuration of the insect alkaloid is currently being determined.

The ratio of the main components of the secretion of the pygidial defense glands—1,8-cineole *(1)* and stenusin *(2)*—amounts to 1:14. We may therefore assume that *St. comma* survives primarily owing to the properties of stenusin. However, the most striking property of stenusin is its extremely high spreading effect. If a spreading pressure-time diagram is plotted for constant spreading area with the aid of a film balance developed by *Hans Kuhn* (Göttingen) then a spreading pressure of p = 28.5 dyn/cm is found for *(2)*, and only 2.2 dyn/cm for *(1)*! The large difference arises from the tenfold lower water solubility of stenusin *(2)* compared to 1,8-cineole *(1)* (0.03 and 0.3 %, respectively). From these values it may be assumed that *(2)* is the actual spreading substance. Velocity-displacement curves that we have determined by means of a cine camera show a propagation rate of 32.5 cm/s for *(2)* and only 18 cm/s for *(1)*. Hence *(2)* spreads much faster than *(1)* and is therefore more valuable for the nonswimmer *St. comma*. Both substances are terpenoid in character; in the course of evolution the oxygen heterocycle *(1)* was transformed into the faster spreading nitrogen heterocycle *(2)*—a terpenoid alkaloid. Compound *(1)* is active against various microbes[4]. The presence of the *original (1)* and the *derived* defense substance *(2)* in the same organism constitutes the highly interesting finding of a comprehensive analysis of the defense substances of a staphylinid.

Received: January 24, 1975;
in shortened form: March 17, 1975 [Z 205 IE]
German version: Angew. Chem. 87, 421 (1975)

CAS Registry numbers:
(2), 54985-88-5

[1] *D. Berger*, Dissertation, Universität Heidelberg 1968.
[2] *J. Connert*, Dissertation, Universität Heidelberg 1973.
[3] *N. Orfanides*, Diplomarbeit, Universität Heidelberg 1975.
[4] Ullmanns Encyklopädie der Technischen Chemie, 3rd. Edit., Vol. 14, p. 773. Urban und Schwarzenberg, München 1963.

[*] Prof. Dr. H. Schildknecht [+], Dr. D. Krauss, Dr. J. Connert, Dipl.-Chem. H. Essenbreis, and N. Orfanides
Organisch-Chemisches Institut der Universität
69 Heidelberg, Im Neuenheimer Feld 270 (Germany)
[+] To whom correspondence should be addressed.

[**] Part 60 of Arthropod Defense Substances. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft. We are grateful to *V. Puthz* (Schlitz/Hesse) for identification of the beetle and to Prof. Dr. *H. Kuhn* and Dr. *D. Möbius* (Göttingen) for determination of thrust-time diagrams.—Part 59: *H. Schildknecht, H. Holtkotte, D. Krauss*, and *H. Tacheci*, Liebigs Ann. Chem., in press.

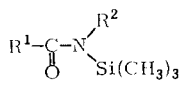
1,3-S,N-Silyl Shift in Silylated Thioamides[**]

By *Wolfgang Walter* and *Hans-Wolfgang Lüke*[*]

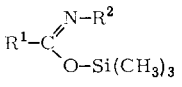
Trimethylsilylamides exist in the amide form (*N*-silylation), the imidate form (*O*-silylation), or as an equilibrium mixture of the two forms[1].

[*] Prof. Dr. W. Walter [+] and Dipl.-Chem. H.-W. Lüke
Institut für Organische Chemie und Biochemie der Universität
2 Hamburg 13, Papendamm 6 (Germany)
[+] To whom correspondence should be addressed.

[**] This work was supported by the Verband der Chemischen Industrie.



amide



imidate

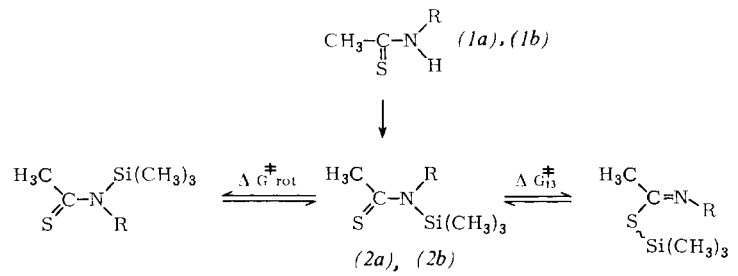
On silylation, primary thioamides R—CS—NH_2 are converted into *N*-trimethylsilylthioamides, whereas some secondary thioamides having bulky substituents attached to the thiocarbonyl carbon and the nitrogen atom also afford *S*-trimethylsilyl thioimidates[2].

We have now silylated *N*-isopropyl-*(1a)* and *N*-neopentylthioacetamide *(1b)* [conditions: 1) *n*-BuLi, 2) $(CH_3)_3SiCl$, reactions in hexane]; these secondary thioamides bear bulky groups only on the nitrogen.

The NMR spectra of the resulting silyl compounds *(2a)* and *(2b)* contain the signals of two isomeric forms; coalescence occurs on warming (*ca.* 130°C). On cooling, the signal of only one of the isomers undergoes splitting after passing through a second coalescence point, so that finally at *ca.* −60°C the signals of three equilibrating forms can be distinguished (for the isomerization parameters $\Delta G^{\neq}$ see Table 1).

Table 1. Isomerization parameter $\Delta G^{\neq}_{1,3}$ of the S,N-silyl shift [3] and $\Delta G^{\neq}_{rot}$ of the rotation.

Cpd.	R	$\Delta G^{\neq}_{1,3}$ [kcal/mol]	$\Delta G^{\neq}_{rot}$ [kcal/mol]
(2a)	*i*-C_3H_7	22.6	11.4
(2b)	$CH_2C(CH_3)_3$	21.4	13.9
(2c)	CH_3		16.7
(2d)	C_2H_5		16.7



(1a), (1b)

(2a), (2b)

From these observations and from the data listed in Table 1 we conclude that on cooling the *N*-silylated forms of *(2a)* and *(2b)* isomerize owing to hindered rotation about the partial double bond (*E*/*Z* isomerism); other silylated thioamides behave in similar fashion. The *E*/*Z* isomerism is also indicated by the shift of the newly appearing groups of signals on dilution with arenes. The isomerization occurring on warming can then only be attributed to a 1,3-S,N-silyl shift. Both processes are reversible.

The *S*-silylated derivatives occurring in equilibrium appear to exist in only one configuration. The long-range coupling constant $J_{CH_3-C=N-CH_2} = 1.4$ Hz in *(2b)* proves the presence of the *Z* form.

Received: February 21, 1975 [Z 206 IE]
German version: Angew. Chem. 87, 420 (1975)

CAS Registry numbers:
(1a), 5310-11-2; *(1b)*, 54986-09-3; *N*-silyl-*(2a)*, 54986-10-6; *S*-silyl-*(2a)*, 54986-11-7; *N*-silyl-*(2b)*, 54986-12-8; *S*-silyl-*(2b)*, 54986-13-9

[1] *C. H. Yoder, W. C. Copenhafer*, and *B. Du Beshter*, J. Amer. Chem. Soc. *96*, 4283 (1974); *J. Pump* and *E. G. Rochow*, Chem. Ber. *97*, 627 (1964); *J. F. Klebe*, Accounts Chem. Res. *3*, 299 (1970); *M. Fukui, K. Itoh*, and *Y. Ishii*, J. C. S. Perkin II *1972*, 1043.

[2] *W. Walter, H.-W. Lüke*, and *J. Voss*, Liebigs Ann. Chem., in press.

[3] The free energies $\Delta G^{\neq}$ of isomerization were determined by an approximate procedure (*H. S. Gutowsky* and *C. H. Holm*, J. Chem. Phys. *25*, 1228 (1956)). The error was taken as ±0.2 kcal/mol (*D. Kost, E. H. Carlson*, and *M. Raban*, Chem. Commun. *1971*, 656).

Aziridinimines, Diaziridinimines, Diaziridinones, and Carbodiimides by Photolysis of 2-Tetrazolines[**]

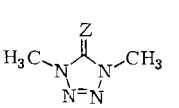
By *Helmut Quast* and *Lothar Bieber*[*]

A possible entry to hetero analogs of trimethylenemethane[1,2] could be provided by ring systems *(1)* which are transformed into methylenecyclopropane analogs *(2)* on photolysis. Loss of CO and N_2 respectively from compounds of type *(1a)* actually provided proof of singlet and triplet

(1) *(2)*

	A	X, Y	Z
(1)	—CO— or —N=N—	C and/or hetero atom	
(1a)	—CO— or —N=N—	C	C
(1b)	—CO—	$C(CH_3)_2$	O
(1c)	—CO—	CH_2	O
(1d)	—N=N—	$C(CH_3)_2$	O

trimethylenemethane[1]. However, *(1b)* and *(1c)* did not give rise to any species detectable by ESR spectroscopy[1a]. Whereas methylenecyclopropanes[1,3] and cyclopropanones[4] were obtained from *(1)* and the photochemical generation of cyclopropanimines[4] and aziridinones[5] could be established from the secondary reaction products, no cyclopropanone was formed on photolysis of the thermally and photochemically surprisingly stable compound *(1d)*[6]. We have now discovered a photochemical synthesis of several hetero-methylenecyclopropanes [*(4)*, *(7)*, *(9)*] from 2-tetrazolines *(3)*[7].



(3a), Z = O
(3b), Z = S
(3c), Z = N-CH_3
(3d), Z = $C(CH_3)_2$
(3e), Z = CH-$C(CH_3)_3$

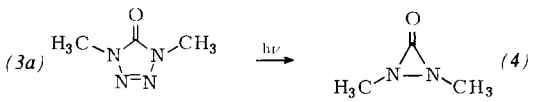
Photolysis of the thermally highly stable tetrazolone *(3a)* in ether or 2-propanol afforded only secondary products of

[*] Doz. Dr. H. Quast [+] and Dipl.-Chem. L. Bieber
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

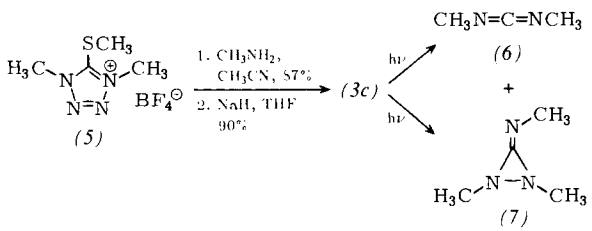
[+] To whom correspondence should be addressed.

[**] Photochemical Formation of Methylenecyclopropane Analogs, Part 1.— This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The results are taken from the Diplomarbeit of *L. Bieber*, Universität Würzburg 1972, and his planned Dissertation.

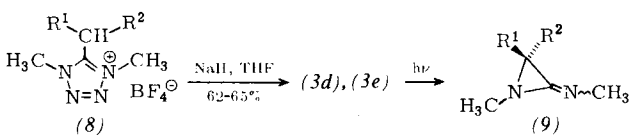
radical reactions with the solvent[8]. After irradiation[9] in CD_3CN we found the sole product to comprise a compound which we regard as 1,2-dimethyldiaziridinone *(4)*[10] on the basis of its ^{1}H-NMR spectrum ($\delta = 2.96$ ppm) and an IR band at 1882 cm^{-1}.



Under the same conditions, the thione *(3b)* [readily accessible by dealkylation of *(5)*, CH_3OSO_3 instead of BF_4[11], with triethylamine in acetonitrile] is quantitatively converted into sulfur and dimethylcarbodiimide *(6)*, which was identified by its ^{1}H-NMR and IR spectrum[12] and by hydrolysis to *N,N'*-dimethylurea. This reaction possibly proceeds *via* the same intermediate as was recently trapped by 3+2 cycloaddition during the thermolysis of 5-imino-1,2,3,4-thiatriazolines[13].



Preparation of the very hygroscopic imine *(3c)* in two steps from *(5)* is an example of a new synthesis, which readily permits variation of the substituent attached to the imino nitrogen atom of 2-tetrazolin-5-imines. Photolysis[9] of *(3c)* in D_8-THF affords 14—17% of *(6)* and 83—86% of diaziridinimine *(7)* which is identical with an authentic sample[14]. The methyl azide expected to accompany *(6)* apparently decomposes under the reaction conditions.



(3d), $R^1 = R^2 = CH_3$; *(9d)*, *E/Z* = 90 : 10
(3e), $R^1 = H$, $R^2 = C(CH_3)_3$; *(9e)*, *E/Z* = 94 : 6

On treatment of *(8)* with sodium hydride in tetrahydrofuran we obtained the methylenetetrazolines *(3d)* and *(3e)* as intensely yellow, extremely air- and moisture-sensitive distillable oils. Their photolysis[9] at −60 °C in D_8-THF (Pyrex filter) quantitatively afforded the aziridinimines *(9)*, whose structure and configuration were confirmed by spectral comparison with authentic compounds[15]. The *E/Z* isomer ratio remained unchanged for weeks at −20 °C. The high stereoselectivity of this photolysis is remarkable. Methylenediaziridines could not be detected.

Received: February 12, 1975;
in shortened form: March 14, 1975 [Z 207 IE]
German version: Angew. Chem. 87, 422 (1975)

CAS Registry numbers:
(3a), 13576-20-0; *(3b)*, 54986-14-0; *(3c)*, 35151-69-0; *(3d)*, 54986-15-1; *(3e)*, 54986-16-2; *(4)*, 54986-17-3; *(5)*, 54986-19-5; *(6)*, 4852-30-6; *(7)*, 54986-20-8; *(8)*, $R^1 = R^2 = CH_3$, 54986-22-0; *(8)*, $R^1 = H$, $R^2 = C(CH_3)_3$, 54986-24-2; *Z-(9d)*, 54986-25-3; *E-(9d)*, 54986-26-4; *Z-(9e)*, 27270-90-2; *E-(9e)*, 27270-91-9

[1] a) *P. Dowd*, Accounts Chem. Res. *5*, 242 (1972); b) *J. J. Gajewski, A. Yeshurun*, and *E. J. Bair*, J. Amer. Chem. Soc. *94*, 2138 (1972); *J. A. Berson, L. R. Corwin*, and *J. H. Davis, ibid. 96*, 6177 (1974).
[2] *J. F. Liebman* and *A. Greenberg*, J. Org. Chem. *39*, 123 (1974), and references cited therein; *M. E. Zandler, C. E. Choc*, and *C. K. Johnson*, J. Amer. Chem. Soc. *96*, 3317 (1974), and references cited therein; *B. K. Carpenter*, J. C. S. Perkin II *1974*, 1.
[3] *W.-D. Stohrer, P. Jacobs, K. H. Kaiser, G. Wiech*, and *G. Quinkert*, Fortschr. Chem. Forsch. *46*, 181 (1974); *S. D. Andrews* and *A. C. Day*, J. Chem. Soc. *B 1968*, 1271; *R. J. Crawford, D. M. Cameron*, and *H. Tokunasa*, Can. J. Chem. *52*, 4025 (1974).
[4] *H. H. Wasserman, G. M. Clark*, and *P. C. Turley*, Fortschr. Chem. Forsch. *47*, 73 (1974), and references cited therein; *K. G. Srinivasan* and *J. H. Boyer*, J. C. S. Chem. Comm. *1974*, 379.
[5] *J. A. Schutyser* and *F. C. De Schryver*, Chem. Ind. (London) *1972*, 465.
[6] *P. S. Engel* and *L. Shen*, Can. J. Chem. *52*, 4040 (1974).
[7] Photolysis of 1,4,5-trisubstituted 2-tetrazolines: *T. Akiyama, T. Kitamura, T. Isida*, and *M. Kawanisi*, Chem. Lett. *1974*, 185.
[8] *W. S. Wadsworth, Jr.*, J. Org. Chem. *34*, 2994 (1969).
[9] All photolyses conducted in sealed NMR sample tubes, previously repeatedly degassed at 10^{-5} torr, with a 150 or 450 W Hg lamp.
[10] Only 1,2-di-*tert*-alkyl-substituted diaziridinones are so far known: *F. D. Greene, J. C. Stowell*, and *W. R. Bergmark*, J. Org. Chem. *34*, 2254 (1969).
[11] *S. Hünig* and *K. H. Oette*, Liebigs Ann. Chem. *641*, 94 (1961).
[12] *G. Papi* and *G. Sbrana*, J. Amer. Chem. Soc. *93*, 5213 (1971).
[13] *E. van Loock, J.-M. Vandensavel, G. L'Abbe*, and *G. Smets*, J. Org. Chem. *38*, 2916 (1973); *R. Neidlein* and *K. Salzmann*, Synthesis *1975*, 52; *M. Revitt*, J. C. S. Chem. Comm. *1975*, 24.
[14] *K.-H. Ross*, Dissertation, Universität Würzburg 1974.
[15] *(10d)*: *H. Quast* and P. Schäfer, unpublished. *(10e)*: *H. Quast* and *E. Schmitt*, Angew. Chem. *82*, 395 (1970), Angew. Chem. internat. Edit. *9*, 381 (1970).

Change in Conformation of a Cystine Peptide on Transition from the Crystal to Solution

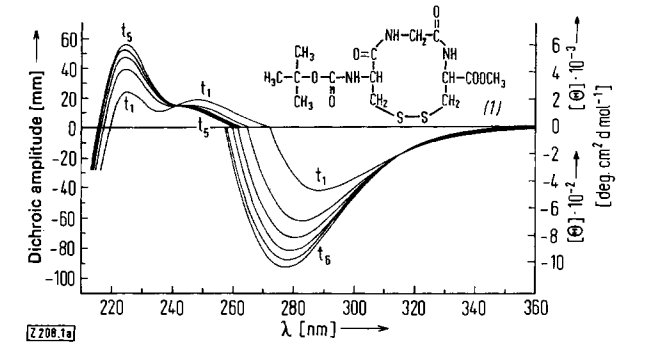
By *Günther Jung, Michael Ottnad, Peter Hartter*, and *Heinrich Lachmann*[*]

Dedicated to Professor Eugen Müller on the occasion of his 70th birthday

During investigations on the chiroptical behavior of the disulfide chromophore in peptides[1] an initially surprising effect was observed. On repetitive recording of the CD spectrum of *tert*-butyloxycarbonyl-L-cysteinylglycylcysteine disulfide methyl ester *(1)* a hypsochromic shift of the longest wavelength negative Cotton effect and a simultaneous increase in ellipticity were registered; in addition, hypsochromism of the disulfide Cotton effect at 245 nm and hyperchromism of the Cotton effect at 225 nm (Fig. 1a) also occurred. Since chemical reactions can be ruled out, it appears likely that the time-dependent changes are related to a conformational transition on going from the crystal to the solution. During such a process a twisting of the disulfide group and *E/Z* isomerization of the two peptide bonds in the heterodetic ring and the urethane bond can occur simultaneously or consecutively. In order to establish whether the time-dependent change of the CD and UV absorption (Fig. 1b) is due to only one or to several of these processes we undertook a kinetic-spectroscopic analysis[2].

Merely the appearance of an isosbestic point in the UV spectra and of two analogous points of constant ellipticity in the CD spectra suggest that the overall conformational change proceeds in a spectroscopically uniform manner. This can be tested with the aid of extinction (*E*) diagrams, extinction

[*] Prof. Dr. G. Jung [+] and Dr. M. Ottnad
Chemisches Institut der Universität
74 Tübingen 1, Auf der Morgenstelle (Germany)
Dr. P. Hartter
Physiologisch-chemisches Institut der Universität Tübingen
Dr. H. Lachmann
Physikalisch-chemisches Institut der Universität Tübingen
[+] To whom correspondence should be addressed.



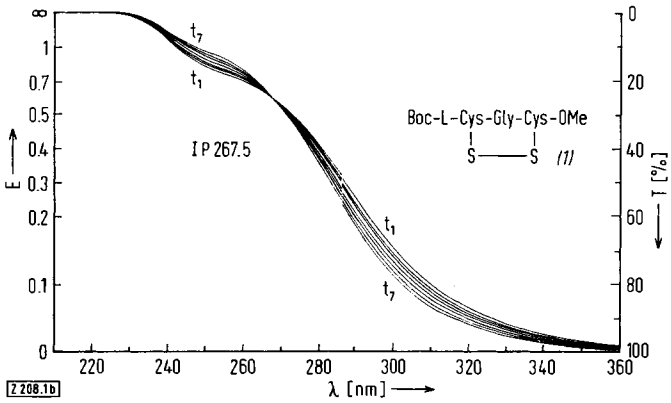


Fig. 1. a) Time-dependence of the CD spectra of *(1)* in 95% ethanol. $c \approx 10^{-3}$ mol/l; 20°C; $d = 20$ mm ($\lambda > 260$ nm), $d = 2$ mm ($\lambda < 260$ nm); $t_i = 5$, 30, 60, 100, 150, 230 min after dissolution of *(1)*. b) Time-dependence of the UV spectra of *(1)* in 95% ethanol. $c \approx 10^{-3}$ mol/l; 20°C; $d = 20$ mm, $t_i = 5$, 15, 35, 70, 120, 240, 500 min after dissolution of *(1)*.

difference (*ED*) diagrams[2] (Fig. 2), and ellipticity diagrams (Fig. 3). Plotting of extinction values $E_\lambda(t_i)$ taken from the time-dependent UV spectra (Fig. 1b) at a particular wavelength *versus* the analogous $E_\lambda(t_i)$ values taken at another wavelength yields an *E* diagram. For small changes, but very different absolute values, of $E_\lambda(t_i)$ (as in Fig. 1b) it is better to calculate the differences $\Delta E_\lambda = E_\lambda(t_i) - E_\lambda(t_1)$ in each case and to plot them against one another (*ED* diagrams, Fig. 2).

If [θ] values or dichroic amplitudes are taken from the time-dependent CD spectra (Fig. 1a) and plotted against each other in analogous manner then ellipticity diagrams[2e] are obtained (Fig. 3). In the case of spectroscopically uniform reactions all these diagrams should afford straight lines for any combination of wavelengths; this requirement is well satisfied in the present case.

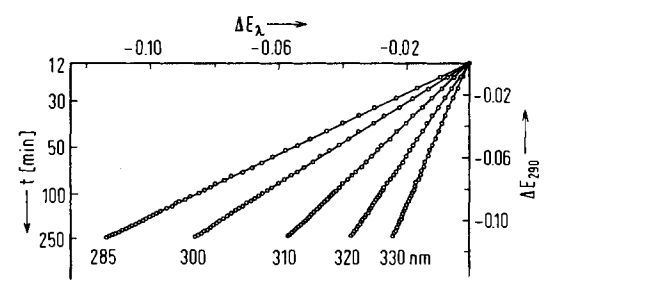


Fig. 2. Extinction difference diagrams: the values are taken from automatically repeated UV spectra (recording conditions as for Fig. 1b, except for d = 50 mm; nonlinear time scale as auxiliary axis).

Consideration of models of *(1)* show that mutually independent isomerizations of the disulfide group and the intraannular peptide bonds are impossible. If all processes within the heterodetic ring occur synchronously with twisting of the inherently

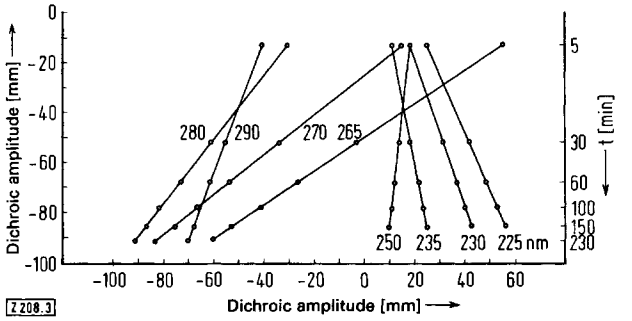


Fig. 3. Ellipticity diagrams: dichroic amplitudes at 275 nm taken from Fig. 1a and plotted against the corresponding values at eight other wavelengths (nonlinear time scale as auxiliary axis).

dissymmetric CSSC grouping or with strict mechanical coupling to this twisting (linear dependence), then the conformational change occurring on transition from the crystal to solution takes place in a spectroscopically uniform manner. Thus the assumption is confirmed that twisting of the disulfide group—accompanied by conformational changes of the entire heterodetic ring—occurs in *(1)* on transition from the crystal to solution. The possible *E/Z* isomerization of the urethane bond does not appear to be incorporated in the observed temperature dependence of the CD and UV spectra of *(1)*.

Many of the spectroscopic data for peptides and other nonrigid molecules which were previously considered to be independent of time should be subjected to critical scrutiny. The relevance of these phenomena, which we have already observed for various other examples, to the interpretation of X-ray structure analyses and of structure-activity relations is obvious.

Received: March 6, 1975 [Z 208 IE]
German version: Angew. Chem. *87*, 448 (1975)

CAS Registry numbers:
(1), 52071-43-9

[1] a) *G. Jung* and *M. Ottnad*, Angew. Chem. *86*, 856 (1974); Angew. Chem. internat. Edit. *13*, 818 (1974); b) *M. Ottnad, C. Ottnad, P. Hartter*, and *G. Jung*, Tetrahedron, 31, 1155 (1975); c) *M. Ottnad, P. Hartter*, and *G. Jung*, Hoppe-Seyler's Z. Physiol. Chem., in press, and references cited therein.

[2] a) H. Mauser, Z. Naturforsch. *23b*, 1021, 1025 (1968); b) *H. Lachmann, H. Mauser, F. Schneider*, and *H. Wenck*, *ibid.* *26b*, 629 (1971); c) *H. Lachmann*, Dissertation, Universität Tübingen 1973; d) *H. Mauser*: Formale Kinetik. Bertelsmann-Universitäts-Verlag, Düsseldorf 1974; e) *H. Lachmann*, to be published.

Formation of Radical Cations from 1,2- and 1,4-Dimethoxybenzene by Electron Transfer to Tl^{2+} and Ag^{2+} in Aqueous Solution. A Pulse Radiolysis and *in situ* Radiolysis EPR Study

By *Peter O'Neill, Steen Steenken*, and *Dietrich Schulte-Frohlinde*[*]

In a previous publication[1] it was shown that Tl^0 reacts with 1,4-dicyanobenzene and 1,4-dinitrobenzene, even in strongly acidic solution, by transfer of an electron to produce radical anions and Tl^+. We now report electron transfer from 1,2- and 1,4-dimethoxybenzene *(1)* and *(2)*, respectively, to Tl^{2+} and Ag^{2+} to yield radical cations and Tl^+ and Ag^+.

[*] Dr. P. O'Neill, Dr. S. Steenken, and Prof. Dr. D. Schulte-Frohlinde [+]
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
433 Mülheim/Ruhr, Stiftstrasse 34—36 (Germany)
[+] To whom correspondence should be addressed.

The radical cations were identified by *in situ* radiolysis EPR[2]. The optical absorption spectra and lifetimes of the radical cations and the rate constants reported (Table 1) were determined by pulse radiolysis. The aqueous solutions used were saturated with N_2O and contained 10^{-3} mol/l of Tl_2SO_4 and 10^{-4} mol/l of *(1)* or *(2)*. The pH was adjusted with perchloric acid.

Irradiation of water with 2.8 MeV electrons produces the species e_{aq}^- (2.7), OH (2.8), H (0.55), H_2 (0.45), H_2O_2 (0.7), H^+ (3.2), OH^- (0.5). The values in parentheses indicate the number of particles formed per 100 eV of absorbed energy. The hydrated electron e_{aq}^- reacts with N_2O to produce OH radicals:

$$e_{aq} + N_2O + H_2O \rightarrow OH + OH + N_2$$

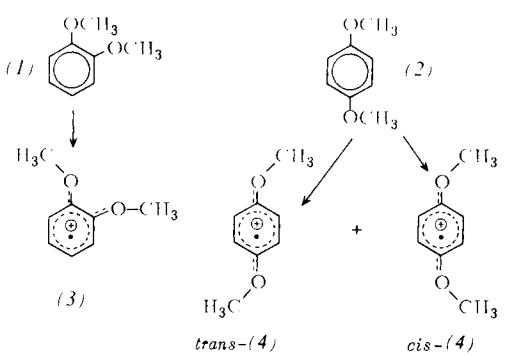
Thus in N_2O saturated solutions the radiolytically formed primary radical species present immediately after the pulse comprise 90% OH radicals and 10% H atoms. The OH radicals react with Tl^+ *via* electron transfer to yield OH^- and Tl^{2+}[3, 4]:

$$OH + Tl^+ \rightarrow OH^- + Tl^{2+}$$

This reaction occurs preferentially at pH values below 4.7[5]. Above this value the complex $[TlOH]^+$[5] is formed. The ions Tl^{2+} and $[TlOH]^+$ are correlated *via the* equilibrium[5]:

$$Tl^{2+} + H_2O \rightleftharpoons [TlOH]^+ + H^+; \quad pK = 4.7$$

On production of Tl^{2+} in the presence of *(1)*, using the procedure described, species *(3)* was observed which is characterized by an absorption spectrum with maxima at 290 and 400 nm and a lifetime of several tenths of a second. In the presence of *(2)* species *(4)* was detected. *(4)* has absorption maxima at 300, 440, and 460 nm and a lifetime of several seconds. Using the *in situ* radiolysis EPR method[2], *(3)* and *(4)* were identified as the radical cations of *(1)* and *(2)*, respectively. *(4)* exists in *trans* and *cis* forms; at 5 °C, the *trans/cis* ratio was found to be 1.12:1. *(3)* exists in only one isomeric form, probably *trans*.



The spectral parameters of *trans-(4)* and *cis-(4)* in aqueous solution are very similar to those[6] in concentrated sulfuric acid.

Table 1. Rate constants k in aqueous solution at 20 °C.

Reaction	k [l mol^{-1} s^{-1}]	Ref.
$Tl^+ + OH \rightarrow [TlOH]^+$	1.0×10^{10}	[4, 5]
$[TlOH]^+ + H^+ \rightarrow Tl^{2+} + H_2O$	1.4×10^{10}	[5]
$Tl^{2+} + H_2O \rightarrow [TlOH]^+ + H^+$	3.5×10^5 [a]	[5]
$Tl^{2+} + (1) \rightarrow Tl^+ + (3)$	6.0×10^8	
$Tl^{2+} + (2) \rightarrow Tl^+ + (4)$	6.5×10^8	
$[TlOH]^+ + (1)$	1.2×10^9	
$[TlOH]^+ + (2)$	4.5×10^8	

[a] Dimensions: s^{-1}

In the absence of Tl^+ under otherwise identical conditions no radical cations were observed at the end of the pulse. From this it follows that the OH radical does not in the primary step react by electron transfer with *(1)* and *(2)*. The dependence of the radical cation concentration, as measured by pulse radiolysis, upon the pH value of the solution corresponds to that of the species Tl^{2+}. Hence it is concluded that only Tl^{2+} reacts completely with *(1)* and *(2)* by electron transfer, in contrast to $[TlOH]^+$. The complex $[TlOH]^+$ reacts with *(1)* and *(2)* with about the same k values as Tl^{2+} (Table 1). Thus the presence of *(1)* or *(2)* does not disturb the equilibrium between Tl^{2+} and $[TlOH]^+$. The radical cations *(3)* and *(4)* can also be generated by reaction with Ag^{2+}, produced[7, 8] by oxidation of Ag^+ with OH, or by reaction with $SO_4^{\bullet -}$.

Received: March 20, 1975 [Z 209 IE]
German version: Angew. Chem. 87, 417 (1975)

CAS Registry numbers:
(1), 91-16-7; *(2)*, 150-78-7; *(3)*, 55012-64-1; *(4)*, 34478-03-0; Tl^{2+}, 14877-28-2; Ag^{2+}, 15046-91-0

[1] *E. A. Robinson* and *D. Schulte-Frohlinde*, J. C. S. Faraday Trans. I, 69, 707 (1973).
[2] *K. Eiben* and *R. W. Fessenden*, J. Chem. Phys. 75, 1186 (1971).
[3] *B. Cercek, M. Ebert*, and *A. J. Swallow*, J. Chem. Soc. *A 1966*, 612.
[4] *H. A. Schwarz, D. Cornstock, J. K. Yendell*, and *R. W. Dodson*, J. Phys. Chem. 78, 488 (1970).
[5] *P. O'Neill* and *D. Schulte-Frohlinde*, J. C. S. Chem. Comm. *1975*, 387.
[6] *W. F. Forbes* and *P. D. Sullivan*, Can. J. Chem. 44, 1501 (1966).
[7] *J. Pukies, W. Roebke*, and *A. Henglein*, Ber. Bunsenges. Phys. Chem. 72, 842 (1968).
[8] *G. C. Barker* and *P. Fowles*, Trans. Faraday Soc. 66, 1661 (1970).

Mode of Formation of Triphenylverdazyl from Triphenylverdazylium Salts or from Triphenylformazan

By *E. A. Ponomareva, P. V. Tarassenko*, and *G. F. Dvorko*[*]

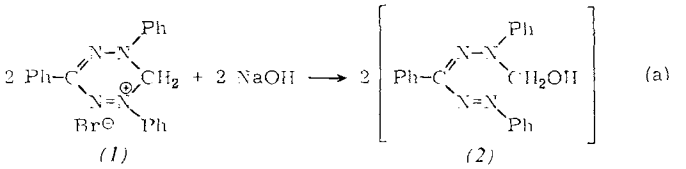
1,3,5-Triphenylverdazylium bromide *(1)* formed from triphenylformazan *(6)*, formaldehyde, and HBr is converted quantitatively into the radical 1,3,5-triphenylverdazyl *(5)* by treatment with NaOH and CH_2O. The reaction mechanism was hitherto unknown[1]. In this communication we report experiments intended to elucidate the individual steps of this and similar reactions.

We have found that in the absence of CH_2O compound *(1)* reacts with an equimolar amount of NaOH in a stream of O_2 or N_2, two thirds undergoing conversion into *(5)* and one third into 5-formyl-1,3,5-triphenylformazan *(3)*. An excess of NaOH does not alter the yield of radical, but compound *(6)* is obtained instead of compound *(3)* [in the same yield as *(3)* in the above reaction]. Atmospheric oxidation of *(5)* affords the aldehyde *(3)*, which is decomposed rapidly and quantitatively into *(6)* and formate by the action of NaOH[2]. In our case *(5)* is not oxidized to *(3)*. The experiments were performed in DMF (or CH_3CN)/H_2O (4:1 v/v); the concentration of *(5)* was monitored by spectroscopy ($\lambda_{max} = 720$, $\log \varepsilon = 3.63$).

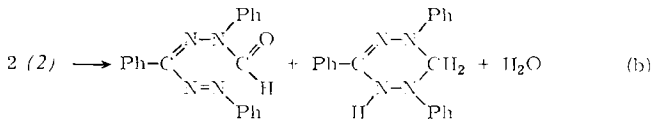
The formation of two moles of *(5)* and one mole of *(3)* from three moles of *(1)* and three moles of NaOH can be explained in terms of the reaction steps (a), (b), and (c).

[*] Doz. E. A. Ponomareva [+], Dipl.-Chem. P. V. Tarassenko, and Dr. G. F. Dvorko
Chemical Faculty of the Kiev Polytechnic Institute
Kiev 56 (USSR)
[+] To whom correspondence should be addressed.

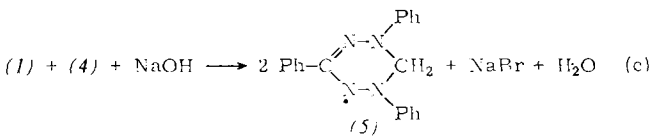
Proof of reaction (a) comes from the finding that *(1)* reacts practically quantitatively with sodium phenoxide to form 5-phenoxymethyl-1,3,5-triphenylformazan; m.p. 97 °C (dec.), UV (dioxane): $\lambda = 236$ nm ($\varepsilon = 29300$) and 343 (19400); 60 MHz ^{1}H-NMR ($CCl_2{=}CCl_2$): $\delta = 2.95$ (d, 2H, N—CH_2—O).



(1) *(2)* + 2 NaBr (a)



(3) *(4)* (b)



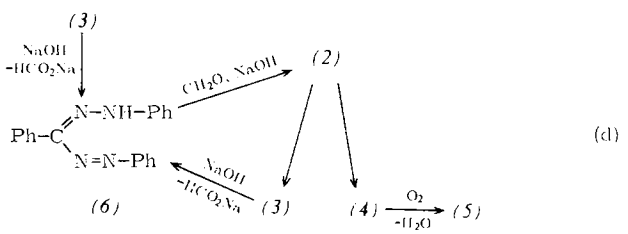
(5) (c)

3 *(1)* + 3 NaOH ⟶ 2 *(5)* + *(3)* + 3 NaBr + 2 H_2O

Confirmation of the proposed reaction (b) is considered to be provided by the finding that alkoxides—dissolved in the corresponding alcohols or alternatively in DMF—quantitatively convert *(1)* into *(5)* in air or in a stream of N_2. The reaction apparently proceeds *via* 5-alkoxymethyl-1,3,5-triphenylformazan which then rapidly decomposes to leucoverdazyl *(4)* and a carbonyl compound.

Reaction (c) is the reversal of the disproportionation of *(5)* in the presence of acid[1]. Kinetic studies in 75 % aqueous CH_3CN have shown that the salt *(1)* undergoes an S_N2 reaction with NaOH. Since reaction (a) is the rate-determining step, the leucoverdazyl *(4)* formed in reaction (b) is able to react quantitatively with *(1)*, thus permitting formation of *(5)* and *(3)* in the ratio 2:1.

On the basis of these results it is now possible to explain the quantitative formation of *(5)* in the reaction of *(6)* or *(1)* with CH_2O and NaOH. An essential feature is the cyclic reaction of 5-formylformazan *(3)*. With an excess of NaOH and CH_2O, *(3)* finally yields the radical *(5)* *via* the intermediates *(6)*, *(2)*, and *(4)*.



(d)

The leuco compound *(4)* is dehydrogenated to *(5)* by atmospheric oxygen[1]: this reaction is fast in alkaline solution[3]. The validity of the proposed scheme (d) is confirmed by the fact that *(3)* and *(6)* give *(4)* in a stream of N_2, but *(5)* in a stream of O_2. On mixing with CH_2O and NaOH, compound *(1)* cannot be reduced directly to *(4)* by formaldehyde, as has previously been assumed[1], since in this case the radical *(5)* is formed, both in a stream of N_2 and in a stream of O_2. Formate formation can also be explained by scheme (d).

Received: March 24, 1975 [Z 211 IE]
German version: Angew. Chem. *87*, 453 (1975)

CAS Registry numbers:
(1), 51940-11-5; *(3)*, 17135-56-7; *(4)*, 22459-57-0;
(5), 2154-65-6; *(6)*, 531-52-2; 5-phenoxymethyl-1,3,5-triphenylformazan, 55162-20-4

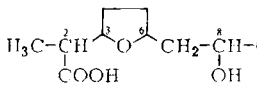
[1] *F. A. Neugebauer*, Angew. Chem. *85*, 485 (1973); Angew. Chem. internat. Edit. *12*, 455 (1973).
[2] *R. Kuhn, F. A. Neugebauer*, and *H. Trischmann*, Monatsh. Chem. *98*, 726 (1967).
[3] *O. M. Polumbrik, G. F. Dvorko*, and *O. M. Grischin*, Ukr. Khim. Zh. *35*, 1046 (1969).

Highly Stereoselective Synthesis of Racemic Nonactic Acid and Synthesis of Dextrorotatory (2*S*,3*S*,6*R*,8*R*)-Nonactic Acid

By *Hans Zak* and *Ulrich Schmidt*[*]

The macrotetrolides nonactin, monactin, dinactin, and trinactin, specific complexing agents for potassium ions, contain nonactic acid *(1)*; the principal metabolite nonactin is composed of two molecules of dextrorotatory (2*S*,3*S*,6*R*,8*R*)- and two molecules of levorotatory (2*R*,3*R*,6*S*,8*S*)-nonactic acid[1]. A synthesis of a mixture of the diastereoisomeric pairs[2], two syntheses of racemic nonactic acid[3, 4] and a synthesis of levorotatory nonactic acid[4] have recently been reported. All these syntheses display little stereoselectivity and afford nonactic acid and 2-*epi*-nonactic acid in approximately equal concentration, as well as 8-*epi*-nonactic acid and 2,8-di-*epi*-nonactic acid.

By means of almost complete Walden inversion at C-8 we have now succeeded in conducting our synthesis of racemic nonactic acid[4] with a high degree of stereoselectivity[4]. The same principle was also used for "inversion" of the 8-*epi*-nonactic acid, formed during the production of levorotatory nonactic acid[4] from (−)-propylene oxide, to form (+)-(2*S*,3*S*,6*R*,8*R*)-nonactic acid.



(1)

The mixture of four diastereoisomeric pairs produced in our synthesis of racemic nonactic acid[4] was oxidized to a mixture of the 8-keto acid and 2-*epi*-8-keto acid. Catalytic hydrogenation of the keto group with Raney nickel afforded almost exclusively a mixture of 8-*epi*-nonactic acid and 2,8-di-*epi*-nonactic acid. Very good yields were obtained in the formation of the 8-tosyl esters and their reaction with potassium acetate in dimethyl sulfoxide, which was accompanied by Walden inversion. After complete hydrolysis and esterification with diazomethane the reaction product consisted entirely of a mixture of methyl nonactate and methyl 2-*epi*-nonactate (1.5:1), which could readily be separated. Methyl 2-*epi*-nonactate can be equilibrated with sodium methoxide to a mixture of methyl nonactate and methyl 2-*epi*-nonactate (1.5:1); we were unable to confirm the ratio of 4:1 reported in ref.[3].

Starting with (−)-propylene oxide (from (+)-lactic ester), our synthesis[4] furnished a mixture from which 25 % of methyl

[*] Dr. H. Zak and Prof. Dr. U. Schmidt [+]
Organisch-Chemisches Institut der Universität
1090 Wien 9, Währinger Strasse 38 (Austria)
[+] To whom correspondence should be addressed.

(−)-(2*R*,3*R*,6*S*,8*S*)-nonactate could be isolated by column chromatography. The mixture of the other three diastereoisomers—(2*S*,3*R*,6*S*,8*S*), (2*R*,3*S*,6*R*,8*S*), and (2*S*,3*S*,6*R*,8*S*)—were converted by Walden inversion into a mixture from which methyl (+)-(2*S*,3*S*,6*R*,8*R*)-nonactate could be isolated in approximately the same amount as the (−)-antipode by chromatography over silica gel. *Both* the levo- and dextrorotatory nonactic acid present in the natural product are thus accessible by asymmetric synthesis from a *single* optically active starting compound.

Received: April 1, 1975 [Z 212 IE]
German version: Angew. Chem. 87, 454 (1975)

CAS Registry numbers:
(±)-(*1*): 55220-86-5; (+)-(*1*), 16221-10-6

[1] *W. Keller-Schierlein* and *H. Gerlach*, Fortschr. Chem. Org. Naturst. *26*, 161 (1968).
[2] *G. Beck* and *E. Henseleit*, Chem. Ber. *104*, 21 (1971).
[3] *H. Gerlach* and *H. Wetter*, Helv. Chim. Acta *57*, 250 (1974).
[4] *J. Gombos, E. Haslinger, H. Zak*, and *U. Schmidt*, Monatsh. Chem. *106*, 219 (1975).
[5] In ref. [3] these compounds are reduced nonstereospecifically with $NaBH_4$ and primarily to the 8-*epi*-alcohols with lithium tris(1-methylpropyl)hydridoborate.

Arsinidene Complexes: Stabilization of Phenylarsanediyl, C_6H_5As, in $C_6H_5As[Cr(CO)_5]_2$[**]

By *Gottfried Huttner* and *Hans-Georg Schmid*[*]

In contrast to the chemistry of their lower homologs, the nitrenes, R—N, little is known about phosphinidines, R—P, and arsinidenes, R—As. The occurrence of phosphinidenes nevertheless appears likely on the basis of several organic trapping reactions[1], while no such evidence has been obtained for arsinidenes. They are suspected to act as intermediates during the formation of cyclooligoarsanes $(RAs)_n$[2]. We have now succeeded in the first stabilization of the "arsinidene", phenylarsanediyl in a metal complex on synthesis of $C_6H_5As[Cr(CO)_5]_2$ (*1*).

The pale yellow complex $(OC)_5CrAs(C_6H_5)H_2$ (*2*)[3] can be metalated with *n*-butyllithium to the orange $(OC)_5CrAs(C_6H_5)Li_2$ which can be converted into (*1*) by treatment with *N*,*N*-dichlorocyclohexylamine and chromatographic work-up:

$$(OC)_5CrAs(C_6H_5)Li_2 \xrightarrow{C_6H_{11}NCl_2} \underset{(1)}{C_6H_5As[Cr(CO)_5]_2} + LiCl + C_6H_{11}N{=}NC_6H_{11} + \ldots$$

The product (*1*) crystallizes as dark violet platelets with a metallic sheen, which appear blue by transmitted light; it is readily soluble in benzene, toluene, and methylene chloride to give intensely blue-green solutions. At 45 °C/10^{-2} torr the new complex can be sublimed with partial decomposition; it melts at 104 °C under N_2 in a sealed tube. Crystals of (*1*) can be kept for several hours in air, but solutions decompose rapidly.

[*] Doz. Dr. G. Huttner and H.-G. Schmid
Anorganisch-chemisches Laboratorium
Fachbereich Chemie der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

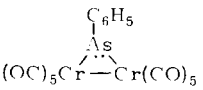
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

The mass spectrum of (*1*) contains the molecular ion at *m/e* 536 (relative to ^{52}Cr). Successive loss of ten CO groups—evidenced by corresponding mass peaks and metastable transitions—leads to $[Cr_2AsC_6H_5]^+$, which decomposes to $[CrAsC_6H_5]^+$ with loss of a chromium atom.

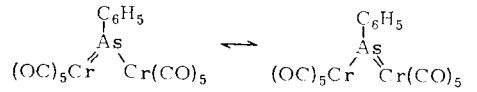
The ^{1}H-NMR spectrum of (*1*) contains no signals apart from a multiplet due to the phenyl protons (δ = 7.5—8.0 ppm, TMS as internal standard).

The IR spectrum of (*1*) displays absorptions in the ν_{CO} region at 2082 (w), 2032 (m), 1984 (vs), and 1953 (w) cm^{-1} (*n*-hexane), whose number indicates a distorted C_{4v} symmetry of the $Cr(CO)_5$ groups. By way of contrast, the ν_{CO} bands of (*2*) lie at lower frequencies: 2068 (s), 1950 (vs), and 1923 (w) cm^{-1} (*n*-hexane). The ν_{AsH} and δ_{AsH} absorptions appearing in the spectrum of (*2*) at 2140 and 775 cm^{-1} cannot of course be observed in the case of (*1*), while the vibrations of the C_6H_5As group in the two compounds appear at about the same wave numbers[4].

Two alternative modes of bonding must be considered for the four-electron ligand C_6H_5—Ȧs: in (*1*):



(*1a*)



(*1b*)

In (*1a*) the potential four-electron ligand would only contribute two electrons to the bond; the chromium atoms would attain the noble gas configuration by one metal-metal and one metal-arsene bond. In (*1b*) the arsenic atom completes its octet of electrons by $Cr_{d\pi}$—$As_{p\pi}$ back bonding; the electron vacancies on the chromium atoms of the $Cr(CO)_5$ groups are filled by the two electron pairs of the arsinidene ligand.

The short wavelength of the ν_{CO} absorption in (*1*) evidences strong metal-ligand back bonding, and thus, like the unusual color of (*1*), points to the structural alternative (*1b*), which has meanwhile been established by structural analysis[5].

We propose the name "arsinidene complexes" for the new type of compound in which an arsanediyl group is stabilized by metal-dπ-arsene-pπ double bonds.

Procedure:

All operations are carried out under N_2. ^{1}H-NMR: Jeol C-60HL; mass spectra: Atlas CH4, ion source TO4.

Compound (*2*) (2.75 g, 7.9 mmol) is dissolved in tetrahydrofuran (100 ml). At −78 °C a solution of *n*-butyllithium (16 mmol) in *n*-pentane (16 ml) is added dropwise within 5 min with vigorous stirring. The orange reaction solution is immediately treated with *N*,*N*-dichlorocyclohexylamine (2 ml, 14.2 mmol) and stirred for 30 min at −50 °C, after which the solvent is drawn off at −20 °C. The orange residue (the calculated amount of LiCl can be detected as toluene-insoluble component) is taken up in CH_2Cl_2 (5 ml) and chromatographed (silica gel, Merck, # 0.063—0.200 mm, 3% H_2O; eluent CH_2Cl_2; column dimensions: length 10 cm, diam. 4 cm). The greenish yellow first runnings contain azocyclohexane and a mixture of cycloarsane-chromium complexes that has not yet been precisely characterized. The greenish black zone of (*1*) develops only slowly and is eluted with 250 ml of CH_2Cl_2. After removal of the solvent at 18 °C, chromatography is repeated at −15 °C (silica gel, as above, 0% H_2O; eluent CH_2Cl_2; column dimensions: length 25 cm, diam. 2 cm). (*1*) migrates as a broad greenish black zone, which affords 0.23 g

(11%) of analytically pure product after removal of solvent and recrystallization from 5 ml CH_2Cl_2/25 ml *n*-pentane at −78 °C.

Received: January 31, 1975;
revised: March 19, 1975 [Z 215 a IE]
German version: Angew. Chem. 87, 454 (1975)

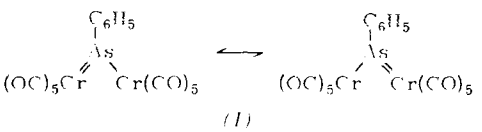
CAS Registry numbers:
$(OC)_5CrAs(C_6H_5)H_2$, 55590-60-8; n-butyllithium, 109-72-8;
$(OC)_5CrAs(C_6H_5)Li_2$, 55590-59-5; *N,N*-dichlorocyclohexylamine 26307-01-7; $C_6H_5As[Cr(CO)_5]_2$, 5590-56-2

[1] *A. Ecker* and *U. Schmidt*, Chem. Ber. *106*, 1453 (1973); and references cited therein.
[2] *O. M. Nefedow* and *M. N. Manakow*, Angew. Chem. *78*, 1039 (1966); Angew. Chem. internat. Edit. *5*, 1021 (1966).
[3] *G. Huttner* and *H.-G. Schmid*, unpublished.
[4] An analysis of the IR spectrum of $C_6H_5AsH_2$ is reported by *H. Stenzenbacher* and *H. Schindlbauer*, Spectrochim. Acta *26 A*, 1713 (1970).
[5] *G. Huttner, J. von Seyerl, M. Marsili*, and *H.-G. Schmid*, Angew. Chem. *87*, 455 (1975); Angew. Chem. internat. Edit. *14*, 434 (1975).

Arsinidene Complexes: Structure and Electronic Spectrum of $C_6H_5As[Cr(CO)_5]_2$[**]

By *Gottfried Huttner, Joachim von Seyerl, Mario Marsili*, and *Hans-Georg Schmid*[*]

A structure having a multiply bonded arsinidene bridging ligand has been considered for phenylarsinidenebis(pentacarbonylchromium), which can be prepared by demetalation of $(OC)_5CrAs(C_6H_5)Li_2$[1]:



(1)

Since this novel structure could not be proved by spectroscopic studies we have carried out a structural analysis of *(1)*[2].

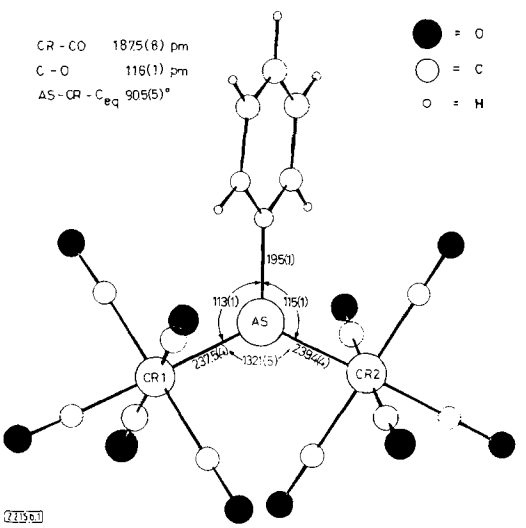


Fig. 1. Structure of *(1)*, a complex with arsenic(I) in trigonal-planar coordination.

[*] Doz. Dr. G. Huttner, J. von Seyerl, M. Marsili, and H.-G. Schmid
Anorganisch-chemisches Laboratorium
Fachbereich Chemie der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

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

The structure of *(1)* depicted in Figure 1 corresponds to the proposed formulation, and exhibits the following features:

1) The arsenic has trigonal-planar coordination. Compound *(1)* is thus the first example of As^I having this coordination geometry.

2) The arsenic-chromium bonds having an average length of 238 pm clearly contain a significant π-bonding component. They are considerably shorter than the As—Cr single bond in $(OC)_5Cr—As(CH_3)_2—Mn(CO)_5$, which contains a tetrahedrally coordinated dimethylarsenido bridge ligand with a Cr—As bond length of 252 pm[3]. Even complexes having terminally bonded arsane ligands, in which the Cr—As bond length should experience considerable shortening by dπ-dπ back bonding, display significantly longer Cr—As bond lengths[4, 5].

3) The observed torsional angles of the substituents $Cr(CO)_5$ and C_6H_5 about the As—Cr and As—C bonds correspond to a particularly favorable steric arrangement: the plane of the phenyl substituent is rotated through 42° relative to the coordination plane of the arsenic. The coordination of the chromium atoms is pseudo-octahedral (maximum deviation of the bond angle from 90 or 180° is 2°); those equatorial axes of the chromium octahedra which lie closest to the coordination plane of the arsenic are displaced by 27° in opposite directions relative to this plane.

The trigonal-planar coordination of the arsenic and the short Cr—As bond lengths indicate that the electron deficiency of the sextet ligand $C_6H_5—\dot{A}s$: is compensated by chromium-dπ-arsenic-pπ back bonding in *(1)*.

The Cr—As—Cr grouping can therefore be approximately described by a model of a three-center 4π system, which can also serve as a basis for qualitative interpretation of the unusual UV spectrum of *(1)* (Fig. 2).

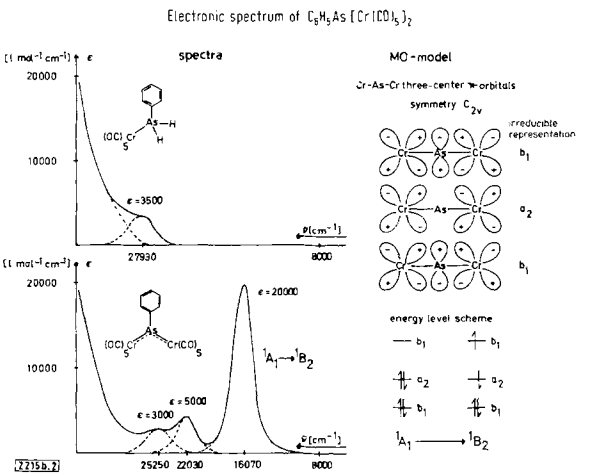


Fig. 2. Electronic spectrum of $C_6H_5As[Cr(CO)_5]_2$ *(1)*.

At 16070 cm^{-1}, in a region where other pentacarbonylchromium ligand complexes show no absorption (see comparison spectrum of $(OC)_5CrAs(C_6H_5)H_2$ in Fig. 2), the spectrum of *(1)* contains a very intense absorption band ($\varepsilon = 20000\,l\,mol^{-1}\,cm^{-1}$)[6]. The new band can be assigned to an electronic transition from the ground state to the first excited state of the three-center 4π system Cr—As—Cr (see Fig. 2). The character of this transition corresponds to a charge-transfer from the metal atoms to the ligand, since although the p-orbital of arsenic participates in the lowest unoccupied molecular orbital it is not involved in the highest occupied molecular orbital. Support for this interpretation comes from the high molar extinction of the observed band.

The arsinidene complex *(1)* is the first representative of a new class of compounds in which arsanediyl groups R—Ä̈s: are stabilized by metal-dπ-arsenic-pπ multiple bonds.

Received: March 19, 1975 [Z 215b IE]
German version: Angew. Chem. *87*, 455 (1975)

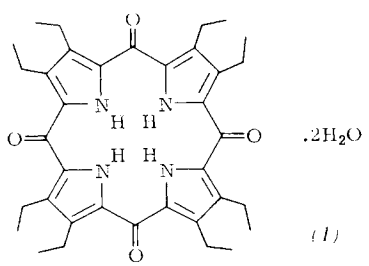
CAS Registry numbers:
(1), 55590-56-2; $(OC)_5CrAs(C_6H_5)H_2$, 55590-60-8

[1] *G. Huttner* and *H.-G. Schmid*, Angew. Chem. *87*, 454 (1975); Angew. Chem. internat. Edit. *14*, 433 (1975).
[2] $R_1 = 0.058$; the structure was solved using a Syntex P 2_1 diffractometer with the Syntex XTL structure-solving system.
[3] *H. Vahrenkamp*, Chem. Ber. *105*, 1486 (1972).
[4] *G. B. Robertson, P. O. Whimp, R. Colton*, and *C. J. Rix*, Chem. Commun. *1971*, 573.
[5] *I. W. Nowell* and *J. Trotter*, J. C. S. Dalton *1972*, 2378.
[6] Since the solutions of the substance decompose during measurement, the value given represents a lower limit.

Structure of Octaethylxanthoporphinogen Dihydrate[***]

By *William S. Sheldrick* and *Jürgen-Hinrich Fuhrhop*[*]

Xanthoporphinogens (Greek xanthos = yellow, porphinogen = porph(yr)in producer) were first obtained by *Fischer* and *Treibs* in 1927 by oxidation of porphyrins with lead dioxide, the yield being almost quantitative[1]. The stimulus to this surprisingly successful experiment came from dehydrogenation experiments on indigo whose structural relation to the porphyrins was at that time considered possible. It was only 40 years later that the structure of these easily crystallizable compounds was elucidated as tetraoxoporphinogens, *e. g. (1)*,



(1)

by *Inhoffen et al.* who used spectroscopic methods[2]. It was then noted that two molecules of water of crystallization could not be removed even by heating in a high vacuum at 150 °C; such stable hydrates have never been observed among porphyrins.

(1) forms tetragonal crystals, $I4_1/a$, with $a = 13.801(1)$, $c = 18.575(6)$ Å; $Z = 4$; $d_{calc.} = 1.19$ g cm^{-3}. The structure was solved by direct methods[3] and refined for 1115 independent reflections (four-circle diffractometer, $F \geq 2.5\sigma(F)$ to $R = 0.075$, $R_G = 0.073$. All the hydrogen atoms could be located in a difference Fourier synthesis and were therefore included together with individual isotropic temperature factors in the last cycles of refinement. All the other atoms were assigned anisotropic temperature factors. The molecule has crystallographic

[*] Dr. W. S. Sheldrick [+] and Doz. Dr. J.-H. Fuhrhop [**]
Gesellschaft für Molekularbiologische Forschung mbH
33 Braunschweig-Stöckheim, Mascheroder Weg 1 (Germany)
[+] To whom correspondence should be addressed.
[**] Institut für Organische Chemie A der Technischen Universität
33 Braunschweig, Schleinitzstrasse (Germany)

[***] This work was supported by the Ministerium für Forschung und Technologie as part of the Technology Program, by the Deutsche Forschungsgemeinschaft, and by the Fonds der Chemischen Industrie.

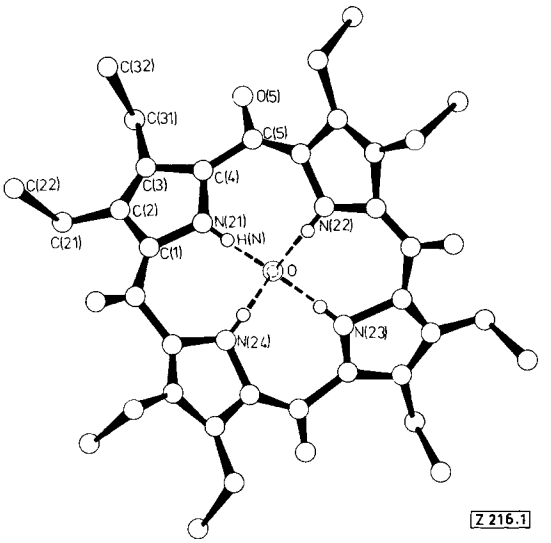


Fig. 1. Projection of *(1)* perpendicular to the S_4 axis; hydrogen bonds (- - -). The most important bond lengths are N(21)—C(1) 1.364(4), N(21)—C(4) 1.384(4), C(1)—C(2) 1.396(5), C(2)—C(3) 1.402(5), C(3)—C(4) 1.401(5), C(4)—C(5) 1.441(5), C(5)—O(5) 1.232(5) Å.

S_4 symmetry (see Fig. 1). The oxygen atoms of the bonded water molecules lie on the S_4 symmetry axis above and below the porphinogen. The atoms bound to a bridging carbon atom, *e. g.* C(5), form dihedral angles of −8.9 or 41.6 with the planes of the neighboring pyrrole rings.

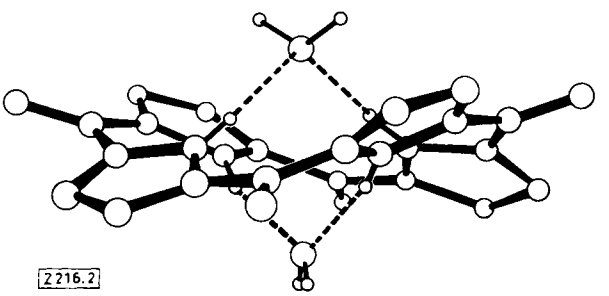


Fig. 2. Projection of *(1)* (without the ethyl-carbon atoms) perpendicular to [010].

The protons on the two opposing nitrogen atoms N(21) and N(23) lie 0.071 Å above the imaginary plane of the molecule, whilst the protons on N(22) and N(24) lie the same distance below the plane. One water molecule lies exactly perpendicularly 2.216 Å above the center of this plane, and a second similarly below it, the oxygen atoms of these water molecules being each linked by hydrogen bridge bonds to two NH protons (separations NH···O 3.016, N—H 0.92, O···H = 2.13 Å). We attribute the twisting of the chromophore mainly to formation of these four hydrogen bridges. The appearance of these bridge bonds which, as mentioned above, are not observed in the related porphyrins, can be explained as being due to the relatively high acidity of α-acyl-substituted pyrroles.

A second effect of the water of crystallization—one that to the best of our knowledge has never been observed before—is the formation of a clathrate-like crystal structure (Fig. 3). The protons of the water molecules form hydrogen bonds to the carbonyl-oxygen atoms of the bridges in the chromophore *(1)*. In this way each of the four hydrogen atoms of the two water molecules interacts with a different ketone-oxygen atom of a neighboring molecule, so that each xanthoporphinogen dihydrate is linked to four other similar molecules. Each chromophore molecule thus fixes two porphinogen

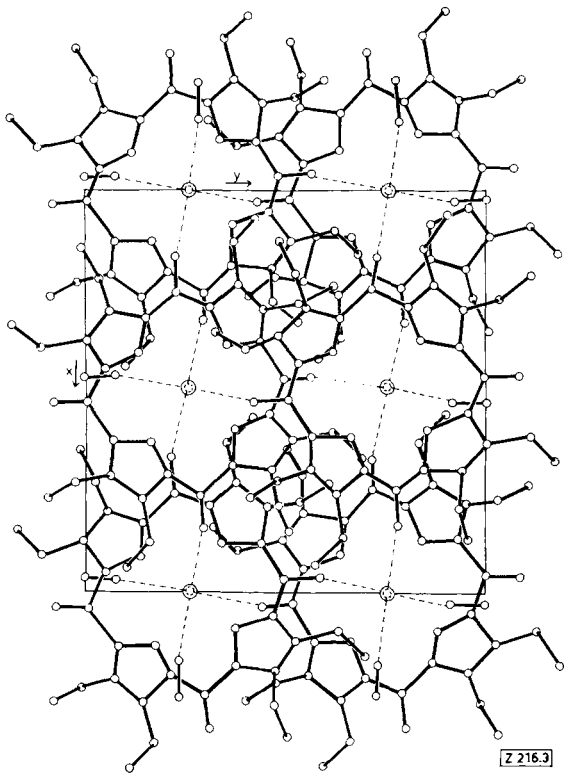


Fig. 3. Projection of the crystal lattice in the direction [001].

molecules on its main axis and each of these in turn bonds two further porphinogen molecules at its periphery. The results of this mode of arrangement is the formation of water-containing, tubular cavities, as depicted in Fig. 3.

Received: March 4;
revised March 24, 1975 [Z 216 IE]
German version: Angew. Chem. 87, 456 (1975)

[1] *H. Fischer* and *A. Treibs*, Liebigs Ann. Chem. *457*, 209 (1927).
[2] *H. H. Inhoffen, J.-H. Fuhrhop*, and *F. von der Haar*, Liebigs Ann. Chem. *700*, 92 (1966).
[3] *G. M. Sheldrick*, program system SHELX, Cambridge (1974).

$Sn_{10}O_4S_{20}^{8-}$: A New Type of Polyanion[**]

By *Willy Schiwy* and *Bernt Krebs*[*]

The chemistry of thioanions of main group elements and transition metals in their highest oxidation states is characterized by the pronounced stability of simple tetrahedral species MX_4^{n-} (X=S or O). Whereas thioanions of, *e.g.*, As^V, Sb^V, Mo^{VI}, and W^{VI} have so far only been detected in their monomeric ortho form, among the thiogermanates(IV) and thiostannates(IV) discrete ions of various stoichiometries and various degrees of condensation have been isolated and characterized in recent years: $Ge_2S_6^{4-}$ and $Sn_2S_6^{4-}$[1], $(GeS_3^{2-})_n$ and $(SnS_3^{2-})_n$[2], $Ge_2S_7^{6-}$ and $Sn_2S_7^{6-}$[3], $Ge_4S_{10}^{4-}$[4], $Sn_3S_8^{4-}$[5]. We have now been able to prepare and characterize (X-ray structure analysis) a new thiostannate which contains isolated polyanions of composition $Sn_{10}O_4S_{20}^{8-}$.

For the preparation, CsOH (7.5 g) is dissolved in H_2O (30 ml) under N_2. H_2S is passed into half of the solution until it is saturated. After filtration and combination with the rest of the solution SnS_2 (6 g) is added portionwise at boiling temperature with exclusion of air. After one hour's stirring and subsequent filtration, colorless $Cs_8Sn_{10}O_4S_{20} \cdot 13H_2O$ is induced to crystallize in a stream of N_2 (monoclinic, C2/c; $a=15.909$, $b=21.256$, $c=18.557$ Å; $\beta=91.71°$; $d_{exp}=3.31$, $d_{calc}=3.377$ g/cm^3; $Z=4$).

The thiooxoanion (Fig. 1) has idealized T_d symmetry and can be described as an arrangement of ten corner-linked SnS_4 tetrahedra; the octahedral sites lying between these tetrahedra are occupied by oxygen atoms. Only the four outer SnS_4 tetrahedra are regular and hardly distorted (terminal bonds with weak π-components: 2.340 Å, bridge bonds 2.403...2.441 Å), whereas for the six inner Sn atoms the coordination number is raised to 6 by bonds (shown bold in Fig. 1, top; 2.047...2.095 Å) to the included oxygen atoms. In the resulting strongly distorted SnO_2S_4 octahedra the Sn—S interatomic distances lie between 2.448 and 2.665 Å.

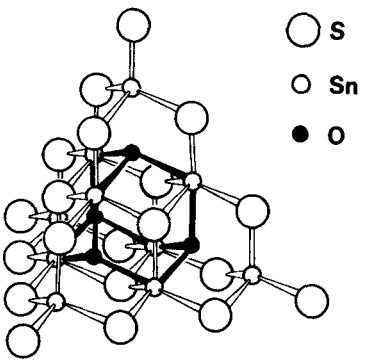


Fig. 1. $Sn_{10}O_4S_{20}^{8-}$ ion in two different representations.

The most important frequencies of the vibrational spectra in the range of stretching and skeletal vibrations are: IR: 150, 260, 281, 320, 346, 360 cm^{-1}; Raman: 193, 327, 336, 357, 385 cm^{-1}. The species $Sn_{10}O_4S_{20}^{8-}$, which is also stable in solution, represents the largest thioanion to be discovered so far, and is a new type of isopolyanion which is also unknown in the chemistry of oxoanions.

Received: March 24, 1975 [Z 219 IE]
German version: Angew. Chem. 87, 451 (1975)

[1] *B. Krebs, S. Pohl*, and *W. Schiwy*, Z. Anorg. Allg. Chem. *393*, 241 (1972).
[2] *J. Olivier-Fourcade, E. Philippot, M. Ribes*, and *M. Maurin*, Rev. Chim. Miner. *9*, 757 (1972); *J. Fenner* and *D. Mootz*, Naturwissenschaften *61*, 127 (1974); *W. Schiwy, C. Blutau, D. Gäthje*, and *B. Krebs*, Z. Anorg. Allg. Chem. *412*, 1 (1975).
[3] *B. Krebs* and *W. Schiwy*, Z. Anorg. Allg. Chem. *398*, 63 (1973); *J. C. Jumas, J. Olivier-Fourcade, F. Vermot-Gaud-Daniel, M. Ribes, E. Philippot*, and *M. Maurin*, Rev. Chim. Miner. *11*, 13 (1974).
[4] *B. Krebs* and *S. Pohl*, Z. Naturforsch. *26b*, 853 (1971); *E. Philippot, M. Ribes*, and *O. Lindqvist*, Rev. Chim. Miner. *8*, 477 (1971).
[5] *J. C. Jumas, E. Philippot*, and *M. Maurin*, J. Solid State Chem., in press.

Alkali Metal Salts of Monothio-, 1,1-Dithio-, and 1,1,2-Trithiooxalic Acid

By *Wolfgang Stork* and *Rainer Mattes*[*]

Of the five possible thio derivatives of the oxalate ion, monothiooxalate *(1)*, 1,1-dithiooxalate *(2)*, 1,2-dithiooxalate

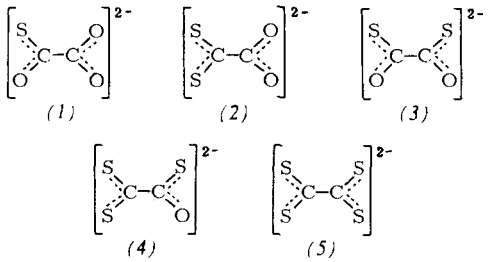
[*] Prof. Dr. B. Krebs and Dr. W. Schiwy
Fakultät für Chemie der Universität
48 Bielefeld, Universitätsstrasse (Germany)

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

[*] Prof. Dr. R. Mattes and Dipl.-Chem. W. Stork
Anorganisch-chemisches Institut der Universität
44 Münster, Gievenbecker Weg 9—11 (Germany)

(3), trithiooxalate *(4)*, and tetrathiooxalate *(5)*, only the anion *(3)* has hitherto been reported[1].

Vibrational spectroscopic[2] and structural studies[3] on *(3)* have also been published, as have reports on its complex



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

chemistry[4]. We have now been able to isolate the ions *(1)*, *(2)*, and *(4)* as their potassium salts, and *(1)* and *(2)* also as their cesium salts.

Our main interest centered on the question of which conformation these anions possess in solution and in the solid state. The oxalate ion is known to have D_{2d} symmetry in solution, but approximate D_{2h} symmetry in the solid state[5]; in contrast, the anion *(3)* has a *gauche* conformation (C_2 symmetry) in solution and in the solid state[2, 3]. For *(1)* and *(4)* resonance formulas having C_s symmetry are conceivable, *i.e.* with a coplanar or orthogonal arrangement of the two (thio)carboxy groups; the corresponding conformations of *(2)* possess higher symmetry, namely C_{2v}. Interest also attaches to the bonding and charge distribution in these anions, and especially to their coordination properties towards metal ions and other coordinatively unsaturated compounds. They also have a certain aesthetic attraction as simple, relatively symmetric compounds.

In order to prepare *(1)* we started from potassium monophenyl oxalate which we saponified with KHS in ethanol. After recrystallization from methanol/water we obtained $K_2C_2O_3S \cdot H_2O$ as thin colorless platelets.—The potassium salt of *(2)* was prepared as follows: trichloroacetic acid was reacted with twice its weight of K_2S dissolved in ethanol. The resulting precipitate was digested with methanol to remove KCl, the $K_2C_2O_2S_2$ precipitated by addition of ether and recrystallized from methanol/water (yellow prisms).—The potassium salt of *(4)* was obtained by reaction of phenyl trichloroacetate with KHS in methanol at 50 °C. $K_2C_2OS_3$ crystallizes as dark yellow prisms. In addition, two modifications of $K_2C_2OS_3 \cdot KCl \cdot H_2O$ are found.—All operations were performed in an inert atmosphere.

Table 1. Vibrational spectra of potassium thioxalates containing the anions *(1)*, *(2)*, and *(4)*.

$K_2C_2O_3S \cdot H_2O$		$K_2C_2O_2S_2$—(1,1)		$K_2C_2OS_3$		Assignment
IR	Raman	IR	Raman	IR	Raman	
1603 vs	1605 (0.5)	1575 vs				$\nu_{as}CO_2$
1531 } vs	1540 (8)					νCO
1517 }	1516 (10)			1510 vs	1510 (0.5)	
1370 s	1376 (5)	1380 vs	1382 (1)			$\nu_s CO_2$
		1030 vs	1030 (0.5)	1024 vs	1020 (1.5)	$\nu_{as}CS_2$
1040 s	1047 (9)		1017 (4.5)	1123 s	1130 (10)	νCC
825 m	825 (2.5)			833 vs	832 (1.5)	νCS
		765 s	767 (4.5)	600 m	602 (9)	$\nu_s CS_2$
785 m	796 (3)	781 s		662 m		
620 m	620 (1)	471 w	476 (10)	550 w	554 (3.5)	
560 m	555 (10)			438 m	438 (9.5)	further bands
	432 (1.5)					
375 m	375 (1)					

Table 1 lists the vibrational frequencies of the anions *(1)*, *(2)*, and *(4)*. Assignment is possible only in the stretching frequency range without any knowledge of the conformations or recourse to model calculations. Raman spectroscopic studies in aqueous solution indicate the anions *(1)*, *(2)*, and *(4)* to have the same conformation in the solid and dissolved states. Structural investigations aimed at determining the conformation are in progress.

Received: March 17, 1975 [Z 220 IE]
German version: Angew. Chem. *87*, 452 (1975)

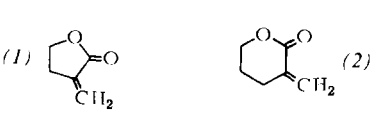
[1] *H. O. Jones* and *H. S. Tasker*, J. Chem. Soc. *95*, 1904 (1909).
[2] *R. Mattes* and *W. Stork*, to be published.
[3] *R. Mattes*, *W. Meschede*, and *W. Stork*, Chem. Ber. *108*, 1 (1975).
[4] *F. J. Hollander* and *D. Coucouvanis*, Inorg. Chem. *13*, 2381 (1974); and literature cited therein.
[5] *G. M. Begun* and *H. W. Fletcher*, Spectrochim. Acta *19*, 1353 (1963).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The synthesis of α-methylene lactones is dealt with in an article by *P. A. Grieco*. The α-methylene-γ-butyrolactone structure *(1)* and, to a lesser extent, the α-methylene-γ-valerolactone structure *(2)* are to be found in a series of natural products,



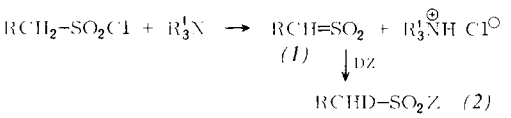
(1) *(2)*

particularly in the sesquiterpenes, which are of interest on account of their biological activities. *(1)* and *(2)* can be pre-

pared, *inter alia*, by reaction of alkynyl alcohols with $Ni(CO)_4$, by reductive amination of α-formyl lactones and subsequent cleavage of trialkylamine, by cyclopropane rearrangement, by Wittig reaction, by reductive elimination of α-formyl lactones, or by a Mannich reaction. Also dealt with is the synthesis of a number of natural products (*e.g. dl*-alantolactone, (+)-arbusculin B, *dl*-avenaciolid, and tulipalin A). [Methods for the Synthesis of α-Methylene Lactones. Synthesis *1975*, 67—82; 69 references]

[Rd 772 IE—M]

Sulfenes *(1)*, the sulfonyl analogs of ketenes, are reviewed in an article by *J. F. King*. Evidence for the existence of the sulfenes is provided *e.g.* by the almost exclusive formation of *(2)* in the reaction of sulfonyl chlorides with bases in



the presence of deuteriated substrates DZ (*e.g.* D_2O, R″OH). Some reactions in which sulfenes are formed, as well as the reactions of these unstable compounds themselves, are collected in tabular form. Typical reactions, besides the sulfonylation of *e.g.* alcohols and amines, are cycloadditions to three- and four-membered rings. [The Return of Sulfenes. Accounts Chem. Res. *8*, 10—17 (1975); 97 references]

[Rd 773 IE—L]

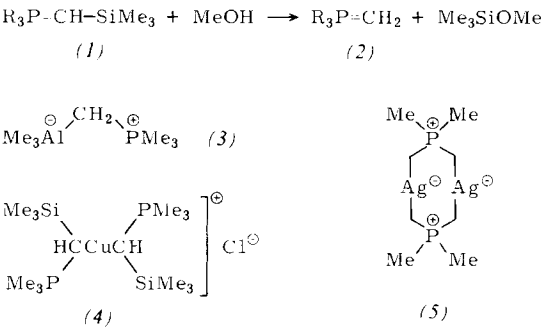
Synthesis and reactions of simple organolithium compounds from weakly acidic C—H compounds such as arylacetic acids, arylalkane- and alkanesulfonic acids, arylalkane- and alkanephosphonic acids, and their derivatives, are summarized in a review article by *D. Ivanov*, *G. Vassilev*, and *I. Panayotov*. After a brief consideration of metalation reactions with aryl-Li and alkyl-Li compounds the reactions of metalated arylacetic acids with α,β-unsaturated ketones, Schiff bases, carboxylic acids, iodine and *N*-bromosuccinimide, 2-benzoylethyl(trimethyl)ammonium iodide, as well as alkylation reactions, are described and compared with those of organomagnesium compounds. The metalation of sulfonic acids and phosphonic acids is also dealt with. Further sections are devoted to the metalation of nitriles, and the esters of aliphatic carboxylic acids. [Syntheses and Reactions of Organolithium Reagents Derived from Weakly Acidic C—H Compounds. Synthesis *1975*, 83—98; 117 references.]

[Rd 775 IE—M]

A classification of photochemical reactions has been carried out by *W. G. Dauben*, *L. Salem*, and *N. J. Turro*. The underlying assumption is that all photochemical reactions of organic molecules are controlled by the generation of primary products which have the characteristics of diradicals. Only one single energy diagram is needed; this enables delineation of the minimum requirements which must be met by a reaction mechanism, as well as prediction of the course of the reaction. Which of the several possible reaction pathways the system chooses is as yet undefinable. [A Classification of Photochemical Reactions. Accounts Chem. Res. *8*, 41—54 (1975); 42 references]

[Rd 776 IE—L]

Inorganic chemistry with ylides is the title of a review by *H. Schmidbauer*. Silicon-containing ylides such as *(1)* undergo desilylation to give salt-free trialkylphosphonium alkylides



(2); complex silicon ylides are accessible by transsilylation. Apart from the homologs of Si and P, main group elements such as Al, Ga, and Mg can also form ylides, *e.g. (3)*. The ylides of transition metals exhibit unusual thermal stability. Thus, *(4)* first begins to decompose at 124°C/0.1 torr, and *(5)* can be sublimed at 150°C/0.1 torr.—Further "ylide formers" are, *inter alia*, Zn, Cd, Hg, Au, Co, Ni, Pd, Pt, and Cr. [Accounts Chem. Res. *8*, 62—70 (1975); 85 references]

[Rd 777 IE—L]

Theory and manifestations of the Jahn-Teller-effects are reviewed by *I. B. Bersuker*. After a brief consideration of the theoretical basis, the adiabatic potentials for orbitally degenerate and pseudo-degenerate states are derived. The results are applied to a qualitative discussion of stereochemistry, crystal chemistry, the shape of electronic broad bands, and polarized luminescence. A more rigorous treatment of the vibronic equations leads to some novel spectral effects, *e.g.*, microwave and ultrasonic absorption, characteristic ESR and Mössbauer spectra, zero-phonon line splitting, *etc.* The consequences of Jahn-Teller instabilities in the field of reaction mechanisms are excluded from the discussion. [The Jahn-Teller Effect in Crystal Chemistry and Spectroscopy. Coord. Chem. Rev. *14*, 357—412 (1975); 105 references]

[Rd 784 IE—H]

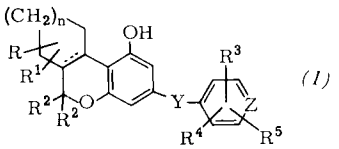
The principle of hard and soft acids and bases (HSAB) in organic chemistry is discussed in a review by *T. L. Ho*. The "hard" species generally have small atomic radii and high effective nuclear charges and are weakly polarizable, while the converse is true for the "soft" species. According to the HSAB principle acids exhibit a higher affinity for bases of the same class (and *vice versa*). The major part of the review deals with the selectivity of reactions such as alkylation and/or acylation in the case of β-propiolactone, the *C*- and/or *O*-alkylation of enolates and related compounds, reactions of organosulfur and organophosphorus compounds, as well as addition reactions. [The Hard Soft Acids Bases (HSAB) Principle and Organic Chemistry. Chem. Rev. *75*, 1—20 (1975); 263 references]

[Rd 779 IE—L]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Benzopyrans of formula *(1)*, suitable for the treatment of states of pain and anxiety, are prepared by various procedures; they have certain advantages in comparison with the natural



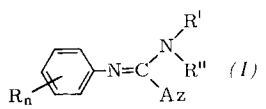
(1)

$n = 1,2$; R, R^1 = H, alkyl; R^2 = alkyl; R^3, R^4, R^5 = H, alkyl, halogen, CF_3; Y = alkylene; Z = CH, N

products on which they are based. [DOS 2415697; Abbott Laboratories, Chicago (USA)]

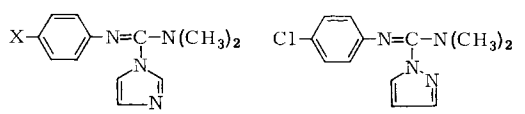
[PR 269 IE—K]

As new weed killers, guanidine-like compounds containing an azolyl group, of formula *(1)*, are used.



(1)

R = halogen, alkyl, Oalkyl, Salkyl; $n = 0$—5; R', R'' = H, alkyl, cycloalkyl, Oalkyl, *etc.*; Az = azolyl group with 1 to 3 nitrogens in the ring

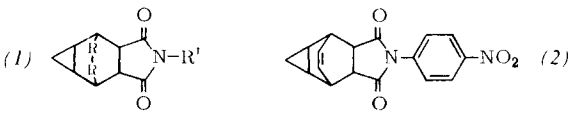


(2), X = H; *(3)*, X = Cl *(4)*

Compounds *(2)*—*(4)* are particularly noted. [DOS 2321330; Bayer AG, Leverkusen (Germany)]

[PR 268 IE—S]

As new pest-control agents dicarboximides of formula *(1)*, and especially *(2)*, are used. R—R is —CH_2—CH_2— or —CH=CH—; R' is, if necessary, substituted phenyl. The

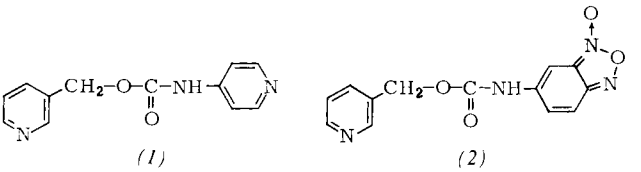


(1) *(2)*

action is directed above all against lepidoptera. [DOS 2417839; Ciba Geigy, Basel (Switzerland)]

[PR 266 IE—S]

A new group of rodenticides consists of the carbamic esters of 3-hydroxymethylpyridine, of formula *(1)* and *(2)*.

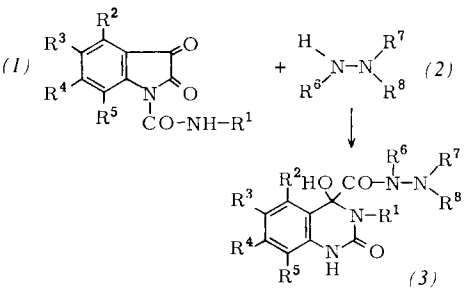


(1) *(2)*

[DOS 2404953; Rohm & Haas Co., Philadelphia (USA)]

[PR 267 IE—S]

New 3-substituted 4-hydroxy-2-oxo-1,2,3,4-tetrahydroquinazoline-4-carbohydrazides *(3)* are obtained by the reaction of



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

R^1 = alkyl, aryl, R^2—R^5 = group not reacting with *(2)*; R^6—R^8 = H, alkyl, aryl

isatin-*N*-carboxamides *(1)* with hydrazines *(2)*. [DOS 2314242; Bayer AG, Leverkusen (Germany)]

[PR 270 IE—K]

BOOK REVIEWS

Einführung in die Radikalchemie (Introduction to Radical Chemistry). By *W. A. Pryor*. Translated by *B. Giese*. Verlag Chemie, GmbH, Weinheim 1974. 1st Edit., ix, 118 pp., 10 figs., 23 tables, bound, DM 24.80.

In 1966 the "Small Pryor" appeared, warmly greeted as a small introductory textbook for radical chemistry. The expert author had selected his material soundly and presented it with didactic skill, together with problems at the end of each chapter, and success was thus assured. Now, eight years later, comes a German translation of the original text. This is surprising, for much has happened since then in radical chemistry. It would have been highly desirable to refer to the literature, which has been enlarged meanwhile and has led to further advances. ESR spectroscopy (pp. 7/8) could today exceed H and CH_3. It is understandable that CIDNP is not yet mentioned. Unfortunately, it is not stated that color is by no means

a specific property of radicals (p. 8). In so short a text it is probably unavoidable that treatment of H-transfer (which does not satisfy one's curiosity about, *e. g.*, the reason for the series primary < secondary < tertiary C), of the transition state, and of the Hammond principle (*e. g.* p. 57) is presented in black-and-white fashion.

The book can be highly recommended to chemists who want a rapid survey and to students of chemistry shortly before or after the "Vordiplom" examination.

W. P. Neumann [NB 258 IE]

Säuren und Basen (Acids and Bases). By *R. P. Bell* (taschentext 19). Translated by *F. Frickel*. Verlag Chemie-Physik Verlag, Weinheim 1974. 1st Edit., vi, 111 pp., 8 figs., 17 tables, paperback, DM 16,80.

This is a German "pocketbook" translation of the 2nd edition (first publication in 1952) of "Acids and Bases: Their Quantitative Behavior" by the author of the well known monograph "The Proton in Chemistry". The Brønsted-Lowry definition is used as a basis for the concepts of acids and bases. The first two chapters deal with elementary matters (the nature of acids and bases; acid-base equilibria in water) which are to be found in introductory textbooks of general or inorganic chemistry. Chapter 3 provides a short review of acids and bases in nonaqueous solvents, and Chapter 4 is devoted to interionic interactions in acid-base equilibria. Very valuable, particularly for students halfway through their course, are Chapters 5—7 [acid-base strength and molecular structure, the rates of acid-base reactions (acid-base catalysis), hydrogen isotopes in acid-base reactions]. The final Chapter 8 is concerned with alternative acid-base concepts, but is very brief since there are very few quantitative relationships.

The author has been at pains to be generally up to date, as appears particularly in Chapters 6 and 7. The explanation of acid-base equilibria in water appears rather thin, and some worked examples would have been useful here. In a new edition a few small errors should be corrected (*e. g.* pp. 65, 90); in particular (p. 107), a Lewis acid should be described as an electron-*pair* acceptor (not an electron acceptor), and a Lewis base as an electron-*pair* donor. A or HA should be used consistently for an acid, but not both. A good point is the literature on further aspects appended to each chapter; here recent monographs and reviews are included. As a whole, this is a readable book and a useful addition to lectures in a student's first years.

Helmut Werner [NB 261 IE]

Organische Chemie I and II (Organic Chemistry I and II). By *L. Eberson*. Translated by *A. Senning*. Verlag Chemie, GmbH, Weinheim 1974. 1st Edit., Vol. I: xiv, 328 pp., 55 figs., 42 tables, paperback DM 17,80; Vol. II: xv, 457 pp., 9 figs., 26 tables, paperback DM 19,80.

This text book of organic chemistry occupies two volumes. The fundamental concepts of structural theory, nomenclature, stereochemistry, energetics and kinetics, and of bonding theory are described in volume I. There follow a section on intermolecular forces and a general treatment of reactions and reaction mechanisms. Later there is a very good description of the usual spectroscopic methods, including X-ray and neutron diffraction; unfortunately, there is no indication of the importance of ^{13}C-NMR spectroscopy. Equally, one misses a short introduction to the Woodward-Hoffmann rules. On the other hand, the clear and detailed treatment of nomenclature questions is welcome, for it is absent from most textbooks.

The first few chapters of volume II describe mainly reactions of organic compounds. The author has selected the traditional division into functional groups for this purpose and he abstains completely from any precise description of individual substances or their preparation. This principle is sensible for a short textbook, for it spares the reader the wealth of individual data that are not essential for understanding organic chemistry.

In later chapters the author considers heterocycles and natural products, where the selection in the natural products section is not so well chosen. For example, most weight is placed here on classical carbohydrate chemistry, while modern aspects such as biogenesis are neglected.

On the other hand, the sections on synthesis and structure demonstration are very successful: the reader is made familiar with planning and performing syntheses (*e. g.* by chain extension) and with the determination of the structures of organic compounds. The last part of volume II treats industrial aspects of organic chemistry, *e. g.* industrial-scale syntheses, drugs, explosives, *etc.*

The arrangement of material in both volumes is easy to follow and clear. The text is to the point and easy to read. Nevertheless, the less experienced reader will in some cases need to turn to further literature in view of the brevity of the presentation, especially for mechanistic considerations. Summarizing, however, it can be said that these volumes, which are particularly suitable for students early in their course, present a useful addition to large textbooks.

Lutz-F. Tietze [NB 262 IE]

Mehr Wissen über Chemie (More Information about Chemistry). By *K. Baumann, H. Fricke*, and *H. Wissing*. Aulis Verlag Deubner & Co. Cologne 1974, Vol. 1: A—H. 1st Edit., 524 pp., numerous formulas, figs. and tables, bound, DM 39.— (later DM 48.—). The two volumes are not sold separately.

This book comprising two volumes, is halfway between a dictionary and a textbook. Volume 1 consists of review articles of one to about 50 pages on around one hundred themes and a keyword index integrated alphabetically into the text with a reference to generally one article. The work is stated by the authors and publishers to be intended for experts and educated laymen, *i. e.* the aim has been to help schoolchildren, laboratory assistants, students, chemistry teachers, and experts. Such an ambitious objective demands very careful selection of the items treated, a balanced and graded level of presentation, and above all materially faultless formulations. In addition, the style must be intelligible linguistically. The reality, alas, is disappointing.

Alongside fairly usable passages there are many sloppy formulations as well as contradictory, half-true, and completely false statements; hardly any could be fully approved. The content of the articles is generally very mixed and arbitrarily assigned; for example, 4 pages on the principles of distillation occur in the Petroleum section. The selection is presumably based on the authors' hobbies. Instead of being gratified, the reader thirsty for facts will instead feel subjected to "quentsching" (Petroleum, page 345).

There is also a lack of didactic skill, particularly in the themes on general chemistry. For example, anyone seeking more knowledge about electronegativity, heats of formation, or bonding forces might be able to guess what the explanations mean, but only if he knew the answers in advance.

There may indeed be a need for a book of this kind. But then it should be a faultless text with a detailed subject index contained in a single volume. In its present form it is a source of annoyance to the expert and an imposition on the interested layman. The claims for this book are in inverse proportion to its quality.

J. F. Cordes [NB 263 IE]

Elektroorganische Chemie (Electro-Organic Chemistry). By *F. Beck*. Verlag Chemie, GmbH, Weinheim 1974, 1st Edit., xvi, 391 pp., 76 figs., 47 tables, bound, DM 88.—.

The author has been completely successful in his aim of presenting this diversified and important boundary area in detail and from a modern point of view. The book stands out clearly from the current flood of monographs about the subject by virtue of its clarity, balance, and adherence to actual practice.

Chapter 1 begins with a brief introduction to the layer model of the electrode/electrolyte phase boundary and to electrode reaction mechanisms (initiation, subsequent reactions, reactive intermediates). The technological advantages of electrosynthesis (control of the products formed, avoidance of co-products) are demonstrated and documented by impressive data from industry. Chapter 2 provides a clear treatment of the important relationships between the potential, current density, concentration, and time (cyclic voltametry, polarography, rotating disk electrodes). The electroanalytical criteria for electrode mechanisms are collected in tables for rapid access. The bibliography lacks only literature references to low-temperature electrolysis [*Reilley*, Anal. Chem. *44*, 142 (1972)] and to recent developments of the combination of electrochemistry with ESR spectroscopy [*Bard*, J. Phys. Chem. 75, 3281 (1971)]. Chapter 3, keeping close to practice, characterizes the cell components (in some cases even giving their suppliers), and the cell and electrolyte types. The description of measuring techniques and electronics is somewhat too brief.

Chapter 4 is the longest section and constitutes the core of the book (140 pages). Here, supplied with 1050 references, some from the patent literature, are described the important possibilities of synthesis, both at the cathode and anode, arranged by classes of compounds. The author finds a good compromise between a strict review presentation (reactions with conditions and yields, mechanistic investigations, industrial data) and the most detailed information. There are detailed treatments of: cathodic hydrogenation of multiple bonds (C=C, C=O, C=N, N=O), cathodic fission (C-Hal, onium ions), anodic oxidation (olefins, aromatic compounds, carboxylic acids, amines), cathodic couplings (activated olefins, carbonyl compounds), anodic couplings (Kolbe electrolysis, aromatic compounds, olefins), electrochemical substitutions, cyclizations, and polymerizations. Chapter 5 gives a brief and stimulating introduction to nonpreparative aspects such as electrochemical production and storage of energy (fuel cells, batteries), surface techniques (electrocoating, corrosion protection), and material separation (dialysis, waste water purification).

Relevant illustrations and carefully thought out formula schemes everywhere aid understanding of difficult material, and reinforce visually the access to information. Extensive subject and author indexes make it possible to find rapidly any desired fact. The printing and the production are immaculate.

The book can be unreservedly recommended to all who wish to occupy themselves or are already engaged in this field, as an introduction and as a comprehensive source of information.

H. J. Schäfer [NB 260 IE]

Atlas of Stereochemistry. Absolute Configurations of Organic Molecules. By *W. Klyne* and *J. Buckingham*. Chapman and Hall, London 1974. 1st Edit., xvi, 311 pp., bound £ 15.00.

This is the first of three attempts known to the reviewer to publish systematic compilations of the absolute configurations of optically active substances. In it the authors have assembled 3000 compounds in 211 full-page tables, for which they concentrated on molecules containing one or two centers of chirality and on selected representatives of the more important classes of natural products. Metal complexes (except for a few metallocenes) and polymers were not included; on the other hand it is very good to see tables of compounds that owe their optical activity to isotopic labeling, a chiral heteroatom (*e.g.* S, P, or Si) or axes or planes of chirality. The literature is covered up to the end of 1971.

Compounds that have been correlated chemically or spectroscopically with one another are always represented on the same page by their stereoformulas; when possible and essential, the sign of α_D and the specification by the (*R*/*S*)-nomenclature in the name are included. Formulas of compounds whose absolute configuration has been determined by the Bijvoet method are marked in special manner. By this method of arrangement the extensive atlas remains very clearly set out in spite of the great wealth of material. Occasionally general rules are added (*e.g.* about the correct way to "read" Fischer projections), or information about review literature. The book closes with formula, author, and subject indexes; these are not wholly free from error.

Everyone concerned with questions of absolute configuration must recognize the enormous amount of work that has gone into the preparation of such an atlas and treasure the result. Searching the literature of optically active natural products is generally easy, as in most cases only one enantiomer occurs in nature; in contrast, for synthetic compounds and degradation products it is often very time-consuming to track down the sources for a correct assignment of the absolute configuration, and here the atlas offers particularly welcome assistance since the relation to examples with truly unambiguously known stereochemistry can be recognized at a glance.

A few blemishes do not spoil the good total impression (the reviewer sought and found, for instance, faulty citation of authors' names, missing notes, and missing substituents on formulas; for A 45.14 there is a prochirality center specified as a chirality center; chaetocin is reproduced by a formula that contains a mirror plane—as does the original paper). This book can be recommended to all who may need to find information rapidly about absolute configuration, and it is likely to become soon an essential part of the libraries in the pharmaceutical industry as increasing attention is paid to the differing activities of enantiomers.

Günther Snatzke [NB 265 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Colorimetric Chemical Analytical Methods. By *L. C. Thomas* and *G. J. Chamberlin*. The Tintometer Ltd., Salisbury 1974. 8th Edit., xli, 626 pp., bound, DM 130.—.

Photobiologie, Band 1: Physikalische Grundlagen. By *R. K. Clayton*. Vol. 33 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. 131 pp., stitched, DM 16.80.

Digitale Elektronik. Grundlagen und Praxis. Eine Einführung für Naturwissenschaftler. By *G. Durcansky*. Physik Verlag GmbH, Weinheim 1975. xii, 217 pp., bound, DM 58.—.

Organometallic Chemistry, Vol. 3. Senior Reporters: *E. W. Abel* and *F. G. A. Stone*. The Chemical Society, London 1975. xx, 487 pp., bound, £ 17.50.—A volume in the series "Specialist Periodical Reports".

Approaches to Camptothecin. By *E. Winterfeldt*/**The Pyrrolizidine Alkaloids.** By *A. Klásek* and *O. Weinbergová*/**Advances in the Chemistry of Glycosaminides.** By *A. Ya. Khorlin* and *S. E. Zurabyan*. Vol. VI of the series "Recent Developments in the Chemistry of Natural Carbon Compounds". Edited by *R. Bognár*, *V. Bruckner*, and *Cs. Szántay*. Akadémiai Kiadó, Budapest 1975. 198 pp., bound, DM 29.—.

Advances in Inorganic Chemistry and Radiochemistry, Vol. 17. Edited by *H. J. Emeleus* and *A. G. Sharpe*. Academic Press, New York 1975. vii, 402 pp., bound, $ 35.00.

Comprehensive Biochemistry. Edited by *M. Florkin* and *E. H. Stotz*. Vol. 31: A History of Biochemistry. Part III: History of the Identification of the Sources of Free Energy in Organisms. By *M. Florkin*. Elsevier Scientific Publishing Company, Amsterdam 1975. xx, 475 pp., bound, Dfl. 110.00.

Catalysis Reviews. Science and Engineering, Vol. 10. Edited by *H. Heinemann* and *J. J. Carberry*. Marcel Dekker, New York 1975. xv, 297 pp., bound, $ 29.50.

Forscher zwischen Wissen und Gewissen. Edited by *F. Cramer*. From the series "Wissenschaft und Öffentlichkeit". Springer-Verlag, Berlin 1974. viii, 126 pp., stitched DM 14.80.

Analytical Profiles of Drug Substances, Vol. 4. Edited by *K. Florey*. Academic Press, New York 1975. xi, 526 pp., bound, $ 26.50.

Amino-acids, Peptides, and Proteins, Vol. 6. Senior Reporter: *R. C. Sheppard*. The Chemical Society, London 1975. xviii, 514 pp., bound, £ 16.50.—A volume in the series "Specialist Periodical Reports".

Mass Spectrometry, Vol. 3. Senior Reporter: *R. A. W. Johnstone*. The Chemical Society, London 1975. xiii, 402 pp., bound, £ 13.50.—A volume in the series "Specialist Periodical Reports".

Lehrprogramm Chemie II. By *J. Nentwig*, *M. Kreuder*, and *K. Morgenstern*. Verlag Chemie, Weinheim 1975. 2. revised edit., XIII, 700 pp., stitched, DM 24.00.

General Chemistry. Principles and Structure. By *J. E. Brady* and *G. E. Humiston*. John Wiley & Sons, New York 1975. x, 733 pp., bound, £ 7.20.

Creativity in Organic Synthesis, Vol. 1. By *J. S. Bindra* and *R. Bindra*. Academic Press, New York 1975. xiv, 322 pp., bound.

Einführung in die Molekülsymmetrie. Ein Lehrprogramm für Hochschulen. By *R. Borsdorf*, *F. Dietz*, *G. Leonhardt*, and *J. Reinhold*. Vol. 32 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. 107 pp., stitched, DM 12.80.

Anwendung der ^{1}H-NMR-Spektroskopie. Ein Lehrprogramm für Hochschulen. By *P. Hallpap* and *H. Schütz*. Vol. 31 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. 103 pp., stitched, DM 12.80.

Handbook of Moisture Determination and Control. Principles, Techniques, Applications. Vol. 3. By *A. Pande*. Marcel Dekker, New York 1975. xi, 585—873 pp., bound, $ 33.50.

Drug Design, Vol. V. Edited by *E. J. Ariëns*. Vol. 11 of the series "Medicinal Chemistry". Edited by *G. de Stevens*. Academic Press, New York 1975. xvi, 356 pp., bound, $ 39.50.

Polymer Molecular Weights, Part I. Edited by *P. E. Slade, Jr.* Vol. 4 of the series "Techniques and Methods of Polymer Evaluation". *P. E. Slade, Jr.* and *L. T. Jenkins*. Marcel Dekker, New York 1975. ix, 286 pp., bound, $ 24.50.

Molecular Rotation Spectra. By *H. W. Kroto*. John Wiley & Sons, London 1975. xi, 311 pp., bound £ 9.75.

Introduction to Chemistry. By *T. R. Dickson*. John Wiley & Sons, New York 1975. 2nd Edit., xix, 457 pp., bound. £ 5.75.

Pyridine and its Derivatives, Supplement Part 4. Edited by *R. A. Abramovitch*. John Wiley & Sons, New York 1975. xiii, 720 pp., bound, £ 32.00.

Die Symmetrie von Molekülen. Eine Einführung in die Anwendung von Symmetriebetrachtungen in der Chemie. By *J. M. Hollas*. Walter de Gruyter, Berlin 1975. 232 pp., stitched, DM 38.—.

Gas Cleaning for Air Quality Control. Industrial and Environmental Health and Safety Requirements. Edited by *J. M. Marchello* and *J. J. Kelly*. Vol. 2 of the series "Chemical Processing and Engineering". Edited by *L. F. Albright*, *R. N. Maddox*, and *J. J. McKetta*. Marcel Dekker, New York 1975. vii, 420 pp., bound, $ 23.50.

Problems for General Chemistry and Qualitative Analysis. By *C. J. Nyman* and *G. B. King*. John Wiley & Sons, New York 1975. viii, 347 pp., stitched, £ 3.00.

Synthetic Peptides, Vol. 3. By *G. R. Pettit*. Academic Press, New York 1975. vii, 438 pp., bound, $ 39.50.

Water and Aqueous Solutions. Introduction to a Molecular Theory. By *A. Ben-Naim*. Plenum Press, New York 1974. XVI, 474 pp., bound, $ 29.50.

International Conference on Modern Trends in Activation Analysis. Edited by *T. Braun* and *E. Bujdosó*. Reprinted from the "Journal of Radioanalytical Chemistry". Elsevier Scientific Publishing Company, Amsterdam/Akadémiai Kiado, Budapest 1975. VIII, 684 pp., bound Dfl. 225.00.—Proceedings of the conference held on 2.—6. October 1972 in Saclay/France.

Organic Syntheses via Boranes. By *H. C. Brown*. With Techniques by *G. W. Kramer*, *A. B. Levy*, and *M. Mark Midland*. John Wiley & Sons, New York 1975. XIX, 283 pp., bound, £ 9.45.

Foreign Compound Metabolism in Mammals, Vol. 3. Senior Reporter: *D. E. Hathway*. The Chemical Society, London 1975. XVI, 727 pp., bound, £ 26.00.—A volume of the series "Specialist Periodical Reports".

Soil Biochemistry, Vol. 3. Edited by *E. A. Paul* and *A. D. McLaren*. From the series "Books in Soils and the Environment". Edited by **A. D. McLaren.** Marcel Dekker, Inc., New York 1975. XV, 334 pp., bound, $ 27.50.

Analysis of Silicones. Edited by *A. L. Smith.* From the series "Chemical Analysis". Edited by *O. J. Elving* and *I. M. Kolthoff.* John wiley & Sons, New York 1975. VIII, 407 pp., bound £ 12.50.

Analytical Chemistry of Germanium. By *V. A. Nazarenko.* From the series "Analytical Chemistry of the Elements". Edited by *A. P. Vinogradov.* John Wiley & Sons, New York/Israel Program for scientific Translations, Jerusalem 1975. XII, 306 pp., bound, £ 12.25.

Developments in Biological Standardization, Vol. 27: International Symposium on Purity of Human Plasma Proteins (11.—14. September 1973, Budapest/Hungary). S. Karger, Basle 1974. X, 274 pp., 57 figs., 89 tables, bound, SFr. 75.–.

Progress in Surface and Membrane Science, Vol. 9. Edited by *D. A. Cadenhead, J. F. Danielli,* and *M. D. Rosenberg.* Academic Press, New York 1975. XI, 316 pp., bound, $ 33.00.

Soil Biochemistry, Vol. 4. Edited by *E. A. Paul* and *A. D. McLaren.* From the series "Books in Soils and the Environment". Edited by *A. D. McLaren.* Marcel Dekker, Inc., New York 1975. XIII, 277 pp., bound, $ 23.75.

Biosynthesis, Vol. 3. Senior Reporter: T. A. Geissman. The Chemical Society, London 1975. VIII, 293 pp., bound, £ 11.00.—A volume of the series "Specialist Periodical Reports".

Sulfur Ylides. Emerging Synthetic Intermediates. By *B. M. Trost* and *L. S. Melvin, Jr.,* Vol. 31 of the series "Organic Chemistry". Edited by *A. T. Blomquist* and *H. H. Wasserman.* Academic Press, New York 1975. X, 344 pp., bound, $ 39.50.

Inorganic Chemistry of the Main-group Elements, Vol. 2. Senior Reporter: *C. C. Addison.* The Chemical Society, London 1975. XIII, 726 pp., bound, £ 24.00.—A volume of the series "Specialist Periodical Reports".

Immobilized Enzymes in Food and Microbial Processes. Edited by *A. C. Olson* and *Ch. L. Cooney.* Plenum Press, New York 1975. X, 268 pp., bound, $ 21.90.

Introduction to Bioelectrodes. By *C. D. Ferris.* Plenum Press, New York 1974. 243 pp., bound, $ 22.90.

The Laboratory Recorder. By *G. W. Ewing* and *H. A. Ashworth.* Vol. 1 of the series "Laboratory Instrumentation and Techniques". Edited by *G. W. Ewing.* Plenum Press, New York 1974. VII, 129 pp., bound, $ 21.60.

Enzyme Engineering, Vol. 2. Edited by *E. K. Pye* and *L. B. Wingard, Jr.* Plenum Press, New York 1974. XIV, 470 pp., bound, $ 32.50.

The Practice of NMR Spectroscopy with Spectra-Structure Correlations for Hydrogen-1. By *N. F. Chamberlain.* Plenum Press, New York 1974. XXIV, 424 pp., bound, $ 34.90.

Critical Stability Constants. Vol. 1: Amino Acids. By *A. E. Martell* and *R. M. Smith.* Plenum Press, New York 1974. XIII, 469 pp., bound, $ 27.60.

Zum Ablauf ionischer Polymerisationsreaktionen. By *G. Heublein.* Akademie-Verlaf, Berlin 1975. VIII, 316 pp., bound, *ca.* DM 58.—.

Stripping Voltammetry in Chemical Analysis. By *Kh. Z. Brainina.* John Wiley & Sons, New York/Israel Program for Scientific Translation, Jerusalem 1975. XII, 222 pp., bound, £ 9.35.

Chemical Applications of Pattern Recognition. By *P. C. Jurs* and *Th. L. Isenhour.* John Wiley & Sons, London 1975. VII, 184 pp., bound, £ 8.25.

The Properties of Electrodeposited Metals and Alloys. By *W. H. Safranek.* Americal Elsevier Publishing Company, New York 1975. IX, 517 pp., bound, $ 35.50.

Die chemische Bindung. Eine verständliche Einführung. By *H. Preuss* and *F. L. Boschke.* Vol. 161 of the series "Heidelberger Taschenbücher". Springer-Verlag, Berlin 1975. VIII, 82 pp., stitched, DM 16.60.

Transport Phenomena. By *W. J. Beek* and *K. M. K. Muttzall.* John Wiley & Sons, London 1975. X, 298 pp., bound, £ 9.85.

EPR of Free Radicals in Radiation Chemistry. By *S. Ya. Pshezhetskii, A. G. Kotov, V. K. Milinchuk, V. A. Roginskii,* and *V. I. Tupikov.* John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1975. VIII, 446 pp., bound, £ 18.70.

Datensammlung Chemie in SI-Einheiten. By *G. H. Aylward* and *T. J. V. Findlay.* Vol. 17 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. X, 158 pp., stitched, DM 14.80.

Topics in Nonbenzenoid Aromatic Chemistry. Edited by *T. Nozoe, R. Breslow, K. Hafner, S. Itô,* and *I. Murata.* John Wiley & Sons, New York 1975. 295 pp., bound, £ 10.50.

Quantitative Biologie. By *C. S. Hammen.* Vol. 36 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. VIII, 133 pp., stitched, DM 14.80.

Thermal Analysis: Comparative Studies on Materials. Edited by *H. Kambe* and *P. D. Garn.* Kodansha Ltd., Tokio/John Wiley & Sons, New York 1975. X, 326 pp., bound, £ 8.75.—Proceedings of the U.S.-Japan Joint Seminar held in Akron, Ohio, on April 8—12, 1974.

Organic Molecular Photophysics, Vol. 2. Edited by *J. B. Birks.* From the series "Wiley Monographs in Chemical Physics". Edited by *J. B. Birks* and *S. P. McGlynn.* John Wiley & Sons, London 1975. XIX, 653 pp., bound, £ 24.00.

Lehrprogramm Stereochemie. By *F. D. Gunstone.* Vol. 39 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. 129 pp., stitched, DM 14.80.

Chemical Process Economics. By *J. Happel* and *D. G. Jordan.* Vol. 1 of the series "Chemical Processing and Engineering". Edited by *L. F. Albright, R. N. Maddox,* and *J. J. McKetta.* Marcel Dekker, New York 1975. 1. Edit., XII, 511 pp., bound, $ 19.75.

Chemistry. The Science and the scene. By *R. D. Clark* and *R. L. S. Amai.* Hamilton Publishing Company, Santa Barbara 1975. VII, 355 pp., bound, £ 5.90.

Technique of Electroorganic Synthesis. Edited by *N. L. Weinberg*. Vol. V, Part II of the series "Techniques of Chemistry". Edited by *A. Weissberger*. John Wiley & Sons, London 1975. X, 1070 pp., bound, £ 22.00.

Formulations, Part I. Edited by *R. R. Myers* and *J. S. Lond*. Vol. 4 of the series "Treatise on Coatings". Edited by *R. R. Myers* and *J. S. Long*. Marcel Dekker, New York 1975. XV, 587 pp., bound, $ 68.00 (Subscr.-price $ 54.00).

Organic Chemistry: A Brief Course. By *J. R. Holum*. John Wiley & Sons, New York 1975. XII, 446 pp., bound, £ 7.00.

Elektrolytgleichgewichte und Elektrochemie. By *G. Ackermann, W. Jugelt, H.-W. Möbius, H. D. Suschke*, and *G. Werner*. Lehrbuch 5 of the series "Fachstudium chemie". Verlag Chemie, Weinheim 1975. 292 pp., stitched, DM 34.—.

Elektrochemie I. Leitfähigkeit, Potentiale, Phasengrenzen. By *C. H. Hamann* and *W. Vielstich*. Vol. 41 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. X, 192 pp., stitched, DM 26.80.

Analysis of Water. By *J. Rodier*. John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1975. XVII, 926 pp., bound, £ 22.50.

Time Dependent Chemical Processes—With Special Reference to Their Simulation and Optimisation. By *E. R. Robinson*. Applied Science Publishers Ltd., London 1975. VII, 370 pp., bound, £ 12.00.

The Interpretation of Infrared Spectra. A Programmed Introduction. By *R. R. Hill* and *D. A. E. Rendell*. Heyden & Son, London 1975. XI, 196 pp., bound, £ 4.40.

More Spectroscopic Problems in Organic Chemistry. By *A. J. Baker, T. Cairns, G. Eglinton*, and *F. J. Preston*. Heyden & Son, London 1975. 2. Edit., X, 129 pp., stitched, £ 2.50.

The Spectroscopy of Flames. By *A. G. Gaydon*. Chapman and Hall, London 1974. 2. Edit., XII, 412 pp., bound, £ 8.00.

Particle Size Measurement. By *T. Allen*. From the series "Powder Technology Series". Edited by *J. C. Williams*. Chapman and Hall, London 1975. 2. Edit., XVIII, 454 pp., bound, £ 8.50.

Metal-to-Metal Bonded States of the Main Group Elements. By *M. J. Taylor*. Academic Press, London 1975. V, 211 pp., bound, £ 5.80.

Carbohydrate Chemistry, Vol. 7. Senior Reporter: *J. S. Brimacombe*. The Chemical Society, London 1975. XII, 611 pp., bound, $ 22.00.—A volume of the series "Specialist Periodical Reports".

Aliphatic Chemistry, Vol. 3. Senior Reporter: *A. McKillop*. The Chemical Society, London 1975. XII, 409 pp., bound, £ 13.50.—A volume of the series "Specialist Periodical Reports".

Soil Biochemistry, Vol. 4. Edited by *E. A. Paul* and *A. D. McLaren*. From the series "Books in Soils and the Environment". Edited by *A. D. McLaren*. Marcel Dekker, New York 1975. XIII, 277 pp., bound, $ 23.75.

Equilibrium Statistical Mechanics. By *F. C. Andrews*. John Wiley & Sons, New York 1975. 2. Edit., X, 256 pp., bound, £ 5.60.

Drug Design, Vol. VI. Edited by *E. J. Ariëns*. From the series "Medicinal Chemistry". Edited by *G. de Stevens*. Academic Press, New York 1975. XVII, 364 pp., bound, $ 39.50.

Experimental Quantum Chemistry. By *P. Hedvig*. Academic Press, New York 1975. 533 pp., bound, $ 24.00.

Radiochemical Separation Methods. Edited by *T. Braun* and *E. Bujdosó*. Elsevier Scientific Publishing Company, Amsterdam 1974. 591 pp., bound, Dfl. 155.00.—Proceedings of the 7th Radiochemical Conference, Marianske Lázne (CSSR), 24.—28. 4. 1973.

Principles of Electrochemical Machining. By *J. A. McGeough*. Chapman and Hall, London 1974. XV, 255 pp., bound, £ 6.00.

Warning on copyright

Before photocopying, xerocopying or reproducing an article from this journal please check whether you may be violating the legal provisions of copyright and thus rendering yourself liable to prosecution.
Copyright law allows the photocopying of individual articles only, and then only as single copies for private or personal use. The production of copies for any other purpose is not permitted without payment of copyright fees.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. - Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 14036, Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Huti*), 111 Fifth Avenue, New York 3, N.Y., USA, and Berkeley Square House, Berkeley Square, London, W. 1., England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), D-6940 Weinheim, Pappelallee 3, P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 Number 7
July 1975
Pages 445–506

Biosynthesis of Ribonucleic Acids

By John P. Richardson[*]

Biosynthesis of ribonucleic acids involves the polymerization of ribonucleotides on deoxyribonucleic acid templates and the conversion of these primary gene transcripts to mature RNA molecules. The present report reviews briefly our current understanding of these processes.

1. Introduction

RNA is a significant and essential cellular component that can comprise as much as a quarter of the dry weight of a cell[1, 2]. Most RNA is involved in protein synthesis, but a small amount is needed in the replication of DNA and some RNA may also have a regulatory function. About half the RNA that is synthesized at any given moment goes into molecules that are stable. These are the ribosomal RNAs (rRNAs), which are structural components of ribosomes, and the transfer RNAs (tRNAs), which serve to adapt the amino acids to the genetic code during protein synthesis. The other half goes into RNA molecules with very low metabolic stability. These are the messenger RNAs (mRNAs), which are the templates for protein synthesis; many of the nuclear RNA molecules, which are precursors to the stable RNAs and mRNA; and the RNA intermediates involved in DNA replication. The lifetime of these RNAs is often less than one-tenth the cell generation time. Because such a large fraction of the RNA is unstable, the cell composition under-represents the fraction of the synthetic capacity devoted to RNA; hence, on a weight basis, RNA synthesis accounts for $^1/_3$ of all macromolecular synthesis.

Chemically, RNA is a linear polymer of ribonucleotides linked together by phosphodiester bonds between the 5′ carbon of one ribonucleotide and the 3′ carbon of an adjacent ribonucleotide. The four common ribonucleotides in RNA have the bases adenine, guanine, cytosine, and uracil; but the stable RNAs, especially the tRNAs, also have small but significant fractions of other ribonucleotides that are formed by modification of the four common ones.

In many of its chemical properties, RNA is similar to DNA. The major chemical differences are in the sugar moieties, where RNA has ribose instead of 2′-deoxyribose found in DNA, and in the presence of uracil as a common base instead of the thymine (5-methyluracil). Also, RNA molecules are usually smaller than DNA molecules, and they are generally single-stranded while DNA is usually double-stranded. Nonetheless, there are enough similarities for RNA to form stable complexes with DNA[3]. The structure of these complexes is a hybrid regular double-helix with the RNA strand antiparallel to a complementary DNA strand[4]. The ability

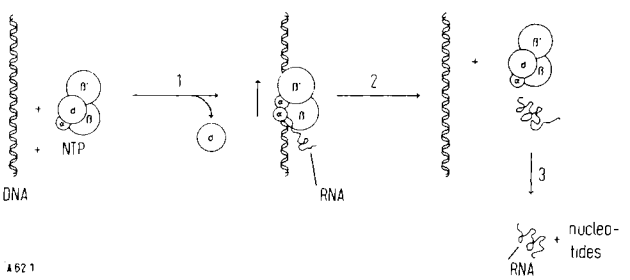


Fig. 1. Scheme for RNA biosynthesis. When RNA polymerase ($2\alpha,\beta,\beta',\sigma$) is incubated with DNA in the presence of substrates (NTPs) (step 1) RNA molecules are synthesized from complexes of RNA polymerase and DNA. The σ factor dissociates from the enzyme shortly after initiation of the RNA chain. When the enzyme reaches a transcription termination signal, it dissociates from the template and liberates the free RNA molecule (step 2). The synthesis of the RNA is completed in many cases by the action of nucleases that cleave segments of the initial transcript and of modification enzymes that alter specific nucleotides (step 3).

[*] Prof. Dr. J. P. Richardson
Department of Chemistry
Indiana University
Bloomington, Indiana 47401 (USA)

to form these structures is significant because it is a clue to a possible mechanism for directing the polymerization of RNA.

The biosynthesis of RNA molecules involves two major processes: polymerization of ribonucleotides and post-transcriptional maturation. These are shown schematically in Figure 1.

2. Polymerization of Ribonucleotides

2.1. RNA Polymerases

Nearly all RNA is polymerized directly from DNA templates by a process called transcription. This is inferred from the facts that nearly all RNA is homologous to sequences of DNA from the same organisms[5]; that most RNA synthesis activity is found in DNA-dependent enzymes[6]; and that all RNA synthesis can be blocked by certain drugs, such as actinomycin D, known to bind very tightly to DNA[7].

An obvious exception to this rule is that some viral RNAs are replicated directly from RNA templates. In addition, ribonucleotides can be added to the 3′ ends of some RNAs without a template in reactions catalyzed by nucleotidyl transferases. Although it had long been considered possible that cellular RNAs might be duplicated on RNA templates there was no evidence to support this hypothesis until it was recently found that rabbit reticulocytes contain an RNA-dependent RNA polymerase[8]. Since these cells no longer have DNA, their remaining mRNA, principally globin mRNA, might be replicated by such an enzyme. However, this has yet to be established.

The enzyme responsible for RNA synthesis from DNA templates is called a DNA-dependent RNA polymerase. In bacteria one basic form, or core structure, of this enzyme has been identified[9]. It is sensitive to inhibition by rifampicin, and can be modified either by the binding of other protein factors or by chemical alterations. Another form has been postulated to be responsible for the RNA synthesis involved in chromosomal replication[10] since this synthesis is apparently not inhibited by rifampicin[11]. However, the RNA polymerase responsible for this activity has not been isolated.

In eukaryotic cells, four separate forms of RNA polymerases have been clearly distinguished[12]. One is from the mitochondria, and the other three are nuclear enzymes of which one comes from the nucleolus, the site of synthesis of ribosomal RNA precursors. The more abundant of the other two nuclear enzymes is inhibited by low levels of the mushroom toxin α-amanitin. This enzyme is thought to be responsible for the synthesis of precursors to mRNA. The other nuclear enzyme appears to be responsible for the synthesis of 5S rRNA and tRNA[13].

Most RNA polymerases are complicated, apparently asymmetric proteins, containing several subunits. With *E. coli* RNA polymerase the smallest unit that has any RNA polymerase activity, known as the core, has a molecular weight of 390000[9, 14]. It consists of four subunits and contains a tightly bound zinc ion[15]. One polypeptide, the α subunit, is present in two copies. The other two, called β and β′, are very large polypeptides with molecular weights >150000 and although they are similar in size, they are distinctly different[16]. Highly purified enzyme also usually contains two other polypeptides. One of these, called σ, is a factor required for initiation of transcription from certain DNA templates and although it binds tightly enough to the free enzyme to be considered a subunit, it is released when the enzyme starts polymerization of an RNA chain. RNA polymerase with σ is called the holoenzyme. The other polypeptide, called ω, has a molecular weight of about 10000 and may actually be a contaminant even though enzyme preparations with ω generally have slightly higher specific activity than preparations without it.

There is no evidence that nucleic acids are an important permanent component of RNA polymerase. However, covalently bound nucleotides and phosphate are known to be present under certain conditions and these substituents could play an important role in modulating enzyme activity[17]. Core RNA polymerase isolated from exponentially growing *E. coli* appears to have less than 0.2 mole of phosphorous per mole of enzyme, so these substituents do not seem to be required for activity during normal cell growth. On the other hand, it has been reported that phosphorylation of σ factor by a protein kinase from rabbit muscle can activate RNA polymerase extensively[18]. The significance of this is not clear but it could be related to the presence of inactive polypeptides the same size as σ factor in some enzyme preparations[19].

The nucleolar and major nucleoplasmic RNA polymerase isolated from both calf thymus and rat liver nuclei are even larger proteins than the *E. coli* enzyme[12]. They are also made up of several subunits including some peptides that are even larger than *E. coli* β,β′ subunits. It is not known yet whether any of these subunits are initiation factors analogous to σ.

In contrast, RNA polymerase isolated from the mitochondria of *Neurospora crassa* consists of an aggregate of a single polypeptide with molecular weight of 64000[20], and the enzymes coded by bacteriophages T3 and T7 have single polypeptides with molecular weight of about 107000[21, 22]. Thus a complex protein structure is not a prerequisite for an RNA polymerase. However, these enzymes act on simpler genomes and the bacteriophage enzymes have rigid specificities. The more complicated structures of the bacterial and nuclear enzymes, therefore, may be characteristic of enzymes that recognize several kinds of genetic regions under strict regulation.

2.2. The Biosynthetic Reaction

All RNA is synthesized by the polymerization of ribonucleoside triphosphates (ATP, GTP, CTP, and UTP) in a reaction that requires a divalent cation, usually Mg^{2+} ions. For each nucleotide added to the growing chain, a molecule of pyrophosphate is liberated. The postulated mechanism for the polymerization reaction is shown in Figure 2. The 3′ hydroxyl group of the 3′ terminal ribonucleotide of the nascent RNA chain is activated to perform a nucleophilic attack on the α (*i.e.* the first) phosphorus of a correctly aligned nucleoside triphosphate. The resulting phosphodiester bond is formed at the expense of the anhydride link between the α and β phosphorus atoms, producing pyrophosphate as the leaving group. The correct alignment of the incoming nucleotide presumably depends on its binding to the enzyme and to the DNA template.

Although the net change in free energy for the addition of monomer is not large ($\Delta G^{0\prime} \approx -0.5$ kcal/mol)[23], the reac-

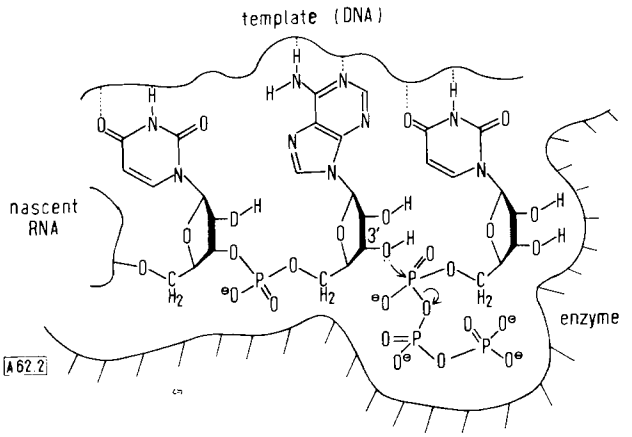


Fig. 2. Scheme for addition of a nucleotide to the 3′ end of a nascent RNA chain.

tion proceeds well as long as the concentration of pyrophosphate is low. Physiologically, this is achieved by hydrolysis of the pyrophosphate to orthophosphate, which is a highly favorable reaction ($\Delta G^{0\prime} = -7.0$ kcal/mol) catalyzed by ubiquitous pyrophosphatases. There is no indication that any further breakdown of nucleoside triphosphates is needed to drive the polymerization. The pure enzyme does not appear to catalyze any nucleotide hydrolysis reaction and the rate of RNA chain polymerization *in vitro* is essentially identical to that *in vivo* when physiological levels of substrates are used[24, 25]. In *E. coli* growing at 37 °C, this rate is 50 nucleotides per second for all RNAs of different types and size[26, 27]. It thus takes about one minute to synthesize an RNA molecule the size of the larger ribosomal RNA, which has a molecular weight of 1.1×10^6. This compares with an overall rate of nearly 900 nucleotides per second per nascent chain needed to replicate the DNA in that cell.

The direction of RNA chain growth for the reaction catalyzed by *E. coli* RNA polymerase is as shown in Figure 2; each incoming nucleotide is added to the end with the free 3′ hydroxyl group[29]. Chain synthesis can be initiated by the same reaction used for elongation, except that the acceptor "RNA" is just another nucleoside triphosphate instead of the 3′ end of a nascent RNA chain. This first nucleotide is the only one incorporated into the chain as a triphosphate; that is, without loss of its β and γ phosphorus atoms.

In general, this initiating nucleotide is always either ATP or GTP[27]. Although it is certainly possible that this specificity is a characteristic of all the different kinds of initiation sites recognized, the interaction of the purine nucleotides with the enzyme could also affect the positioning of the enzyme in an initiation site. ATP and GTP both bind to two sites on the free enzyme whereas UTP and CTP bind rather weakly to only one of these[29]. The extra binding site for the purine nucleotides may be involved in the initiation reactions including the proper positioning of the enzyme with respect to the DNA template.

2.3. The Role of DNA

With the DNA-dependent RNA polymerases, DNA acts as the template for the assembly of RNA. Without the template and without all the nucleoside triphosphates specified by the template, no RNA is synthesized. The best templates for most enzymes are double-helical DNAs, but single-stranded DNA—and even RNA under some conditions—can substitute for double-helical DNA, but with much lower activity; with saturating amounts of DNA, *E. coli* RNA polymerase is less than one-tenth as active with a single-stranded DNA than with a good double-helical DNA[6].

Analysis of the regions transcribed from a denatured DNA indicate that the enzyme is less discriminating when the template is in its single-stranded form[30]; evidently RNA polymerase can initiate synthesis from many more regions on single-stranded DNA than on double-helical DNA and these include regions that are apparently not transcribed in the cell. The lower rate of RNA synthesis is not because of a lack of initiation sites but rather because RNA chain growth is slower, termination is more frequent, and possibly initiation is slower[28, 31].

The overall transcription reaction on a double-helical DNA is fully conservative with respect to the structure of the DNA[32]; no permanent alteration of the DNA occurs during the course of RNA synthesis. However, while it is used as a template, the DNA is firmly complexed with the enzyme and the nascent RNA chain[33]. In some cases the enzyme can be denatured and the RNA will remain attached to the DNA[34], but usually removal of the enzyme will result in a spontaneous dissociation of the RNA[33]. Furthermore, most of the nascent RNA is susceptible to ribonuclease digestion. These facts suggest that the RNA is involved in a direct interaction with the DNA but that the site of this interaction is probably small and dependent on the enzyme for stability.

Two basic models have been proposed as mechanisms for how a double-helical DNA can be used as a template for the assembly of a free single-stranded RNA without permanently altering the DNA structure. In one[35, 36], a short single-stranded segment of the DNA, exposed by local unwinding, acts as a template by a mechanism similar to the process proposed by *Watson* and *Crick* for the duplication of DNA; a particular base in the DNA strand would only allow binding in the enzyme of the nucleotide that forms the correct Watson-Crick base pair (Fig. 3a). Presumably in this case, the RNA and the free template DNA strand would form a short hybrid

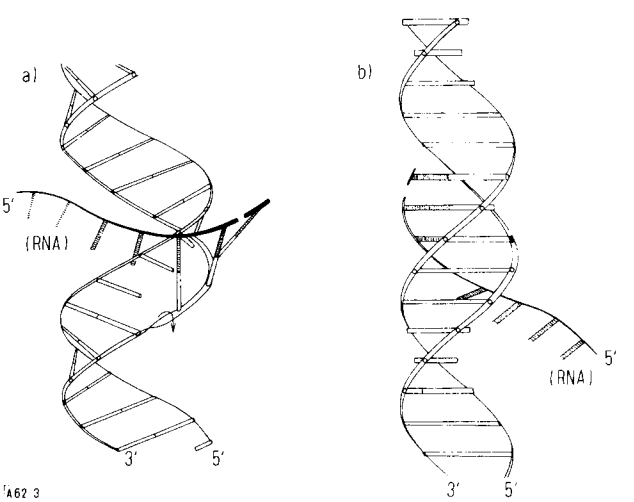


Fig. 3. Models of nascent RNA molecules forming interaction with nucleotides on only one DNA template strand (a) or on both DNA template strands (b). The DNA in (a) is in the "A" form and the DNA in (b) is in the "B" form.

helix which, however, would be displaced by reformation of the more stable DNA-DNA helix during polymerization.

In the alternative model[37], the two DNA strands do not separate completely and the RNA is assembled in the major groove of DNA by binding of the monomer ribonucleotides to *both* bases of each DNA pair. The specific interactions required for this binding have been demonstrated by model building[38] (Fig. 3b).

The major distinction between the two models is that a single DNA strand acts as the template in one whereas both strands are required in the other. The strongest evidence in favor of the former model is that single-stranded DNA can be used as a template, which suggests that the enzyme can use Watson-Crick base pairing for the interaction[35]. However, the slower chain growth and frequent termination that occurs on the single-stranded DNA suggests that the second DNA strand must play some important role in stabilizing the interaction. Since both models require a distortion and partial unwinding of the helix, the fact that RNA polymerase does cause DNA to unwind about 180° per enzyme[39] is not sufficient evidence to support either model. Instead, it is necessary to demonstrate the involvement of either one or both strands as template, and this has yet to be accomplished.

3. Selectivity of Transcription

3.1. Initiation

The synthesis of specific RNA molecules is a result of the initiation and termination of transcription at specific points on the DNA template[40]. The *E. coli* DNA-dependent RNA polymerase has the ability to select the site on the DNA to be used for initiation; initiation does not occur at random, and as long as σ factor is present these initiation sites can be regular double-helical sections of the DNA. The core enzyme also has a limited capacity to initiate specific RNA synthesis; it can use certain single-stranded segments and may be able to initiate slowly from double-helical segments. The main functions of the σ factor are to stabilize the interaction between the enzyme and the initiation site, and to destabilize the nonspecific interaction that RNA polymerase can make with almost any region of DNA. It was originally suggested that σ factor might direct the recognition of a particular DNA region[41], but no new σ factors that confer obviously different specificities on the activity of *E. coli* core RNA polymerase have been purified. Thus, strong support of this model has yet to be found.

A second sigma factor from *E. coli* has been isolated as a component of a minor RNA polymerase fraction. This new protein called σ′ has a molecular weight of 56000 and binds more tightly to the core enzyme than σ[42]. It apparently performs the same functions, and σ does not further activate enzyme saturated with σ′. No differences have been distinguished yet in their specificity except that σ′ more readily catalyzes the *de novo* synthesis of ribohomopolymers and the DNA-dependent synthesis of poly A[43]. In its size, σ′ from *E. coli* is similar to the σ isolated with *B. subtilis* RNA polymerase. Since *E. coli* σ will substitute for the *B. subtilis* σ factor, it appears that a basic interaction between factor and core has been conserved in different bacterial species[44].

The model for recognition of the initiation site on DNA by RNA polymerase favored currently[40] postulates that the enzyme rapidly associates and dissociates from random sites on DNA molecules until it recognizes a special site, where it can form a tight binary complex (Fig. 4). This complex in turn is in equilibrium with another one in which the DNA strands unwind to expose the DNA bases. It is enzyme in this latter complex that is able to initiate an RNA chain. Many elements of this model have been supported by studying the binding of RNA polymerase to T7 DNA in the absence of nucleoside triphosphates and the conditions necessary for rapid chain initiation from complexes between RNA polymerase and DNA. The schema does not take into account the effect that the nucleoside triphosphates might have on the binding and recognition steps, but it is believed that the RNA polymerase can bind very close to the initiation site without the involvement of nucleoside triphosphates.

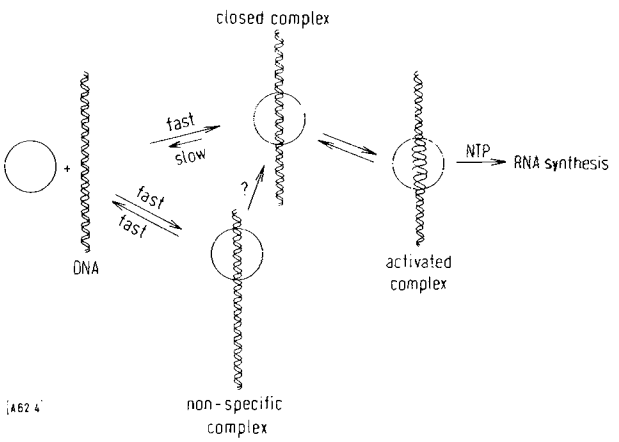


Fig. 4. Model for recognition and activation of the initiation site on DNA by RNA polymerase (circle). NTP = any nucleoside triphosphate (adapted from ref. [40]).

The genetic element that is thought to govern initiation of RNA chain is called the promoter[45]; mutants in promoter regions affect the rate of transcription from the genetic unit governed by that promoter. Two such promoter mutants that govern the transcription of the N gene in λ, have been mapped at about 33 nucleotides from the DNA sequence that specifies the 5′ terminal end of the RNA transcript for the λ N gene[46–48]. Even though the promoter site is neither coincident with nor immediately adjacent to the DNA sequences for the transcript it controls, it is within the 40 base pairs that presumably can be spanned by a single RNA polymerase molecule. It is thus close enough to influence directly the ability of the enzyme to use the template sequences for the start of the RNA molecule.

The segment of DNA between the start of the N gene transcript and the site for its promoter mutations has been sequenced[48] and the sequence contains several two-fold rotational symmetries (see Fig. 5). Certain of these symmetries are probably recognized by various λ regulator proteins including the λ repressor, and one of them may be important for RNA polymerase recognition. If this is the case then there is likely also to be a symmetry in the structure of RNA polymerase. This would have to involve the α subunit because it is the only one that is present in duplicate. A site in this λDNA sequence recognized by the Hind RII restriction nuclease is also indicated. When RNA polymerase is bound to λDNA the restriction nuclease no longer cleaves at that

site[47, 49]. Other sites on λDNA and on several other DNA molecules recognized by this restriction enzyme are also protected from its nuclease activity when RNA polymerase is bound[49]. However, most of the sites recognized by this nuclease on these DNA molecules are not protected by RNA polymerase. Thus, the sequence recognized by the nuclease is not sufficient to define the complete recognition site for RNA polymerase binding, but it may be a necessary sequence for at least one kind of polymerase binding site.

Fig. 5. Nucleotide sequence of a λ operator-promotor region. Sequence taken from ref. [48]. The overlined segment (GAT) indicates the start of the N gene transcript. Several two-fold rotational symmetries occur in this sequence. The axis of symmetry for the enclosed sequences is located by the vertical arrow above the sequence. The axes for two other symmetries are located by the two vertical arrow below the sequence. The site of cleavage by the Hind restriction nuclease is also indicated. R = purine nucleotide; Y = pyrimidine nucleotide.

Although no σ factors with proven differences in specificity have been purified, there are many proteins that act in conjunction with the holoenzyme that affect the selectivity of transcription. The best characterized proteins of this sort are the repressors for the lactose[50] and galactose[51] operons and for the early transcription units on bacteriophage λDNA[52]. These repressors specifically inhibit transcription of the genetic regions they control. With a bacteriophage DNA carrying sequences of the lactose operon, the lactose repressor only inhibits transcription of those sequences and not the sequences of the bacteriophage genes[53]. Similarly, λ repressor specifically inhibits transcription from the early region of λ DNA but does not inhibit transcription of bacteriophage 434 DNA, a closely related DNA that is immune to the action of the λ repressor[52].

The repressor molecules are known to bind very tightly and specifically to the operator region of the appropriate DNAs. Since these operator regions are near or overlap with the regions recognized by RNA polymerase for the initiation of the synthesis of the genetic unit controlled by the repressor, it is quite possible that the repressor binding physically prevents interaction with RNA polymerase. This has been demonstrated with the λ repressor[54]. Alternatively, the repressor could just prevent the enzyme from moving through or away from the DNA regions blocked by it; there is also some evidence to support this mode of action as well[55]. The λ DNA sequences given in Figure 5 include a site recognized by the λ repressor. In this case transcription appears to start just outside of the region recognized by the repressor. However, the transcript of a lactose operator containing an especially active promotor mutation includes the sequences for the lactose operator[56, 57]. Thus there may be several ways in which repressor-operator interactions can affect transcription of the genetic unit regulated.

Two factors have been isolated that specifically *activate* transcription of particular genetic regions. One of these is the C gene product of the arabinose operon of *E. coli*. This protein in the presence of L-arabinose stimulates the transcription of the DNA region coding for the enzymes of L-arabinose metabolism[58, 59]. Its mechanism of action still remains to be elucidated. The other factor, which is known by several names including catabolite gene activator protein and cyclic-AMP receptor protein, is required along with its allosteric effector 3'-5' cyclic AMP for transcription, among others, of sequences coding for the proteins for lactose, galactose and arabinose utilization[60]. This factor binds to DNA and requires the presence of 3'-5' cyclic AMP to function[61]. It has been suggested that it may act to lower this activation temperature for unwinding DNA at the initiation sites for the affected transcription units[40].

Several other protein factors have also been demonstrated to activate transcription of various DNA templates under certain conditions, but the role of many of these factors remains unclear[40]. On the other hand, certain proteins known to be required for the activation of certain genetic regions on T4 DNA have been found as subunits of RNA polymerase isolated from T4-infected *E. coli*[62, 63]. Again, it is not known how these proteins effect this activation.

3.2. Termination

Specific termination of transcription is required on bacterial and the larger bacteriophage genomes to prevent continued transcription from one genetic unit into an adjacent unit that should be controlled independently. Certain sequences in DNA are evidently recognized by *E. coli* RNA polymerase as termination signals because many of the transcripts synthesized *in vitro* are discrete molecular species that correspond to particular genetic units on the DNA[40]. The specificity of this termination recognition is also reflected in the characteristic sequence of -U-U-U-U-U-U that has been found at or near the 3' ends of several RNAs synthesized *in vitro*; in most cases this sequence is Purine-$(U)_6A_{OH}$[64, 65].

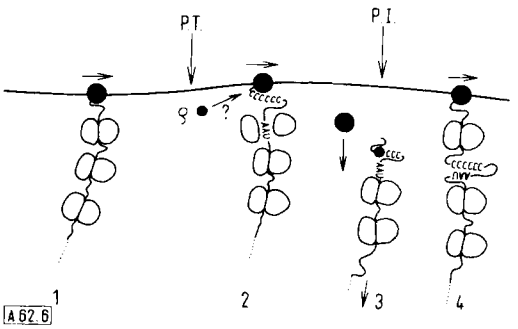


Fig. 6. Model for ρ function. P.T. and P.I. indicate genetic positions for protein synthesis termination and initiation signals, respectively. State 1 shows nascent RNA with ribosomes nearing a termination site. State 2 shows a ribosome being released at the protein synthesis termination signal (UAA) on nascent RNA, and it shows a C-rich RNA stretch emerging from the RNA polymerase (large black circle). State 3 shows the RNA and RNA polymerase that have been released by action of ρ that recognized the C-rich region on the RNA (it also shows a ρ molecule still attached to the C-rich RNA region). State 4 shows a nascent RNA whose synthesis was not terminated by ρ action. If the termination signal (P.T.) should arise as the result of a mutation to a nonsense codon within a cistron (structural gene), ρ might have a chance to act at C-rich regions on the nascent RNA that would normally be obscured or blocked by the presence of a ribosome translating the RNA. This model could account for the strong polar effects caused by nonsense codons.

At least one other type of termination signal also exists. This is the signal recognized when an added protein, called ρ factor, is also present[66]. However, in this case there is evidence that a nucleotide sequence is recognized on the RNA, not the DNA[67]. Some recent experiments suggest that ρ interacts with specific sequences on nascent RNA molecules

to activate a nucleoside triphosphate phosphohydrolase (or phosphotransferase) activity that is essential for the ρ-induced termination of RNA synthesis[68, 69]. This sequence is probably near rather than at the 3′ end of the terminated RNA chain because it is unlikely that ρ could fit into the polymerization site of RNA polymerase. From studies with the effects of ρ on transcribing the DNA region for the gal and lac operons, it has been suggested that ρ function may be to decrease the expression of genes at the end of a transcription unit compared to the genes near the beginning of that transcription unit[70]. A model for ρ function is presented in Figure 6.

4. Post-transcriptional Maturation Reactions

The synthesis of many RNA molecules requires several biochemical steps in addition to the transcription of the nucleotide sequences for the RNA from the DNA template. These steps include cleavage of extra nucleotides from the transcripts, modification of some nucleotides and, in some cases, the addition of nucleotides at the 3′ end of the RNA by a synthetic reaction that does not depend on a DNA template.

4.1. Removal of Extra Nucleotides

The clearest examples of cleavage of sequences has come from studies of the synthesis of ribosomal RNAs in eukaryotic cells[71]. In HeLa cells, for example, the 18S, 28S, and 7S rRNAs are all derived from a single precursor molecule that is nearly twice as large as the combined size of the rRNA products. This precursor has large stretches of RNA nucleotides that are degraded in the maturation process.

In bacteria the sequences for the 16S and 23S rRNAs are also in single transcription units[72], but in this case a full length RNA containing both 16S and 23S rRNA sequences is rarely detected because the cleavage of the portion with the 16S rRNA sequence occurs before the synthesis of the 23S portion is finished. However, significant amounts of this full length RNA molecule are found in a mutant that contains reduced levels of ribonuclease III, an endonuclease specific for double-stranded RNA[73]. This suggests that RNase III is responsible for the cleavage of the portion containing the 16S sequences from the portion containing the 23S sequences. Further steps in the maturation of the ribosomal RNAs in *E. coli* involve the removal of a few extra nucleotides from the 5′ and 3′ ends of the cleaved precursors. In all, about 22% of the nucleotides from the initial transcript are removed[74]. Thus a greater fraction of the ribosomal RNA transcript is conserved in *E. coli* than in HeLa cells.

The synthesis of tRNA molecules also appears to depend on a similar pattern of cleavage and trimming. Several genes for tRNA molecules are found clustered on the chromosomes of *E. coli*[75] and bacteriophage T4[76, 77]. When a short labeling time is used it is also possible to detect labeled RNA molecules that contain the sequences for two or more tRNA molecules. Since segments containing sequences for other tRNAs could also have been cleaved during RNA polymerization the transcription units for the tRNA may contain sequences for several species plus spacer regions that are degraded when the primary transcripts are converted to mature tRNA molecules. An outline for these steps is given in Figure 7.

Isolation of a precursor for the tyrosine tRNA ($ptRNA^{Tyr}$) from *E. coli* has made it possible to assay some of the

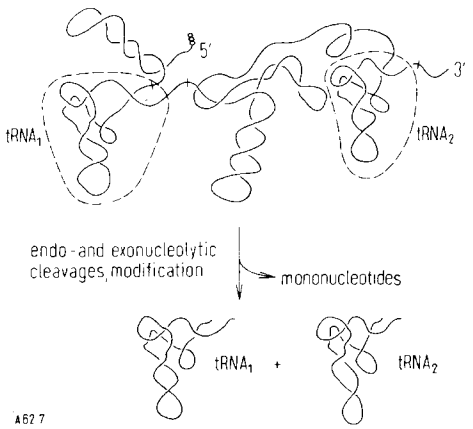


Fig. 7. Scheme for processing of a transcript containing sequences for two mature tRNA molecules. $tRNA_1$ and $tRNA_2$. The circles at the 5′ end indicate a triphosphate group.

enzymes involved in the removal of extra nucleotides from the 5′ and 3′ ends of the precursor. A ribonuclease called RNase P (for precursor) has been identified with this assay[78] and mutants with a temperature-sensitive form of this enzyme have been isolated[79]. When incubated at the restrictive temperature, these mutant strains accumulated precursors containing as many as four tRNA sequences in a single RNA.

Cleavage reactions are also believed to be very important in converting gene transcripts found in the nuclei of eukaryotic cells into the messenger RNA molecules found in the cytoplasm of these cells[80]. Most of the nuclear RNA molecules are much larger than the messenger RNAs in eukaryotic cells; molecules with molecular weights up to 2×10^7 have been found for the former, whereas even the largest mRNA molecules are less than one-tenth that size. The nuclear RNA molecules are also metabolically very labile. Over 90% of the larger RNA molecules synthesized in the nucleus are broken down there and only a small fraction is transferred to the cytoplasm. This fraction appears to correspond to the 10% of the RNA at the 3′ end of the nuclear transcripts and is believed to be the source of mRNA.

Although definite evidence for specific cleavage of precursor to a bacterial messenger RNA is lacking, many bacteriophage mRNA molecules are synthesized as long transcription units *in vitro*. The T7 RNA synthesized *in vitro* with *E. coli* RNA polymerase has a molecular weight of 2.5×10^6[81], yet the early T7 species found after infection in normal cells are all considerably smaller. However, when T7 infects a strain of *E. coli* that has a defective ribonuclease III, the T7 RNA is as large as the *in vitro* products[82]. Thus ribonuclease III may be involved in processing of mRNA as well as rRNA.

4.2. Modification of Nucleotides

Maturation of many RNA molecules also involves modification of selected nucleotides in the initial transcripts. Examples of some modified nucleotides are given in Figure 8. These modifications are most extensive in the synthesis of tRNA molecules but are also important for the synthesis of ribosomal RNA molecules and may be important for the synthesis of some mRNA molecules[83–85]. The most common modification reaction is the addition of a methyl group to a nucleotide. The donor of the methyl group is *S*-adenosylmethionine and the reactions are catalyzed by specific methyl transferase enzymes that recognize the nucleotide to be modified in a

specific location. The products are primarily base methyl derivatives, but some 2'-*O*-methylribose derivatives and some dimethyl derivatives are also made.

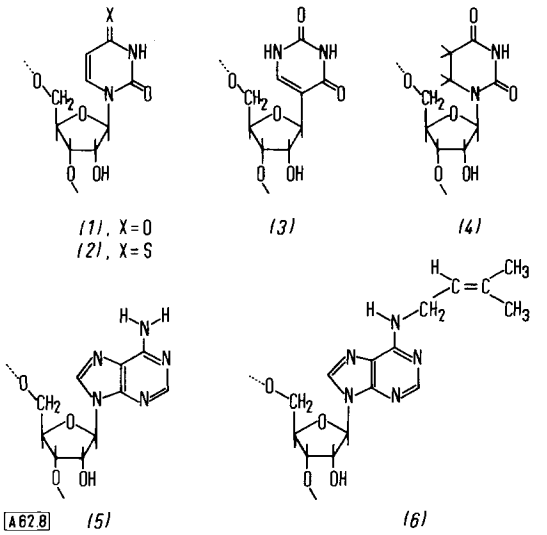


Fig. 8. Structures of uridine *(1)*, adenosine *(5)*, and their modified derivatives 4-thiouridine *(2)*, pseudouridine (5-β-D-ribofuranosyluracil) *(3)*, 5,6-dihydrouridine *(4)*, and N^6-(2-isopentenyl)adenosine *(6)*.

Another important modification is the isomerization of certain uridylate residues to pseudouridylate (5-ribosyluracil nucleotide). Almost every tRNA molecule has at least one pseudouridylate residue and many have two or more. This isomer has also been found in ribosomal RNAs of both eukaryotes and prokaryotes. An enzyme system that catalyzes the isomerization reaction for uridylate residue in tRNA molecules has been isolated from *E. coli*[83], and mutants of *Salmonella typhimurian* have been found that are lacking one of these enzymes; these mutant strains are defective in the regulation of certain amino acid biosynthetic pathways[86].

Other modification reactions appear to occur exclusively in tRNA molecules. These include thiolation of uridylate residues, reduction of certain uracil bases to dihydrouracil, and the addition of isopentenyl group to 6-amino group of adenosine residues near certain anticodons. Many of these modifications are essential for function while others have roles that have not been identified.

For both tRNA and rRNA some of the modification reactions can occur on the larger precursors. However, the unmodified $tRNA^{Tyr}$ from *E. coli* that has been trimmed to its final size is a better substrate for modification than its larger precursor[87] and some of the modifications of rRNA occur only after certain ribosomal proteins have bound[72]. Thus, nucleotide modifications can occur on the initial transcript but the completion of all the reactions may be one of the final steps in maturation of tRNA and rRNA molecules.

4.3. Addition of Residues

Finally, an important but not well understood maturation step for some RNA molecules involves the addition of nucleotides to the 3' end of the RNA in a reaction catalyzed by terminal nucleotide transferases that do not depend on a DNA template[80]. Many of the large nuclear RNAs and mRNAs in eukaryotic cells have sequences of poly(A) at their 3' end that are from 150 to 300 nucleotides long. The evidence that these adenylate residues are added by a post-transcriptional reaction is that the appropriate template sequences for a poly(A) as long as 300 nucleotides have not been found in the DNA; that enzymes isolated from both nuclei and cytoplasm of many types of cells catalyze the attachment of adenylate residues to RNA; and that certain drugs selectively inhibit the synthesis of the poly(A) sequences. The exact function of these poly(A) sequences is not yet clear, but their addition appears to be a necessary step in the maturation of some mRNA species in higher organisms. The fact that they are found at the 3' end of both the large nuclear RNA molecules and mRNA molecules is a further indication that the 3' end of the nuclear RNA is a precursor to the mRNA. Although an enzyme capable of catalyzing the addition of adenylate residues to RNA has been found in bacteria, no evidence has been presented that such sequences are present in any bacterial RNA.

Bacteria and other organisms also have enzymes that can add cytidylate and adenylate residues to tRNA molecules lacking the -pCpCpA$_{OH}$ sequence found at the 3' terminal of every mature tRNA[88]. The one precursor tRNA that has been sequenced already, the $ptRNA^{Tyr}$ of *E. coli* contains internally the -pCpCpA- sequence of mature tRNA[89]. Thus the function of the enzymes that catalyze the addition may only be to replace this end if it is removed during the trimming process. However, the pCpCpA$_{OH}$ sequence may not be present in the primary gene products for all the tRNAs. In such cases, the post-transcriptional addition reaction catalyzed by the enzyme would be an important maturation step for the synthesis of these tRNA molecules.

I thank Dr. T. Blumenthal for a critical reading of this review. I am supported by a U.S. National Institutes of Health Career Development Award (GM-70, 422).

Received: October 30, 1974 [A 62 IE]
German version: Angew. Chem. 87, 497 (1975)

[1] *O. Maaløe* and *N. O. Kjeldgaard:* Control of Macromolecular Synthesis. Benjamin, New York 1966.
[2] *J. E. Darnell, Jr.*, Bacteriol. Rev. *32*, 262 (1968).
[3] *B. D. Hall* and *S. Spiegelman*, Proc. Nat. Acad. Sci. USA *47*, 137 (1961).
[4] *G. Milman, R. Langridge*, and *M. J. Chamberlin*, Proc. Nat. Acad. Sci. USA *57*, 1804 (1967).
[5] *D. Kennell*, J. Mol. Biol. *34*, 85 (1968).
[6] *J. Hurwitz* and *J. T. August*, Progr. Nucl. Acid Res. *1*, 59 (1963).
[7] *J. M. Kirk*, Biochim. Biophys. Acta *42*, 167 (1960); cf. also *H. Lackner*, Angew. Chem. *87*, 400 (1975); Angew. Chem. internat. Edit. *14*, 375 (1975).
[8] *K. M. Downey, J. J. Byrnes, B. S. Jurmark*, and *A. G. So*, Proc. Nat. Acad. Sci. USA *70*, 3400 (1973).
[9] *M. J. Chamberlin* in *P. D. Boyer:* The Enzymes. 3rd Edit., Vol. 10. Academic Press, New York 1974, p. 333.
[10] *R. Schekman, W. Wickner, O. Westergaard, D. Brutlag, K. Geider, L. L. Bertsch*, and *A. Kornberg*, Proc. Nat. Acad. Sci. USA *69*, 2691 (1972).
[11] *A. Sugino, S. Hirose*, and *R. Okazaki*, Proc. Nat. Acad. Sci. USA *69*, 1863 (1972).
[12] *P. Chambon* in *P. D. Boyer:* The Enzymes. 3rd Edit., Vol. 10. Academic Press, New York 1974, p. 261.
[13] *R. Weinmann* and *R. G. Roeder*, Proc. Nat. Acad. Sci. USA *71*, 1790 (1974).
[14] *R. R. Burgess*, J. Biol. Chem. *244*, 6168 (1969).
[15] *M. Scrutton, C. Wu*, and *D. Goldthwait*, Proc. Nat. Acad. Sci. USA *68*, 2497 (1971).
[16] *W. Zillig, K. Zechel, D. Rabussay, M. Schachner, V. S. Sethi, P. Palm, A. Heil*, and *W. Seifert*, Cold Spring Harbor Symp. Quant. Biol. *35*, 47 (1970).
[17] *C. G. Goff* and *K. Weber*, Cold Spring Harbor Symp. Quant. Biol. *35*, 101 (1970).
[18] *O. J. Martelo, S. L. C. Woo, E. M. Reimann*, and *E. W. Davie*, Biochemistry *9*, 4807 (1970).

[19] C. Nüsslein and B. Heyden, Biochem. Biophys. Res. Commun. 47, 282 (1972).
[20] H. Küntzel and K. P. Schäfer, Nature New Biol. 231, 265 (1971).
[21] M. J. Chamberlin, J. McGrath, and L. Waskell, Nature 228, 227 (1970).
[22] E. K. F. Bautz, FEBS Lett. 36, 123 (1973).
[23] A. L. Lehninger: Bioenergetics. Benjamin, New York 1965, p. 210.
[24] J. P. Richardson, J. Mol. Biol. 49, 235 (1970).
[25] R. W. Davis and R. W. Hyman, Cold Spring Harbor Symp. Quant. Biol. 35, 269 (1970).
[26] H. Bremer and D. Yuan, J. Mol. Biol. 38, 163 (1968).
[27] H. D. Manor, D. Goodman, and G. Stent, J. Mol. Biol. 39, 1 (1969).
[28] U. Maitra and J. Hurwitz, Proc. Nat. Acad. Sci. USA 54, 815 (1965).
[29] D. A. Goldthwait, D. D. Anthony, and C. W. Wu, LePetit Colloq. Biol. Med. 1, 10 (1970).
[30] E. N. Brody and E. P. Geiduschek, Biochemistry 9, 1300 (1970).
[31] H. Bremer, M. Konrad, and R. Bruner, J. Mol. Biol. 16, 104 (1966).
[32] E. P. Geiduschek, T. Nakamoto, and S. B. Weiss, Proc. Nat. Acad. Sci. USA 47, 1405 (1961).
[33] H. Bremer and M. W. Konrad, Proc. Nat. Acad. Sci. USA 51, 801 (1964).
[34] M. Hayashi, Proc. Nat. Acad. Sci. USA 54, 1736 (1965).
[35] M. Chamberlin and P. Berg, J. Mol. Biol. 8, 297 (1964).
[36] V. L. Florentiev and V. I. Ivanov, Nature 228, 519 (1970).
[37] G. S. Stent, Advan. Virus Res. 5, 95 (1958).
[38] P. A. Riley, Nature 228, 522 (1970).
[39] J. M. Saucier and J. C. Wang, Nature New Biol. 339, 167 (1972).
[40] M. J. Chamberlin, Annu. Rev. Biochem. 43, 721 (1974).
[41] R. R. Burgess and A. A. Travers, Fed. Proc. 29, 1164 (1970).
[42] R. Fukuda, Y. Iwakura, and A. Ishihama, J. Mol. Biol. 83, 353 (1974).
[43] Y. Iwakura, R. Fukuda, and A. Ishihama, J. Mol. Biol. 83, 369 (1974).
[44] R. G. Shorenstein and R. Losick, J. Biol. Chem. 248, 6170 (1973).
[45] W. Epstein and J. Beckwith, Annu. Rev. Biochem. 37, 411 (1968).
[46] B. Allet and R. Solem, J. Mol. Biol. 85, 475 (1974).
[47] R. Maurer, T. Maniatis, and M. Ptashne, Nature 249, 221 (1974).
[48] T. Maniatis, M. Ptashne, B. G. Barrell, and J. Donelson, Nature 250, 394 (1974).
[49] B. Allet, R. J. Roberts, R. F. Gesteland, and R. Solem, Nature 249, 217 (1974).
[50] B. Müller-Hill, Angew. Chem. 83, 195 (1971); Angew. Chem. internat. Edit. 10, 160 (1971).
[51] S. Nakanishi, S. Adhya, M. Gottesman, and I. Pastan, Proc. Nat. Acad. Sci. USA 70, 334 (1973).
[52] M. Ptashne in A. D. Hershey: The Bacteriophage Lambda. Cold Spring Harbor Laboratory, 1971, p. 221.
[53] B. de Crombrugghe, B. Chen, W. Anderson, P. Nissley, M. Gottesman, I. Pastan, and R. Perlman, Nature New Biol. 231, 139 (1971).
[54] P. Chadwick, V. Pirrotta, R. Steinberg, and M. Ptashne, Cold Spring Harbor Symp. Quant. Biol. 35, 283 (1970).
[55] A. M. Wu, S. Ghosh, and H. Echols, J. Mol. Biol. 67, 423 (1972).
[56] N. M. Maizels, Proc. Nat. Acad. Sci. USA 70, 3585 (1973).
[57] W. Gilbert and A. Maxam, Proc. Nat. Acad. Sci. USA 70, 3581 (1973).
[58] J. Greenblatt and R. Schleif, Nature New Biol. 233, 166 (1971).
[59] G. Wilcox, K. Clemetson, D. Santi, and E. Englesberg, Proc. Nat. Acad. Sci. USA 68, 2145 (1971).
[60] W. Anderson, A. Schneider, M. Emmer, R. Perlman, and I. Pastan, J. Biol. Chem. 246, 5959 (1970).
[61] A. D. Riggs, G. Reiness, and G. Zubay, Proc. Nat. Acad. Sci. USA 68, 1222 (1971).
[62] A. Stevens, Proc. Nat. Acad. Sci. USA 69, 603 (1972).
[63] H. Horvitz, Nature New Biol. 244, 137 (1973).
[64] P. Leibowitz, S. M. Weissman, and C. M. Radding, J. Biol. Chem. 246, 5120 (1971).
[65] J. E. Dahlberg and F. R. Blattner, Fed. Proc. 32, 664 Abs (1973).
[66] J. W. Roberts, Nature 224, 1168 (1969).
[67] J. P. Richardson, Cold Spring Harbor Symp. Quant. Biol. 35, 127 (1970).
[68] C. Lowery-Goldhammer and J. P. Richardson, Proc. Nat. Acad. Sci. USA 71, 2003 (1974).
[69] G. Galluppi, C. Lowery-Goldhammer, and J. P. Richardson, unpublished observations.
[70] B. de Crombrugghe, S. Adhya, M. Gottesman, and I. Pastan, Nature New Biol. 241, 260 (1973).
[71] G. Attardi and F. Amaldi, Annu. Rev. Biochem. 39, 183 (1970).
[72] N. R. Pace, Bacteriol. Rev. 37, 562 (1973).
[73] N. Nikolaev, L. Silengo, and D. Schlessinger, Proc. Nat. Acad. Sci. USA 70, 3361 (1973).
[74] N. Nikolaev, D. Schlessinger, and D. K. Wellauer, J. Mol. Biol. 86, 741 (1974).
[75] A. Ghysen and J. F. Celis, Nature 249, 418 (1974).
[76] C. Guthrie, J. G. Seidman, S. Altman, B. G. Barrell, J. D. Smith, and W. H. McClain, Nature New Biol. 246, 6 (1973).
[77] D. P. Nierlich, H. Lamfrom, A. Sarabhai, and J. W. Abelson, Proc. Nat. Acad. Sci. USA 70, 179 (1973).
[78] S. Altman and H. D. Robertson, Mol. Cell. Biochem. 1, 83 (1973).
[79] P. Schedl and P. Primakoff, Proc. Nat. Acad. Sci. USA 70, 2091 (1973).
[80] R. A. Weinberg, Annu. Rev. Biochem. 42, 329 (1973).
[81] J. J. Dunn and F. W. Studier, Proc. Nat. Acad. Sci. USA 70, 1559 (1973).
[82] J. J. Dunn and F. W. Studier, Proc. Nat. Acad. Sci. USA 3296 (1973).
[83] D. Söll, Science 173, 293 (1971).
[84] U. Z. Littauer and H. Inouye, Annu. Rev. Biochem. 42, 439 (1973).
[85] R. P. Perry and D. E. Kelley, Cell 1, 37 (1974).
[86] C. E. Singer, G. R. Smith, R. Cortese, and B. N. Ames, Nature New Biol. 238, 72 (1972).
[87] K. P. Schaeffer, S. Altman, and D. Söll, Proc. Nat. Acad. Sci. USA 70, 3626 (1973).
[88] M. P. Deutscher, Progr. Nuel. Acid Res. Mol. Biol. 13, 51 (1973).
[89] S. Altman and J. D. Smith, Nature New Biol. 233, 35 (1971).

Asymmetric Membranes: Preparation and Applications

By H.-D. Saier and H. Strathmann[*]

The separation of molecular mixtures by semipermeable membranes under the driving force of hydrostatic pressure has assumed major importance in recent years. Among other factors the development of membranes with asymmetric structure which, while having the same separating properties, afford a filtration output many times greater than that of the previously known symmetrical membranes, was decisive for this method. In the present progress report the structures of asymmetric membranes are discussed, as well as their preparation from various polymers and their application to the separation of molecular mixtures.

1. Introduction

Selective mass transport through membranes has been the subject of numerous scientific investigations for more than a century. In this work attention was first focused on biological membranes, the importance of which for metabolic processes in living organisms was recognized very early, but more recently synthetic membranes in particular and their application to separation problems in chemistry and industry have acquired economic significance. For example, membrane filtration is nowadays used to extract drinking water from the sea, for fractionating, concentrating, and purifying macromolecular solutions, for the treatment of industrial waste waters, and for the recovery of valuable constituents. Membrane filtra-

[*] Dr. H.-D. Saier [+] and Dr. H. Strathmann
Forschungsinstitut Berghof GmbH
74 Tübingen-Lustnau, Berghof (Germany)
[+] To whom correspondence should be addressed.

tion has proved particularly useful in the treatment of thermally sensitive substances in biochemistry, pharmacology, and the food industry[1-9]. Here and in many other problems of separation it is often greatly superior to the more conventional distillation, crystallization, extraction, and other processes, for it can often be carried out faster, more economically, and under milder conditions.

In view of the wealth of possible applications of membrane filtration and their economy it is surprising that its industrial exploitation became possible only a few years ago, even though the principle of the process and its industrial potential have been known for almost a century from *Pfeffer*'s investigations[10] and *van't Hoff*'s theoretical studies[11] on osmosis. However, the industrial application of the method was held back not least by the difficulty of developing membranes with sufficient filtration efficiency. Only the studies of *Loeb* and *Sourirajan*[12-15], which led to the integral-asymmetric membranes, have made industrial scale membrane filtration feasible, and this stimulus was followed by some very hectic development, particularly in the desalination of seawater and brackish waters. Recent progress in polymer chemistry considerably extended the scope of membrane filtration.

Asymmetric membranes consist, in principle, of a relatively thick, highly porous carrier and the actual membrane, the latter being only 0.1 to 0.5 μm thick. They are characterized primarily by a greatly increased rate of filtration.

2. The Principle of Membrane Filtration

Membrane filtration is based fundamentally on a simple principle[16]. A molecular mixture is brought by convection onto the surface of a membrane. While some of the components pass through the membrane under the influence of hydrostatic pressure, others are retained more or less completely. Viewed superficially, membrane filtration differs from conventional filtration only by the size of the particles to be separated. The real difference, however, is that a conventional filter acts as a sieve and separates a mixture of substances simply according to particle sizes, whereas in membrane filtration specific interactions between the mixture components and the membrane matrix are, or can also be, responsible for the separation. It is thus possible not only to carry out separations in the molecular range but also to separate substances having the same or nearly the same molecular dimensions.

Terminologically, a distinction is made in membrane filtration between reverse osmosis and ultrafiltration[7, 17]. The process is called reverse osmosis when the osmotic pressure difference between the starting solution and the filtrate is not negligible compared with the hydrostatic pressure applied; this is the case when low-molecular compounds are to be separated from a solution, *e. g.* in the desalination of seawater. When, however, the aim is to separate macromolecular substances with molecular weights of about 10000, the osmotic pressure difference between the starting solution and the filtrate is negligibly small compared with the hydrostatic pressure applied, and the process is one of ultrafiltration.

Although at first sight this differentiation may appear to be very arbitrary, it has a degree of justification in respect of the membranes used and the hydrostatic pressure required, and there are also genuine differences between the techniques used for reverse osmosis and ultrafiltration (see Section 7).

3. Phenomenological Description of Membranes and Membrane Transport Processes

Since the membrane itself is decisive for the success of membrane filtration, this section will be devoted to a short discussion of membrane construction and of mass transport through membranes.

Quite generally, a membrane is defined as a liquid or solid intermediate phase separating two homogeneous phases and offering different resistances to the passage of different chemical substances. The mass transport through this intermediate phase can be described by the following phenomenological relationship[18]:

$$J_i = \sum_{k=1}^{n} L_{ik} X_k \qquad i = 1, 2, 3, \ldots n \tag{1}$$

where J_i is the material flow of the component i, L_{ik} is a phenomenological coefficient, and X_k is a generalized driving force provided by the chemical and electrochemical potential gradients of the component k in the membrane. The applicability of eq. (1) is restricted by boundary conditions set by the limited validity of linear laws in thermodynamics of irreversible processes in discontinuous systems[19-21]. Although eq. (1) describes the transport process in membranes in such a way that it includes all the interactions between the particle flows as well as chemical reactions, its value for the description of membrane filtration processes is limited because the phenomenological coefficients are mathematically difficult to obtain and because the equation is strictly valid only in a state close to equilibrium.

The generalized definition of a membrane is also of little value when membranes are to be developed for special purposes, because this phenomenological description, like eq. (1), does not take into account the membrane structure or the molecular interactions between the transported particles and the membrane matrix. For the development of membranes in practice it is therefore often more advantageous to work with membrane models.

4. Membrane Models

There are two models for the description of filtration membranes, each representing an idealized limiting case: the "pore membrane" and "the solubility membrane".

The ideal pore membrane comes nearer in its structure to a conventional filter. Here mass transport takes place through well-defined pores and the selectivity of the membrane is determined by the pore diameter. Pore membranes can be used only for the separation of substances that differ in molecular dimensions.

In contrast, the ideal solubility membrane is a homogeneous polymer layer through which all the components are transported independently of one another by molecular diffusion. The selectivity of the solubility membrane depends on differences between the diffusion coefficients and concentrations of individual components in the membrane matrix.

4.1. Model of a Pore Membrane

The mass transport during filtration through an ideal pore membrane depends on volume flow through the pores and

can be described by the Hagen-Poiseuille equation. For a system consisting of a solvent and a dissolved component the volume flow density J_v is given by the relation[23]:

$$J_v = L_p(\Delta p - \sigma \Delta \pi) \quad (2)$$

Here L_p is the hydrodynamic permeability, Δp the specified hydrostatic pressure, $\Delta \pi$ the difference between the osmotic pressures in the original solution and the filtrate, and σ a so-called reflection coefficient[24] that is a measure of the separating characteristics of the membrane. For a strictly semipermeable membrane $\sigma = 1$[21].

The hydrostatic permeability L_p is given by:

$$L_p = \omega r^2/(8\pi\lambda\eta\Delta x) \quad (3)$$

Here ω is the porosity, r the mean pore radius, η the viscosity, λ a correction factor for pore length, and Δx the thickness of the membrane. For dilute solutions and membranes with good selectivity the flow density J_1 of the solvent is equal, in the first approximation, to the volume flow density J_v. For the dissolved component the flow density J_s is given by the following relationship[21]:

$$J_s = J_v c_s^m - D_s^m(\mathrm{d}c_s^m/\mathrm{d}x) \quad (4)$$

Here c_s^m and D_s^m are, respectively, the concentration and the diffusion coefficient of the dissolved component in the membrane, and $\mathrm{d}c_s^m/\mathrm{d}x$ is the concentration gradient of the dissolved component in the membrane. Eq. (4) consists of two additive terms: the first describes convective transport of the dissolved component with the volume flow, and the second diffusion of this component in the volume flow. The second term is negligible in membranes with high filtration efficiency[22].

The two partial flows of solvent and solute yield a further parameter that can in general be used to characterize a membrane. This is the membrane's retention capacity R for the dissolved component[25]:

$$R = 1 - (J_s/J_v c_s^o) \quad (5)$$

Putting $J_s = J_v c_s^f$ we obtain:

$$R = 1 - c_s^f/c_s^o \quad (6)$$

Here c_s^o and c_s^f are the concentrations of the dissolved component in the original solution (o) and the filtrate (f). For a strictly semipermeable membrane J_s and thus $c_s^f J_v = 0$ and $R = 1$, whereas for a membrane with no separating capacity $R = 0$.

4.2. Model of a Solubility Membrane

In an ideal solubility membrane the transport of the components depends on molecular diffusion in which coupling of the material flows is neglected. The flow density of any one component through the membrane can be described by the following equation[2, 26].

$$J_i = \frac{D_i^m k_i c_i}{RT\Delta x}\left(\bar{V}_i \Delta p - \frac{RT}{c_i}\Delta c_i\right) \quad (7)$$

Here, J_i is the mass flow of a component i through the membrane, D_i^m the diffusion coefficient in the membrane, k_i the distribution coefficient between the membrane and the adjoining solution, c_i the concentration in the adjoining solution, and Δc_i the concentration difference of component i between the two sides of the membrane. $\bar{V}_i$ is the partial molar volume of component i, Δp is a specified pressure difference, R is the gas constant, T is the absolute temperature, and Δx is the membrane thickness.

If the filtration flow density is to be derived for a relatively dilute solution, the concentration term $RT\Delta c_i/c_i$ in eq. (7) can be expressed as $\bar{V}_1 \Delta \pi$. The term $\Delta \pi$ is the osmotic pressure difference between the original solution and the filtrate. The filtration flow density for the solvent J_1 is given by eq. (8):

$$J_1 = \frac{D_1^m k_1 c_1 \bar{V}_1}{RT\Delta x}(\Delta p - \Delta \pi) \quad (8)$$

For description of the filtration flow density of the dissolved component J_s in a dilute solution the pressure term $\bar{V}_i \Delta p$ can become negligible in comparison with the concentration term $RT\Delta c_i/c_i$[26]; we then have to a first approximation:

$$J_s = D_s^m k_s \Delta c_s/\Delta x \quad (9)$$

5. Production of Asymmetric Membranes

Equations (2)—(4), and (8), (9) illustrate the difference between a pore membrane and a solubility membrane. While a pore membrane merely differentiates between the particle geometries, *i.e.* acts only as a molecular sieve, the selectivity of a solubility membrane depends mainly on the distribution coefficients of the components between the membrane and the external phases. Because of this, a pore membrane can separate only materials that differ considerably in molecular size, while a solubility membrane can also separate materials having the same—or nearly the same—molecular size if their solubilities in the membrane phase are sufficiently different.

A further difference between solubility and pore membranes lies in their different filtration flow densities. Owing to the diffusion process the filtration flow density of a solubility membrane is 1—2 orders of magnitude lower than that of a pore membrane under the same driving force. In both cases, however, as follows from the transport equations, the filtration flow density is inversely proportional to the membrane thickness.

Nevertheless, for economic reasons the filtration flow density should be as large as possible, *i.e.* the membrane thickness should be minimized. In the present state of the art it is not possible to produce perfect, self-supporting films thinner than about 10 μm on a large scale, whereas to achieve economically justifiable filtration flow densities the membranes must not be appreciably more than 0.1 to 0.5 μm thick. These difficulties are overcome by the use of asymmetric membranes. Figure 1 shows side-by-side scanning electron micrographs of an asymmetric and a symmetrical membrane. The total thickness of the asymmetric membrane amounts to 0.1 to 0.5 mm. It is constructed of a relatively thick, very porous support carrying an extremely thin skin measuring 0.1 to 0.5 μm. This skin is the actual semipermeable membrane, while the coarse, highly porous support has no selective properties and does

not present any significant hydrodynamic resistance to the flow of the filtrate.

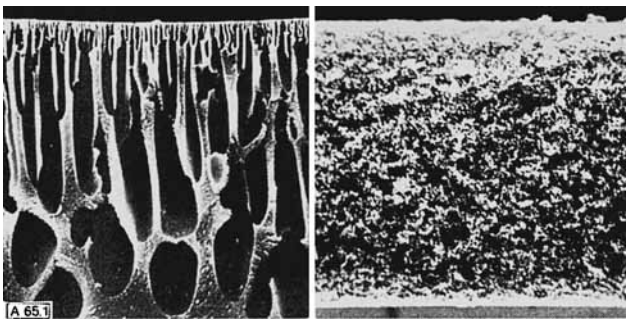


Fig. 1. Scanning electron micrographs of sections through an asymmetric membrane (left) and a symmetrical membrane (right).

Apart from their high rate of filtration, asymmetric membranes have the further advantages that they are not blocked so quickly as the symmetrical ones and can be readily cleaned.

In 1960 *Loeb* and *Sourirajan* prepared the first asymmetric cellulose acetate membrane, which displayed outstanding filtration properties. Subsequent development was at first purely empirical[13, 15, 27, 28]. Numerous detailed recipes were published, but not much was known about the actual membrane formation. It was only through the extensive use of scanning electron microscopy and systematic investigations carried out above all by *Matz*, *Frommer*, *et al.*[29–32] that the processes involved in production of asymmetric membranes became clear. By systematic variation of the preparation parameters, asymmetric membranes can today be prepared from a large variety of polymers and with a wide variety of filtration characteristics.

5.1. Production of Asymmetric Membranes by Phase Inversion Reaction

Loeb and *Sourirajan*'s process for the production of asymmetric cellulose acetate membranes consists of four individual steps:

1) Cellulose acetate is dissolved in a solvent or solvent mixture to a concentration of 20 to 30 wt-%.

2) The highly viscous solution is spread on a glass plate as a film 0.2 to 0.5 mm thick.

3) Part of the solvent is evaporated.

4) The film is dipped into a water bath, the polymer then precipitating with a solid, asymmetric structure.

We now know that this procedure is not restricted to cellulose acetate, but that any film-forming polymer can be used that is soluble in a solvent and can be precipitated by an agent miscible with the solvent[33, 34]. The most important step is the precipitation of the polymer from a homogeneous mixture in a non-solvent. This process is a special case of a reaction that always leads to a porous system[35] and that was called phase inversion by *Kesting*[1]. In a phase inversion reaction a homogeneous polymer solution is converted into a two-phase system: a solid, polymer-rich phase forming the membrane skeleton and a liquid, solvent-rich and polymer-poor phase filling the membrane pores.

Figure 2 shows a typical phase diagram for the production of a membrane. The system as a whole comprises a single-phase region is which the three components are miscible with one another and a region in which the system separates into two phases. The miscibility gap generally lies very close to the solvent-precipitant line, which means that practically no polymer remains in the solution. If we now consider the membrane preparation with the aid of the phase diagram, then point A on the polymer-solvent line corresponds to the composition of the membrane solution; the composition of the precipitated membrane is given by point C on the polymer-precipitant line, *i.e.* at point C two phases exist side by side: a polymer-rich, solid phase, whose composition is given by point S and which forms the membrane skeleton, and a liquid, polymer-poor phase, whose composition is given by point L and which constitutes the content of the pores. The position of point C on the line S-L determines the total porosity of the membrane. During the actual precipitation process the system moves along the path from A to C while the solvent is replaced by the precipitant. At point B the system breaks up into two phases.

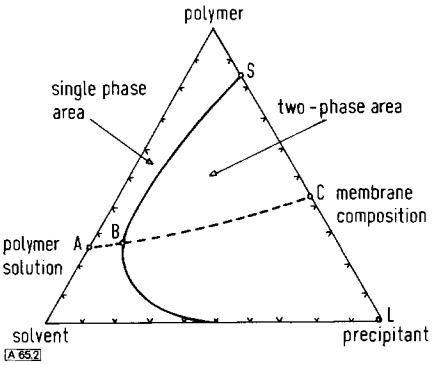


Fig. 2. Phase diagram for membrane preparation. For explanation see text.

The phase inversion reaction need not necessarily be brought about by precipitation. Phase separation can also be effected if the polymer-solvent system is not homogeneously miscible over the whole concentration or temperature interval. If a system has a miscibility gap at low temperature the phase separation can be effected by cooling, and it is this procedure that is nowadays used in practice for membrane production.

According to *Kesting*[36], part of the solvent is evaporated so as to convert a system not miscible over the whole concentration interval into two phases, *i.e.* into a porous membrane.

Although the phase diagram is very useful for an analysis of membrane formation, it provides no information about the microscopic distribution of the phases; on its basis we cannot say whether the membrane contains a few large pores or many small ones, or indeed whether the membrane is asymmetric. The asymmetric structure is determined mainly by kinetic parameters during the precipitation[1, 29, 35]. Either symmetrical or asymmetric membranes can be prepared by varying certain parameters whose influence on the membrane structure is more or less understood. Nevertheless, even today there is still no comprehensive theory that would unambiguously explain the formation of the asymmetric structure.

Phenomenologically, two types of structure, each associated with characteristic membrane properties, can be distinguished for asymmetric membranes (Fig. 3). A foam-like structure with a relatively thick, homogeneous layer above it is mechanically very stable and can be used with pressures up to 100 bar; this asymmetric structure is suitable for the separation of substances of low molecular weight, *e.g.* salt and water, by reverse osmosis. In the case of membranes with finger-like structure we are in general dealing with pore membranes

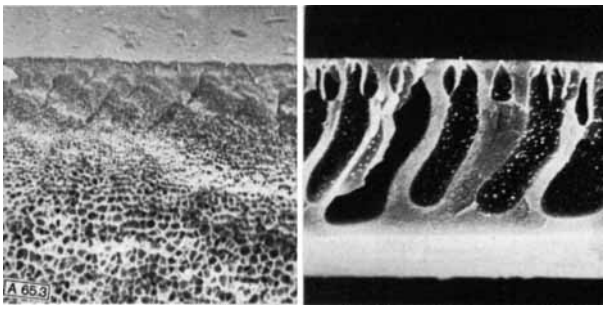


Fig. 3. Scanning electron micrographs of sections through asymmetric membranes with a foam structure (left) and finger structure (right).

allowing high filtration flow densities even at low hydrostatic pressures; these have no ability to retain salts. At pressures above 10 bar the structure collapses and the membranes lose their good filtration properties; such structures are therefore usually reserved for ultrafiltration, *i. e.* for the separation of macromolecular substances at low hydrostatic pressures.

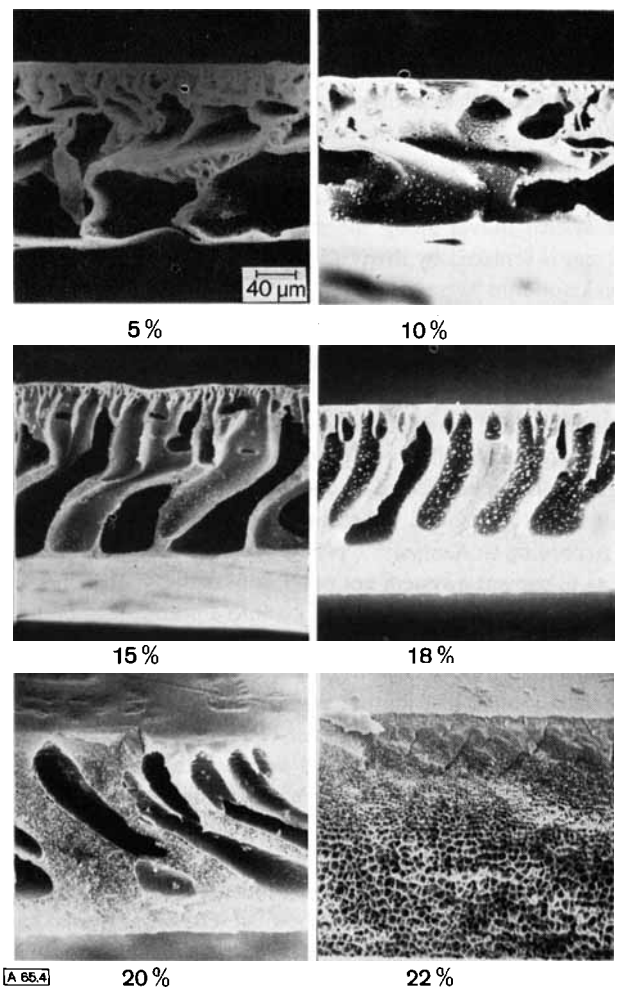


Fig. 4. Scanning electron micrographs of membrane section in dependence on polymer content of the initial solution (figures in wt-%).

These two membrane types are the limiting cases; in practice a continuous transition from one to the other can be achieved by variation of the preparation parameters, and thereby a continuous transition from dense desalting membranes to coarse-pored ultrafiltration membranes (Fig. 4).

5.2. Production of Composite Asymmetric Membranes

Comparatively recently, a "composite" method of construction was devised for the preparation of asymmetric membranes[37-43] that had extremely high filtration flow densities and could be used especially for reverse osmosis. For composite membranes a highly porous, readily permeable, and mechanically very strong support is prepared, on which is placed a homogeneous separating layer 200 to *ca.* 1000 Å thick. For this purpose a very dilute polymer solution is poured—once or several times—onto the support layer and the solvent is evaporated. To prevent the polymer solution from penetrating the support, the latter is usually protected by an inert intermediate layer which is removed in subsequent washing processes.

Present-day composite membranes consist of two materials, since the support must not be attacked by the solvent of the separating layer added. Cellulose acetate, cellulose nitrate mixed polymers, and polysulfones are the main materials used for the highly porous carriers. The pore diameter of the carrier material must be smaller than the thickness of the active film, in order to prevent rupture of the separating layer. Any polymer can be considered for the homogeneous separating layer, provided that the solvent used does not also attack or dissolve the material of the support. The range of materials that can be used is limited by the conditions that can be withstood by both, but this disadvantage is compensated by the very high filtration flow densities.

Other methods of preparing asymmetric membranes are still in the experimental stage, for example spreading[44] of polymers on a liquid foundation which is then applied directly to the porous supporting structure, or coating the porous supports in a plasma stream of monomers which polymerize on the support[44-48].

Very good filtration results for special applications have been achieved with dynamically formed membranes[49-56], which are not true composite membranes although they behave as such. Almost any ultrafiltration membrane can be used for dynamically formed membranes if its pore diameter is not more than about 0.2 µm. During the filtration a very small amount of macromolecular or colloidal substance is added to the initial solution, this additive being retained by the pores of the support and thereby forming a film that can separate even salt from water.

6. Choice of Polymers Suitable for Membrane Production

Membrane materials are required to have high mechanical, chemical, and thermal stability as well as resistance to microbiological degradation. While in pore membranes the material responsible for the separation plays a subordinate role, in solubility membranes it exerts a decisive influence on the separating characteristics. Solubility membranes are always used when molecules of approximately equal size are to be separated, the basis for this being special interactions between the molecules and the membrane matrix.

Transport of water and salt has been the subject of numerous studies, particularly through cellulose acetate but also through other polymers[2, 28, 57]. Water transport is associated with the number of polar groups present in the polymer matrix.

These polar groups serve as adsorption centers with which the penetrating water can interact by hydrogen bonding. According to this view the water molecules are transported through the homogeneous matrix by activated boundary layer diffusion along the polar groups. A prerequisite for this to happen is that the polar groups should be distributed in the polymer matrix as close together and as regularly as possible[58, 59].

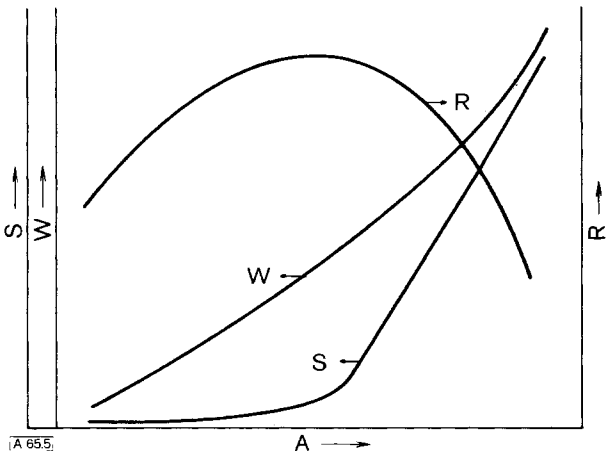


Fig. 5. Relation between the salt flow (S), water flow (W), salt retention capacity (R), and water absorption (A), schematic.

Exclusion of the salt depends on the inability of its unhydrated ions to form hydrogen bonds to any large extent with the polar groups. Hydrated alkali metal and halide ions are, however, too large to penetrate the polymer matrix. Polymers with desalination properties can usually absorb up to about 20 wt-% of water; at high water uptakes water clusters are increasingly formed in the homogeneous polymer, and the hydrated ions of the salt can penetrate, so that the retention capacity is affected. The distribution of water within the polymer matrix can be determined with the aid of a function devised by *Zimm* and *Lundberg*[60]. Clusters can also be present at very small water uptakes—much below 20 wt-%—arising from the all-powerful water-water interactions; such a polymer would be unsuitable for desalination purposes. Figure 5 shows the relation between the salt flow, water flow, salt-retention capacity, and water absorption[57].

7. Problems of Membrane Filtration in Industrial Practice

7.1. Concentration Polarization

Even when an optimally suitable membrane is available for a given problem of material separation, its practical industrial application may run into difficulties seriously detracting from economics of the process. One of the most important problems in technical processes is concentration polarization[61-66]. This appears because, on membrane filtration, a solution is brought to the surface of a semipermeable membrane by *convection*. While the solvent permeates the membrane under the driving force of hydrostatic pressure, the dissolved components are more or less completely retained; they concentrate in the boundary layer on the membrane surface and, owing to the concentration gradient, diffuse back into the original solution; after some time a stationary state is produced, with a constant concentration profile: convective transport of the dissolved particles to the membrane surface is compensated by a diffusion current directed back into the original solution.

Concentration polarization considerably impairs the economics of membrane filtration. With substances of low molecular weight, *e.g.* salts, the osmotic pressure of the original solution, which must be overcome by the hydrostatic pressure, increases with increasing concentration at the membrane surface. Moreover, since in general filtration membranes are not strictly semipermeable, and the amount of material passing through the membrane is also directly proportional to the concentration on the membrane surface, the quality of the filtrate is impaired by the concentration polarization. The separation capacity of the membrane is thus reduced.

During filtration of macromolecular substances it is very often found that, as a result of concentration polarization, the solubility limit is exceeded and a covering film is formed on the membrane surface. Such films act as secondary membranes, which not only drastically reduce the filtration flow densities but can also completely alter the separation characteristics of the original membrane.

Although concentration polarization cannot be wholly avoided, it can be kept in check by suitably arranged flow parallel to the membrane surface, as has been shown by penetrating investigations of transport processes at the laminar boundary of membrane surfaces.

7.2. Development of Membrane Filtration Systems

In large industrial filtration systems the disadvantageous effects of concentration polarization must be kept as small as possible by suitable arrangements for the flow of the original solution and lay-out of the installation. In addition, the filtration unit should be distinguished by a low cost and long service life, and should not occupy much space. Three systems have passed into industrial use (Sections 7.2.1 to 7.2.3).

7.2.1. The Tube Bundle System

The tube bundle system is represented schematically in Figure 6[67]. The tube-shaped asymmetric polymer membranes are placed in porous tubes made of metal or plastic. To maintain the concentration increase at a minimum level, the flow through the tubes must be turbulent, and the relatively large tube diameter (*ca.* 2.5 cm) therefore requires a high pump output. The ratio of the installed membrane surface to the volume of the apparatus, *i.e.* the packing density, is low; the relatively large costs of sealing the ends, support of the

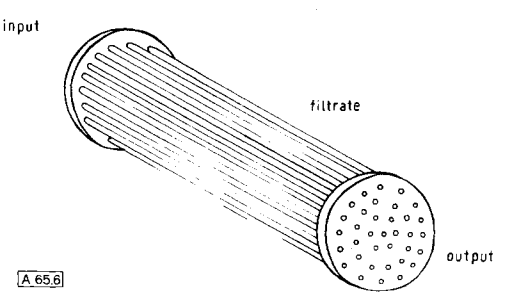


Fig. 6. Construction of the tube bundle module, schematic.

membranes, and changing of the membranes are also unfavorable. However, the possibility of cleaning the membrane surfaces mechanically with small foam balls constitutes an advantage of this system.

7.2.2. The Roga Module

The Roga module[68] consists of two asymmetric membranes separated by an incompressible but porous intermediate layer. Flow is introduced through a lattice on each side of the membrane. Figure 7 gives a schematic representation of the construction. The whole arrangement is rolled up, made watertight, and placed in a pressure tube. This mode of construction gives a filtration module with favorable cost and compactness. However, here too problems arise with controlling the concentration polarization, particularly when colloidal or macromolecular material has to be separated.

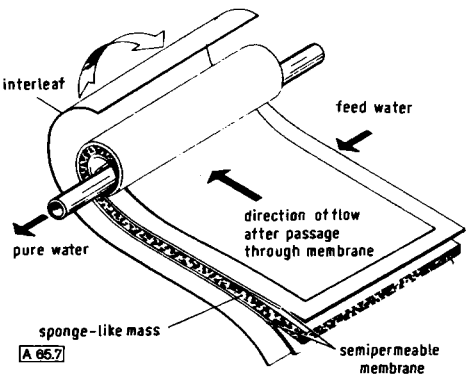


Fig. 7. Construction of the Roga module, schematic.

7.2.3. The Hollow Fiber System

The membranes developed by DuPont[69, 70] are in the form of hollow fibers of asymmetric structure; the actual separating layer is on the outside of the fibers. The fibers are bundled together, bent into a U-shape, inserted in a pressure tube, and sealed up. The packing density of such a module is extremely high. The fibers are selfsupporting, so that for work at pressures up to about 60 bar only a pressure-tight outer tube of steel, aluminum, or fiberglass-reinforced plastic is required. Filtration units can then be constructed from hollow fiber modules distinguished by very small bulk and favorable cost characteristics, which have proved valuable above all for desalination. They appear to be unsuitable for the separation of macromolecular substances because precipitates are formed on the membrane. The precipitates formed on the outside of the hollow fibers can only be partially removed by the insufficient flow running over the fiber surfaces, so that a very large part of the membrane surface becomes unavailable for filtration.

The Amicon[71] and Berghof companies[72] have developed a different hollow-fiber concept, in which the active separating layer is in the interior of the hollow fibers. This filtration from the inside to the outside, even with low flow rates in the laminar flow region, can reduce the concentration polarization to economically acceptable levels. Figure 8 is a schematic representation of the filtration process. This new hollow-fiber concept combines the advantages of the DuPont module and the tube bundle module. So far it has only been used for ultrafiltration, since the resistance of the fibers to pressure does not yet satisfy the demands of reverse osmosis.

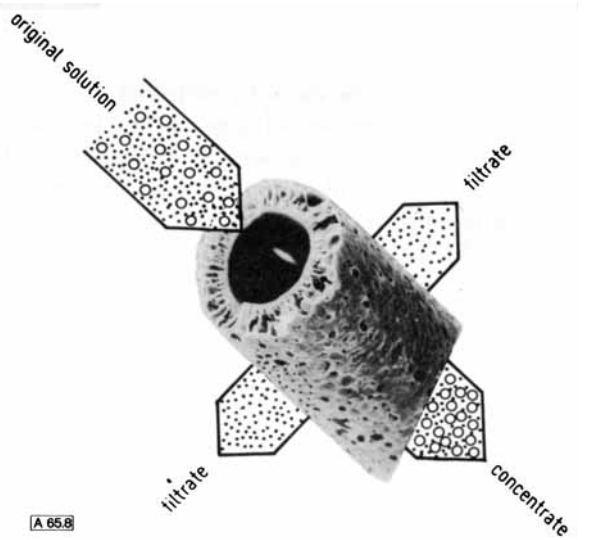


Fig. 8. Schematic representation of filtration through hollow fibers with an inner active layer.

All hollow-fiber filtration systems give not only purified filtrates but also highly concentrated solutions. The latter can be further evaporated and finally dumped or, simply burnt, if their content of organic matter is high.

8. Present and Future Applications of Asymmetric Membranes

The main applications of asymmetric membranes are in the field of desalination of sea water, brackish waters, and river waters. Desalination plants have been built especially in the USA, in Israel, and recently in the Federal Republic of Germany. The water obtained from these plants is sterile, desalted, and completely free from particles.

The recent progress in polymer chemistry now makes it possible to purify the sometimes extremely corrosive industrial waste waters. Here membrane filtration has the edge over other methods of separation in that its mode of operation conserves energy. It has proved its value particularly in the treatment of waste water from dairy plants, from dipping tanks for electrophoretic coating in the automobile industry, and for the separation of oil emulsions. In this way valuable components such as proteins, varnishes, and oils can be recovered. Other fields of application are in the purification of the waste waters from breweries and from factories dealing with fish, starch, dyeing, and coffee. In the pharmaceutical and clinical industry asymmetric membranes are used principally to provide sterile liquids free from microparticles. It would appear advantageous also to use them as artificial kidneys; it might be possible to replace the slow and relatively unspecific dialysis by membrane filtration of blood that would be faster and give considerably sharper separation.

The industrial application of membrane processes is certainly still in its infancy[73, 74]. The development of asymmetric membranes is being directed toward better selectivity and faster rates of filtration; above all, membranes with still greater chemical, mechanical, and thermal resistance are being sought.

In the development of membranes and membrane systems Nature itself can be taken as a model. In Nature membranes are of decisive importance for life, as they fulfill a variety of functions in plant and animal metabolism. Natural membranes are extremely selective, have variable separating proper-

ties, serve as information carriers, give extremely fast transport rates, and take active part in mass transport. A very large number of new uses will follow if membrane research can incorporate just a few of these properties in synthetic membranes.

Received: December 2, 1974 [A 65 IE]
German version: Angew. Chem. 87, 476 (1975)
Translated by Express Translation Service, London

[1] *R. E. Kesting:* Synthetic Polymeric Membranes. McGraw-Hill, New York 1971.
[2] *U. Merten:* Desalination by Reverse Osmosis. MIT Press, Cambridge, Mass. 1966.
[3] *S. B. Tuwinder:* Diffusion and Membrane Technology. Reinhold, New York 1962.
[4] *R. E. Lacey* and *S. Loeb:* Industrial Processing with Membranes. Wiley, New York 1972.
[5] *W. F. Blatt, B. G. Huson, S. M. Robinson,* and *E. M. Zipilivan,* Nature *216*, 511 (1967).
[6] *R. W. Baker,* J. Appl. Polym. Sci. *13*, 369 (1969).
[7] *A. S. Michaels* in *E. S. Perry:* Advances in Separation and Purification. Wiley, New York 1968.
[8] *H. Strathmann, H.-D. Saier, W. Wysocki,* and *U. Müller,* Lebensmitteltechnik *8*, 3 (1973).
[9] *H.-D. Saier* and *U. v. Mylius,* Deut. Milchwirt. *11*, 307 (1974).
[10] *W. Pfeffer:* Osmotische Untersuchungen. Leipzig 1877.
[11] *J. van't Hoff,* Z. Phys. Chem. *1*, 481 (1887).
[12] *S. Loeb* and *S. Sourirajan,* J. Appl. Polym. Sci. *1*, 33 (1959).
[13] *S. Loeb* and *S. Sourirajan:* Advan. Chem. Ser. *38*, 117 (1962).
[14] *S. Loeb* and *S. Sourirajan:* Univ. of California, Los Angeles, Report 60—60 (1960).
[15] *S. Loeb* and *S. Sourirajan,* US-Pat. 3133132 and 3133137 (1964).
[16] *A. G. Horrath,* US-Pat. 1825631 (1931).
[17] *R. A. Cross* and *H. Strathmann* in *B. L. Karger, L. S. Snyder,* and *C. Horvath:* An Introduction to Separation Science. Wiley, New York 1973.
[18] *S. R. de Groot:* Thermodynamics of Irreversible Processes. North Holland, Amsterdam 1959.
[19] *O. Kedem* and *A. Katchalsky,* Trans. Faraday Soc. *59*, 1918, 1931, 1941 (1963).
[20] *H. Podall,* OSW-R. & D. Rep. 303 (1968).
[21] *R. Schlögl:* Stofftransport durch Membranen. Steinkopf, Darmstadt 1964.
[22] *H. Strathmann, R. W. Baker,* and *F. R. Eirich,* J. Phys. Chem. *76*, 238 (1972).
[23] *O. Kedem* and *K. S. Spiegler,* Desalination *1*, 311 (1966).
[24] *A. J. Staverman,* Trans. Faraday Soc. *48*, 176 (1952).
[25] *J. S. Johnson, L. Dresner,* and *K. A. Kraus,* in *K. S. Spiegler:* Principles of Desalination. Academic Press, New York 1966
[26] *W. E. Clark,* Science *138*, 148 (1963).
[27] *S. Loeb* and *S. Manjikian,* Ind. Eng. Chem. Process Des. Develop. *4*, 207 (1965).
[28] *C. E. Reid* and *E. J. Breton,* J. Appl. Polym. Sci. *1*, 133 (1956).
[29] *M. A. Frommer, I. Feiner, O. Kedem,* and *R. Bloch,* Desalination *7*, 393 (1970).
[30] *R. Matz,* Desalination *11*, 207 (1972).
[31] *R. Matz,* Hydronautics Incorporated R. & D. Report 7005-4 to OSW, April 1970.
[32] *R. Matz,* Proc. 41st. Annual Meeting Israel Chem. Soc., Oct. 1971.
[33] *H. Strathmann, H.-D. Saier,* and *R. W. Baker,* 4th Internat. Symp. on Fresh Water from the Sea, Heidelberg 1973.
[34] *H. Strathmann* and *H.-D. Saier,* Chem. Ing. Tech. *46*, 109 (1974), Mikrofiche MS 014/74.
[35] *H. Strathmann, P. Scheible,* and *R. W. Baker,* J. Appl. Polym. Sci. *15*, 811 (1971).
[36] *R. E. Kesting,* J. Appl. Polym. Sci. *17*, 1771 (1973).
[37] *R. L. Riley, H. K. Lonsdale,* and *C. R. Lyons,* J. Appl. Polym. Sci. *15*, 1267 (1971).
[38] *R. L. Riley, H. K. Lonsdale, C. R. Lyons,* and *L. LaGrange,* OSW-R. & D. Rep. 386 (1969).
[39] *M. Cohen* and *B. Riggleman,* OSW-R. & D. Rep. 400 (1969).
[40] *L. T. Rozelle, J. E. Cadotte,* and *B. R. Nelson,* OSW-R. & D. Rep. 725 (1971).
[41] *L. T. Rozelle,* Polym. Prepr. *12*, 261 (1971).
[42] *B. R. Nelson, L. T. Rozelle, J. E. Cadotte,* and *E. M. Scattergood,* Environmental Protection Agency Program No. 12010 D. R. H. U. S. Government Printing Office, Washington, Nov. 1971.
[43] *P. S. Francis* and *J. E. Cadotte,* OSW-R. & D. Rep. 247 (1967).
[44] *P. S. Francis et al.,* OSW-R. & D. Rep. 177 (1964).
[45] *H. Yasuda,* US-Pat. 3775308 (1974).
[46] *H. Yasuda,* Appl. Polym. Symp. *22*, 241 (1973).
[47] *J. R. Hollahan,* Science *179*, 500 (1973).
[48] *G. Canepa, S. Munari, C. Rossi,* and *R. Vigo,* Desalination *13*, 159 (1973).
[49] *G. Tanny* and *J. Jagur-Grodzinski,* Desalination *13*, 53 (1973).
[50] *E. Hoffer* and *O. Kedem,* Desalination *2*, 25 (1967).
[51] *A. E. Marcinkowsky, K. A. Kraus, H. O. Phillips, J. S. Johnson,* and *A. J. Shor,* J. Amer. Chem. Soc. *88*, 5744 (1966); US-Pat. 3449245 (1969).
[52] *J. R. Fryer, J. L. Hutchison,* and *R. Peterson,* Nature *226*, 149 (1970).
[53] *J. Johnson, A. Shor,* and *K. Kraus,* Desalination *2*, 243 (1967).
[54] *C. Eyraud et al.,* US-Pat. 2022187.
[55] *C. W. Saltonstall* and *H. F. Shney,* OSW-R. & D. Rep. 730 (1971).
[56] *S. B. Sachs* and *H. K. Lonsdale,* J. Appl. Polym. Sci. *15*, 797 (1971).
[57] *H. Strathmann,* OSW-R. & D. Rep. 726 (1971).
[58] *T. A. Jameson* and *T. H. Meltzer,* J. Appl. Polym. Sci. *13*, 267 (1970).
[59] *A. Yasuda* and *C. E. Lamaze,* OSW-R. & D. Rep. 281 (1967).
[60] *B. H. Zimm,* and *J. L. Lundberg,* J. Phys. Chem. *60*, 425 (1956).
[61] *H. Strathmann* and *R. W. Baker,* J. Appl. Polym. Sci. *14*, 1197 (1970).
[62] *H. Strathmann,* Chem. Ing. Tech. *44*, 1160 (1973).
[63] *H. Strathmann,* Chem. Ing. Tech. *45*, 825 (1973).
[64] *H. Strathmann* and *B. Keilin,* Desalination *6*, 179 (1969).
[65] *A. J. Shor, K. A. Kraus, J. S. Johnson,* and *W. T. Smith,* Ind. Eng. Chem. Fundam. *7*, 44 (1968).
[66] *U. Merten,* Ind. Eng. Chem. Fundam. *2*, 229 (1963).
[67] Water Waste Treat. *9*, 147 (1964).
[68] OSW-R. & D. Rep. 313, 341 (1968).
[69] Chem. Eng. *78*, 54 (1971).
[70] *H. I. Mahon,* Nat. Acad. Sci. Publ. *942*, 345 (1963), Proc. Desalination Res. Conf.
[71] *W. F. Blatt,* International Laboratory, p. 14, Nov./Dec. 1972.
[72] German Pat. Appl. P 2318346.2, Firma Berghof (1974).
[73] *U. F. Franck,* Lecture, Achema 1973.
[74] *A. S. Michaels,* Chem. Eng. Progr. *64*, 31 (1968).

Stereochemistry of Reaction Paths as Determined from Crystal Structure Data—A Relationship between Structure and Energy

By Hans-Beat Bürgi[*]

The three-dimensional structure of frequently occurring molecular fragments has been studied systematically. Molecular subunits which were examined include hydrogen bridges (O—H···O), triiodide anions (I_3^-), other linear triatomic fragments (Cl—Sb···Cl, S—S···S, Mo—O···Mo), tetrahedral ions (SO_4^{2-}, PO_4^{3-}, $AlCl_4^-$) and related species (MSO_3, *etc.*), molecules containing both keto- and amino-groups (mostly alkaloids), substituted [10]annulenes and cycloheptatrienes, organic five-membered rings, and five-coordinated metal and nonmetal atoms. The bond distances and angles describing the structure of a giving fragment cover a range that is many times larger than the range of the experimental standard deviations. The changes of the various structural parameters of a fragment are correlated with each other. The observed mutual dependence (structural correlation) may be described by means of *Pauling*'s equation relating bond length r to bond number n: $r = r_0 - c \log n$. The bond numbers n are expressed in terms of bond angles. The sum of bond numbers at a given atom is roughly constant and does not depend on the environment. "Standard bond lengths" of a fragment are determined by a least-squares procedure based on all available data. They are supplemented by curves that describe the observed distortions.

The shape of these correlation curves is reminiscent of the structural changes occurring along the pathways of chemical reactions, *e.g.* nucleophilic substitution at tetrahedrally coordinated atoms (S_N1 and S_N2), nucleophilic addition to carbonyl groups, electrocyclic ring closure of polyenes, pseudo-rotation of five-membered rings or Berry pseudo-rotation. For many of these reactions approximate energy hypersurfaces have been obtained from quantum mechanical calculations, model force fields and from spectroscopic information (IR, NMR). Comparison between reaction pathways determined from structural correlations with those obtained from models of the energy surfaces shows fair agreement.

1. Prologue

Energy, chemical reactivity or biological activity of chemical compounds are being correlated more and more successfully with the three-dimensional structure of the respective molecules. Molecular structure has therefore become an observable of central interest, and the techniques to measure it—microwave spectroscopy, electron, neutron and X-ray diffraction—have been developed into routine procedures yielding reliable and accurate information in most cases.

The enormous amount of accurate structural information available at present provokes questions: Does all the information taken together lead to new points of view? What are they? Numerous answers have been attempted. Many of them have contributed substantially to the understanding of the nature of chemical bonding. If we add another paper to the list, it is because we hope to establish a connection between the "statics" of ordered crystalline substances and the "dynamics" of reacting chemical systems.

2. Structural Parameters and Their Standard Values

The idea that molecules may be looked at as collections of atoms connected by bonds has its origin in 19th century chemistry. The classical formulas of organic chemistry indicate that the number and direction of bonds is a characteristic property of an atom. This idea originated before the electron was discovered and it has influenced chemical thinking ever since. With the development of physical methods it became possible to obtain more and more accurate information about the arrangement of atoms in molecules, complex ions and crystal lattices and to measure molecular structure, *i.e.* constitution, configuration and conformation. The results of structure determinations, mainly X-ray analyses, have thus provided some sort of physical reality to the abstract formulas. They have also put them on a metrical basis which consists of tables of interatomic distances and angles.

Nowadays these tables contain many millions of entries. Attempts to systematize the data have shown repeatedly that the interatomic distances between two atoms of a given kind can be divided into two groups: 1. Distances between atoms which are considered to be chemically bonded. The values cluster around a characteristic value called a standard bond length. 2. Distances between atoms not chemically bonded; in general, these are larger than or equal to a limiting value, the van der Waals distance. Standard distances between bonded and nonbonded atoms are usually expressed as sums of standard radii (covalent, ionic or van der Waals radii)[1a, 2]. Their magnitude depends mainly on the kind of atom involved and only slightly on its interactions with neighboring atoms[3].

Bond angles and torsion angles have been given standard values as well. Based on *Le Bel*'s and *van't Hoff*'s postulate of tetrahedral carbon atoms[4], *Baeyer* assumed—30 years before X-ray methods were available—that the bond angles at four-coordinated carbon are 109°28'[5]. The determination of the atomic structure of diamond confirmed this assumption. Later structure determinations of hydrocarbon molecules have led to refinements of *Baeyer*'s hypothesis, *e.g.*, to the reference

[*] Dr. H. B. Bürgi
Laboratory of Inorganic Chemistry
Swiss Federal Institute of Technology (ETH)
CH-8006 Zürich, Universitätsstr. 6 (Switzerland)

values of 109.5 to 112.5° ascribed to C—C—C angles[6]. The preferred torsion angles of saturated hydrocarbons have been found to be 60°, 180° and 300°[7].

The structures of the peptide group[8], the purines and pyrimidines[9] have been standardized too because they are not influenced significantly by their environment. The availability of standard structures of these macromolecular fragments has become an indispensable prerequisite for crystallographic determinations of the three-dimensional structure of enzymes and nucleic acids.

Attempts to understand the variety of structural phenomena in terms of the sum of properties ascribed to molecular or submolecular fragments are typical for chemistry. Additivity relationships help to systematize experimental observations (structural parameters, thermochemical quantities, chemical shifts). This does not mean, of course, that they also explain them.

3. Deviations from Standard Structures—Two Points of View

1. Attempts to build up the variety of molecular structures from only a few structural units and construction principles are always limited by the fact that certain situations are incompatible with the postulated regularities. *Baeyer* had recognized that the C—C—C angles in cyclopentane, a molecule which was known at the time, had to be smaller than 109°28′; he therefore invented the concept of strained molecules[5]. Whenever experimental results emerge that do not quite fit into a scheme, the deviations from the standard are attributed to additional factors. Conjugation, hyperconjugation, donor-acceptor interactions, electrostatic forces, van der Waals attraction, steric factors and geometric constraints are but a few of the quantitative and qualitative concepts and models that are supposed to influence molecular structure and energy. Some of these models are associated with attractive, bonding interactions between atoms, others with repulsive, nonbonding ones. Of course, there are no rigorous quantum mechanical criteria to distinguish bonding from nonbonding interactions, but this should not deter us from the use of these models if they help to classify observations and to make predictions.

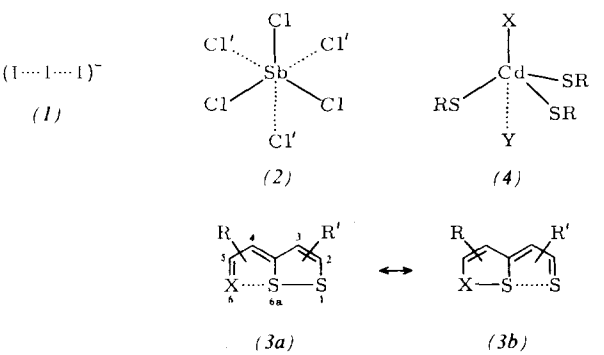
2. In this paper an alternative point of view is developed. We start from the qualitative observation that in many cases *van der Waals* radii are 0.5 to 1.0 Å longer than covalent radii[1a, 2]. As a result the spectrum of interatomic distances should show a gap which separates bonded from nonbonded distances. During the past few years, however, an increasing number of interatomic distances has been found which occupy just this gap between the customary ranges of bonded and nonbonded distances. A good example is the molecular donor-acceptor complex formed by trimethylamine and iodine, $(CH_3)_3N\cdots I—I$[10]. The N···I distance is 2.27 Å, about 0.25 Å more than the sum of the covalent radii (0.70 + 1.33 = 2.03 Å), but 1.4 Å less than the sum of the van der Waals radii (1.5 + 2.15 = 3.65 Å)[1b]. The I—I distance is 2.83 Å, about 0.15 Å longer than the I—I distance in molecular I_2. A list of analogous couples of long bonds and short nonbonded contacts in polyiodide anions and in I_2(s) (Table 1) gives further support to the view that bonded distances cannot always be sharply distinguished from nonbonded distances and that covalent bonds turn into nonbonded interactions continuously.

Table 1. Interatomic distances [Å] in polyiodide anions.

Compound	$d(I^1—I^2)$	$d(I^2—I^3)$	$\sigma(d)$	Ref.
I_2(g)	2.67	4.30	—	[83, 1a]
I_2	2.70	3.54	—	[84]
$[(C_2H_5)_4N]I_7$	2.735	3.435	0.003	[85]
$(NH)_4I_3$	2.791	3.113	0.004	[86]
$[(CH_3)_4N]I_5$	2.81	3.17	0.015	[87]
Cs_2I_8	2.84	3.00	0.03	[88]
CsI_3	2.842	3.038	0.002	[89, 90]
$[(C_5H_5)_2Fe]I_3$	2.85	2.97	0.02	[91]
	2.89	2.97	0.02	
$[(C_2H_5)_4N]I_3$	2.892	2.981	0.004	[92]
	2.912	2.961	0.004	
$[(C_2H_5)_4N]I_7$	2.904	2.904	0.003	[85]
$[(C_6H_5)_4As]I_3$	2.919	2.919	0.001	[89, 93]
$[(C_5H_5)_2Fe]I_3$	2.93	2.93	0.02	[94]
$[(C_2H_5)_4N]I_3$	2.928	2.928	0.003	[92]
	2.943	2.943	0.003	

4. Correlations between Structural Parameters

The simultaneous appearance of a short intermolecular and a long intramolecular distance is a general phenomenon. In the limiting case two indistinguishable interactions are observed. *Bent* has given a graphical correlation of the two distances describing a linear I_3^- fragment *(1)* (Table 1, Figure



(1) *(2)* *(4)* *(3a)* *(3b)*

1a) and found that a hyperbolic curve fits the experimental values with a deviation of less than 0.05 Å. A further example of this type is provided by antimony trichloride. In some crystalline compounds containing $Sb^{III}Cl_3$ the ligand sphere of antimony is completed by three additional chloride ions Cl′ to yield $Cl_3SbCl'_3$ which takes the shape of a distorted octahedron *(2)*. The scatter-plot of the short Sb—Cl distances *trans* to the long Sb···Cl′ distances shows the hyperbolic form also found for I_3^- (Fig. 1)[12].

The two S—S distances in 6a-thiathiophthene derivatives[13] (*(3)*, X = S) are in the range between 2.16 Å and 2.56 Å (Table 2). The long S···S distances are about 0.5 Å longer than the covalent bond in dimethyldisulfane (2.023 Å)[69] and about 1.15 Å shorter than the *van der Waals* contact (3.7 Å). The distribution of the S—S distances (Figure 1c) has the same form as was found for I—I or Sb—Cl distances. The distribution shows a gap between 2.6 and 3.7 Å. In dithiafurophthenes (*(3)*, X = O) the S—S distance is 2.1 Å. The O···S distance is 2.3—2.4 Å, clearly less than the sum of van der Waals radii (3.25 Å). In order to compare the incomparable, *i.e.* O···S distances with S···S distances, we have corrected the observed O···S distances for the difference in covalent radii between O (0.66 Å) and S (1.04 Å)[14]. The corrected distances fill the gap between 2.6 and 3.0 Å (Fig. 1c). The range of distances ob-

served in derivatives of 6a-thiathiophthene indicates that it does not cost much energy to distort the symmetric unsubstituted molecule (*(3)*, X=S, R=R′=H) into an unsymmetrical one, *i.e.* the structure of this type of molecule may be looked at as a sensitive probe for perturbations of many kinds (substituents, crystal lattice, heteroatoms)[148].

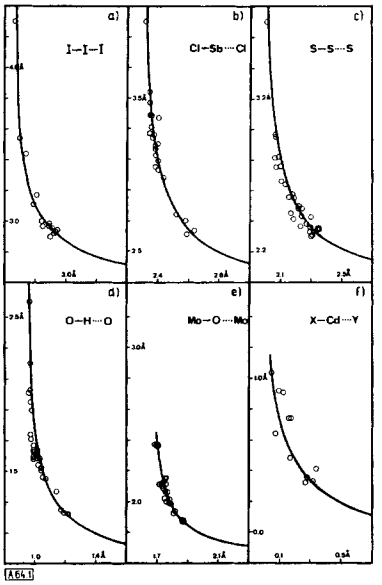


Fig. 1. Scatter plot of interatomic distances in linear three atom molecules and molecular fragments. The curves are described in Section 6.3 equation (15); numerical constants are given in Table 3. a) Polyiodide anions (Table 1). b) Cl—Sb···Cl′ fragments [12]. c) 6a-Thiathiophthenes (Table 2). d) Hydrogen bridges, O—H···O; neutron diffraction data from [17] only (January 1971—March 1972); data from [15] yield the same curve. e) Mo—O···Mo from molybdenum oxides [18]. f) X—Cd(SR)$_3$···Y; observed axial Cd—I, Cd—S and Cd—O distances minus the sum of corresponding covalent radii [14, 16] (cf. Section 6.3).

Other examples of a hyperbolic correlation between the two distances in a linear triatomic fragment are: hydrogen bridges[15, 17], O—H···O (Fig. 1d), oxygen bridges in polymolybdates and molybdenum oxides[18], Mo—O···Mo (Fig. 1e), and trigonal-bipyramidal complexes of cadmium(II)[16], X—CdS$_3$···Y (*(4)*, Fig. 1f).

Correlations of the type described above are not restricted to internuclear distances. An analogous dependence of angles on distances will be illustrated for tetrahedral ions[19]: Most PO$_4$-tetrahedra in phosphates and polyphosphates for example, do not show the highest possible symmetry (T_d). In order to illustrate structural correlations for these ions it is sufficient to discuss PO$_4$-fragments which show approximate C_{3v}-symmetry. These are describable in terms of three parameters (Fig. 2): a unique bond of length r_2, the average $\langle r_1 \rangle$ of the other three bond lengths and the average $\langle \theta_1 \rangle$ of the three bond angles included by r_1 and r_2. If r_2 is longer than $\langle r_1 \rangle$, $\langle \theta_1 \rangle$ is smaller than 109.47°, if r_2 is shorter than $\langle r_1 \rangle$, $\langle \theta_1 \rangle$ is larger

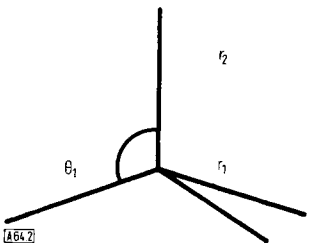


Fig. 2. Parameters describing a tetrahedral molecule with C_{3v} symmetry.

Table 2. S—S, S—O, and S—N distances [Å] in 6a-thiathiophthene and its derivatives *(3)*.

Compound	X	$d(S^1—S^{6a})$	$d(S^{6a}—X^6)$	$\sigma(d)$	Ref.
Dimethyldisulfane	S	2.023	3.7	0.003	[1b, 69]
6a-Thiathiophthene	S	2.361	2.361	0.002	[120]
2,5-Dimethyl-	S	2.358	2.358	0.001	[121]
2,5-Diphenyl-3,4-dimethylene-	S	2.351	2.351	0.001	[122]
2,3,4,5-Tetraphenyl-	S	2.312	2.312	0.002	[123]
2,5-Diphenyl-3,4-dimethyl-	S	2.303	2.303	0.001	[124]
2-(*p*-Dimethylaminophenyl)-4-phenyl-	S	2.348	2.350	0.002	[125]
2,5-Diphenyl-3,4-diaza-	S	2.319	2.328	0.003	[126]
2,5-Diphenyl-	S	2.362	2.304	0.003	[127]
2,3,4-Triphenyl-	S	2.270	2.375	0.003	[128]
2,5-Diphenyl-3-methyl-	S	2.255	2.398	0.001	[129]
2,5-Diphenyl-3,4-trimethylene-	S	2.329	2.288	0.001	[130]
2-Methyl-	S	2.425	2.301	0.002	[131]
2-Methylthio-3-amino-5-phenyl-	S	2.375	2.266	0.004	[132]
2,5-Dianilino-3,4-diaza-	S	2.475	2.225	0.003	[133]
3,4-Diphenyl-	S	2.232	2.434	0.004	[134]
2-Methylthio-3-benzoyl-5-(*p*-bromophenyl)-	S	2.454	2.168	0.008	[135]
		2.561	2.163		
2-Methyl-4-phenyl-	S	2.481	2.242	0.002	[136]
2,4-Diphenyl-	S	2.499	2.218	0.003	[137]
Linear systems with more than three sulfur atoms	S	2.482	2.209	0.001	[138]
	S	2.580	2.183	0.007	[139]
	S	2.583	2.172	0.007	
	S	2.551	2.156	0.002	[140]
1-Bromo-1-nitro-2,4-epidithio-4-phenylbutadiene	O	2.074	2.373	0.007	[141]
2-Nitroso-3,5-epidithio-1,5-diphenyl-2,4-pentadien-1-one	O	2.178	2.034	0.005	[142]
2-(5-Phenyl-1,2-dithiole-3-ylidene)-cyclohexanone	O	2.126	2.255	0.008	[143]
2-(*p*-Dimethylaminophenyl)-4-phenyl-6,6a-dithiafurophthene	O	2.111	2.284	0.004	[144]
	O	2.101	2.443		
2,4-Diphenyl-6,6a-dithiafurophthene	O	2.106	2.382	0.006	[145]
3-Acetamido-1,2,4-dithiazol-5-thione	O	2.064	2.577	0.003	[146]
		2.063	2.567		
3,5-Epidithio-2,5-diphenyl-2,4-pentadienylidene-3-aminoquinoline	N	2.364	1.887	0.007	[147]
2,4-Diphenyl-5-(β-methylthiostyryl)isothiazolium iodide	N	2.814	1.717	0.008	[147]

than 109.47°. For small deviations from T_d symmetry the change in r_2 is roughly equal to minus three times the change in $\langle r_1 \rangle$ (Fig. 3c), *i. e.* the sum of the four bond lengths is approximately constant—a result which also holds for the corresponding t_2 symmetrical normal coordinate of a PO_4-fragment in an environment of T_d symmetry[20]. The ions SO_4^{2-} (Fig. 3a) and $AlCl_4^-$ show the same behavior.

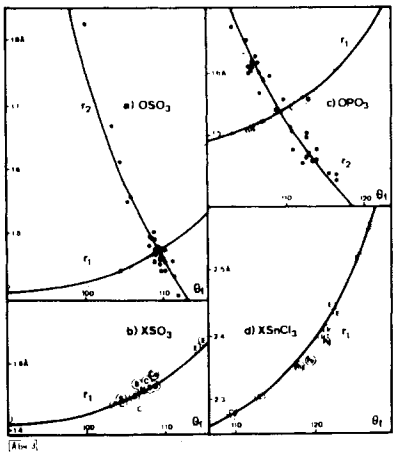


Fig. 3. Scatter plot of distances and angles in approximately C_{3v} symmetrical tetrahedral molecules [19]. Black circles: r_2 *vs* θ_1; open circles: r_1 *vs* θ_1. Letters identify the element M in MSO_3 or $MSnCl_3$, E stands for a lone pair of electrons [22].

The family of $XSnCl_3$ tetrahedra includes compounds containing Sn^{IV} ($SnCl_4$, CH_3SnCl_3) as well as Sn^{II} ($MSn^{II}Cl_3$[22]). In spite of the differences in the nature of the substituents X and of the corresponding differences in the oxidation state of Sn the dependence of $\langle \theta_1 \rangle$ on $\langle r_1 \rangle$ is the same as found for PO_4^{3-} (Fig. 3d). In addition it may be noted that for substituents X of high electronegativity $\langle \theta_1 \rangle$ and $\langle r_1 \rangle$ are smaller than for substituents M of small or vanishing electronegativity[23]. Similar correlations have been observed for XSO_3, XPO_3 and OPX_3 tetrahedra (Fig. 3b).

5. Curve Fitting of the Graphical Correlations by Analytical Formulas

All analytical formulas used to represent the graphical correlations may be obtained from a logarithmic relationship between bond length r and bond strength n originally proposed by *Pauling*[25]:

$$r = r_0 - c \log n \tag{1}$$

In his work on interatomic distances and atomic radii of metals *Pauling* defined the quantity n as the number of electron pairs participating in a bond[26]. The numerical constant r_0 is taken to be the reference bond length of a single bond. The quantity c is an empirical constant; r_0 and c are characteristic of the pair of atoms under consideration.

In order to adapt *Pauling*'s equation for our purposes, n is expressed in terms of structural parameters (rather than in terms of a model that tries to describe the electronic properties of bonds). The description of tetrahedral fragments showing approximate C_{3v}-symmetry is based on the following assumptions

$$n_2 = 9\cos^2\langle \theta_1 \rangle \tag{2}$$
$$n_1 = (4 - 9\cos^2\langle \theta_1 \rangle)/3 \tag{3}$$

The equations have been chosen such that

$$n_2 + 3n_1 = 4 = const. \tag{4}$$

This latter relationship expresses *Pauling*'s postulate, according to which the sum of all bonds around the central atom is a constant[26]. The parameters r_0 and c may be determined by linear regression; they are applicable to the dependence of both $\langle r_1 \rangle$ and r_2 on $\langle \theta_1 \rangle$. The parameters for Al—Cl, Sn—Cl, P—O and S—O bonds are listed, among others, in Table 3. The numerical values of c are found to be equal within their estimated standard deviations (0.02 Å). It is therefore possible to condense all observed pairs $(r - r_0)$ *vs.* $\langle \theta_1 \rangle$ into a single diagram (Fig. 4) and to compare the observed scatter-plots with analytical curves of the form

$$\langle r_1 \rangle - r_0 = 0.5 \log n_1 \tag{5}$$
$$r_2 - r_0 = 0.5 \log n_2$$

This rather surprising result suggests that the characteristic deformations of tetrahedral fragments upon perturbation hardly depend on the type of atoms involved[27]. (An analytical expression for the hyperbolic dependence between two distances in a linear triatomic fragment will be given in Section 6.4.)

Table 3. Numerical values of the constants r_0 and c in equation (1) for various types of bonds (cf. text) [19].

Bond	r_0 [Å]	$-c$ [Å]
Al—Cl [a]	2.125	0.49
Sn—Cl [a]	2.277	0.48
S—O [a]	1.472	0.51
P—O [a]	1.534	0.47
I—I	2.67 [83]	0.85
Sb—Cl	2.26 [b]	1.03
S—S	2.02 [69]	0.83
O—H	0.957 [17]	0.85
Mo—O	1.67 [18]	0.67 [18]
Cd—X		1.05 [16]

[a] Determined by least-squares calculation.
[b] From [1a], corrected according to [3].

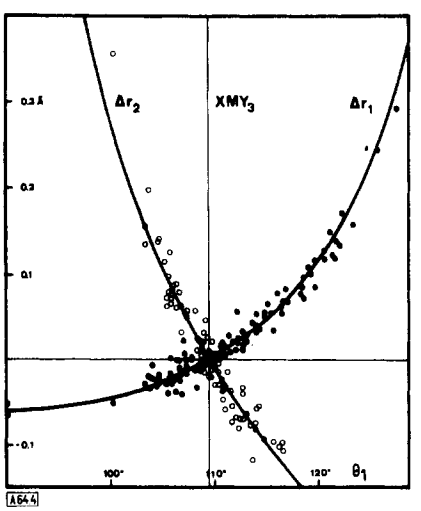


Fig. 4. Scatter plot of distances and angles in approximately C_{3v} symmetrical, tetrahedral molecules. All data referred to a common origin [19].

The correlations shown in figure 4 extend over a range of about 35° in $\langle\theta_1\rangle$ and about 0.4 Å in $\langle r_1\rangle$ or r_2. The deviations of experimental points from calculated curves are in general less than 3° in $\langle\theta_1\rangle$ and less than 0.03 Å in $\langle r_1\rangle$ or r_2; these orders of magnitude are typical also for most other correlation described in this paper.

Equations (1) to (4) should be considered as empirical relationships illustrating the limits between possible and imaginable nuclear arrangements. Interpretations of n in such terms as "bond strength", "bond order" or "bond number" are not normally based on a solid theoretical foundation, but may offer in some instances a clearer visualization of the data. This point of view is further supported by the fact that apart from the logarithmic *Pauling* function, there are various other linear and non-linear relationships between structural parameters[28].

The analytical form of such relationships is unimportant anyway; important is the existence of the correlations which allows us to render more precise and to extend structural concepts such as "standard bond length", "standard bond angle" or "standard structure": The somewhat arbitrary averages over structural parameters from different molecules[29] are replaced by standard structures of high symmetry (if possible). The standard parameters of these (arbitrarily defined) standards are usually not observed experimentally but may be obtained from an appropriate least-squares calculation including all observations. The deviations from such standard structures follow—within narrow limits—curves whose numerical constants are also obtained from the least-squares calculation.

6. Interpretation of Structural Correlation

Although the regularities described in previous paragraphs permit a systematization of a large amount of structural data, there still remains an open question: How can our findings be integrated into the large body of chemical facts and—in particular—how can they contribute to a better understanding of a central chemical phenomenon, namely chemical reactions?

6.1. Chemical Reactions

Our attempts to answer such questions are based on a simple observation: The continuous transition between bonded and nonbonded atomic distances documented by a large body of experimental structural data is a necessary characteristic of any chemical transformation during which existing bonds are broken and new bonds formed.

Currently, chemical reactions are described in terms of their stable starting materials and products as well as their kinetic and mechanistic course. Whereas stable molecules may be characterized fairly exhaustively by means of structure determination, MS, NMR, IR, UV and thermochemistry, many of the postulated reaction mechanisms rely on more or less unique interpretations of kinetic and other mechanistic information. Results of such experiments are cast into the form of simple energy profiles which represent a connection between an energetic coordinate and a structural or reaction coordinate (Fig. 5). In spite of the popularity of such diagrams, their coordinates are rarely given an accurate definition.

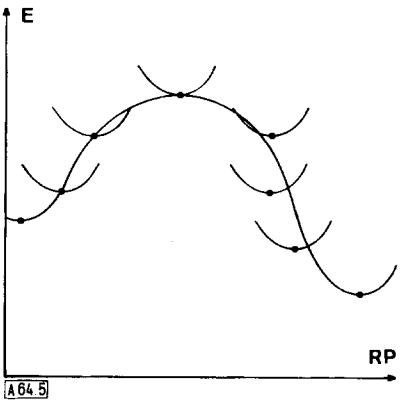


Fig. 5. Energy profile. E = Energy, RP = Reaction path.

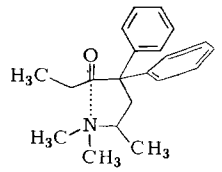
Eyring and *Polanyi*[30] assumed that every chemical reaction is to be described in terms of an energy hypersurface. The path (trajectory) followed by an individual molecule on this surface depends on the magnitude and direction of its momentum which, in general, will be different for every molecule. For the subsequent discussion we neglect the dynamic aspects of a real chemical reaction and consider only the energy hypersurface. On such a surface we define curves which connect the minima (representing starting materials, products and intermediates) along "valleys" and across "passes" (representing activated complexes)[31]. These curves do not depend on the vibrational, rotational and translational energy distribution in the molecules. We call the curves minimum energy pathways or simply reaction paths. Information about the detailed course of such pathways, *i.e.* about the synchronous changes in distances and angles, is scarce. Quantum mechanical calculations and empirical model force field calculations are now beginning to fill this gap; however, for a molecule of chemical interest these methods still require an often prohibitive computational effort.

If it were possible, however, to freeze-in reacting molecules at any desired point along a reaction path, the nuclear configuration at this point could be investigated at leisure. The procedure could be repeated for a sufficient number of points (Fig. 5) and the resulting sequence of "still" photographs, arranged in the right order, could provide the basis for a cinematical animation showing the synchronous nuclear motions along the reaction path. In practice, appropriate molecular or crystalline frameworks have to be found which fix reactive chemical fragments at a certain point of the reaction path. Intra- or intermolecular strain in the framework provides the driving force to push the reactive groups away from the minima and towards an activated complex. Such structures can be investigated by conventional methods of structure analysis.

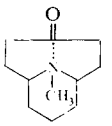
6.2. Nucleophilic Addition to Carbonyl Groups

The ideas outlined above are exemplified by the structures of a series of alkaloid and related molecules [*(5)—(12)*], all of which contain a tertiary amino group and a carbonyl group. The conformations of the C_3- or C_4-chains connecting these groups are such as to permit a close approach of the amine N to the carbonyl C. The shorter the N···C distance the more the carbonyl group is pyramidalized[32]. In the extreme [*(12)*] a tetrahedral intermediate is observed.

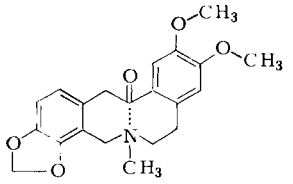
An analytical relationship describes the correlation between the distance d(N···C) and the deviation Δ of the carbonyl



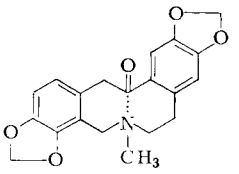
(5)[95]



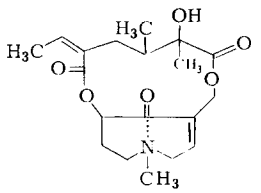
(6)[96]



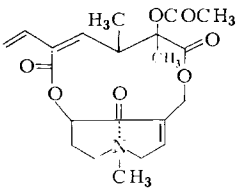
(7)[97]



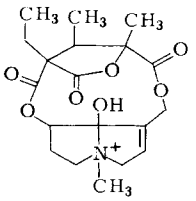
(8)[98]



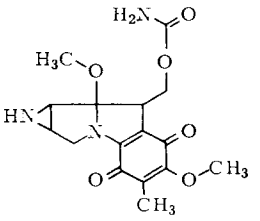
(9)[99]



(10)[100]



(11)[101]



(12)[102]

carbon atom out of the plane defined by its three ligands R, R′ and O (Fig. 6a):

$$d(\mathrm{N\cdots C}) = -c_1 \log n_1 + d(\mathrm{C—N}) \qquad (6)$$

The constant c_1 is 0.85 Å; the standard C—N single bond length d(C—N) is 1.48—1.50 Å; $n_1 = (\Delta/\Delta_{max})^{2}$[119]; Δ_{max}, the value of Δ for a tetrahedral intermediate, is 0.44—0.42 Å (Fig. 6a). A similar relationship may be given for the carbonyl group:

$$d(\mathrm{C{=}O}) = -c_2 \log n_2 + d(\mathrm{C-O}) \qquad (7)$$

Pauling's value of 0.71 Å was chosen for c_2; the standard C—O single bond length is 1.43 Å; we require, as above, that $n_2 = 2 - n_1$ in order to keep the sum of the bonds constant.

The positions of the nitrogen atoms relative to the carbonyl group define a line passing through the carbonyl carbon atom and forming an angle of about 107° with the C=O bond; this line is approximately in the plane bisecting the angle RCR′. Furthermore, this line coincides to within a few degrees with the orientation of the nitrogen lone pairs (estimated on the basis of the three C—N bond directions in the tertiary amine) (Fig. 6b). Replacing nitrogen by a less nucleophilic oxygen but keeping the nucleophile ··· electrophile distance the same, clearly reduces pyramidalization at carbonyl carbon[33]. This finding suggests that the pyramidalization Δ and its dependence on distance may be considered as a structural measure of the nucleophilicity of the entering group[34].

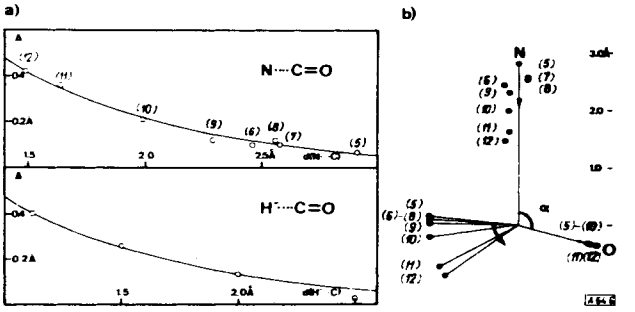
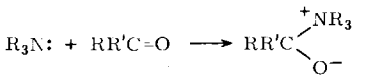


Fig. 6. Reaction path for nucleophilic addition to a carbonyl group a) Δ *vs.* d(N···C), structural data (top): Δ *vs.* d(H⁻···C), computed data (bottom). b) Projection of the RR′C(O)(NR$_3$) group on to the N···C=O plane showing nucleophilic nitrogen (top), carbonyl oxygen (bottom right) and inclination of RCR′ plane (bottom left). Compounds (5)—(12).

The data, ordered with respect to decreasing N···C distance, may be looked at as a series of snapshots along a continuous reaction path describing nucleophilic addition of amine nitrogen to carbonyl carbon:



$$R_3N: + RR'C{=}O \longrightarrow RR'C(^{+}NR_3)(O^{-}) \qquad (8)$$

The nitrogen lone pair approaches the electrophilic carbon of the carbonyl group at an approximately tetrahedral angle. During this process the carbonyl group pyramidalizes and the C—O bond length increases until a tetrahedral four-coordinated carbon—a tetrahedral intermediate—is reached. The same path, traveled in reverse, also describes the decay of the tetrahedral intermediate. This pathway agrees with the generally accepted mechanism of nucleophilic addition[35].

Storm and *Koshland*[36] have measured the highest rates of lactonization for molecules with intramolecular O···C=O angles α (Fig. 6b) of about 98°. Both kinetic and structural data therefore lead to the conclusion that the angle of nucleophilic attack is larger than 90° and amounts to 100—110° along the reaction path and, therefore, also at the transition state[37].

According to our working hypothesis the correlation between d(N···C=O) and Δ (Fig. 6) represents a model for the structural course of the reaction (8) or, in other words, coincides with a valley of the corresponding energy surface. This hypothesis has to be justified, at least in a qualitative sense, because the structural parameters are obtained from molecules and crystal lattices at equilibrium and do not yield direct energetic information. In the present case Hartree-Fock-SCF-LCGO-MO calculations for a simplified model reaction were performed: the formation of a methoxide anion from a formaldehyde molecule and a hydride anion[38]

$$CH_2O + H^- \rightarrow CH_3O^- \qquad (9)$$

The reaction path (Fig. 7) was calculated as a function of the distance d(H⁻···C=O) by minimizing the total energy with respect to the relevant structural parameters Δ and d(C=O). The energy surface is symmetric with respect to the mirror plane perpendicular to the plane of formaldehyde and the entire reaction path is on this mirror plane. For distances d(H⁻···C) > 3 Å the reaction path is in the plane of the formaldehyde molecule and on the HCH bisector. For 3 Å > d(H⁻···C) > 2.5 Å the path curves out of the molecular plane but the H⁻···H distance stays essentially constant at about 2.7 Å. The last part of the reaction path shows the nucleophilic

hydride anion attacking the electrophilic carbon which becomes increasingly pyramidalized and whose distance to oxygen increases. The $H^- \cdots C{=}O$ angle of attack is 120—109° (Fig. 7). The relationship between $d(H^- \cdots C)$ and Δ (bottom of Fig. 6a) is given by

$$d(H^- \cdots C) = -0.9 \log(\Delta/0.4)^2 + 1.13\,\text{Å} \qquad (10)$$

The total energy decreases as the reaction progresses without going through a maximum. It reaches a minimum for the methanolate anion. The total change in energy amounts to 48 kcal/mol. The valley in the energy surface becomes narrower as the interactions between the 1s-orbital of H^- and the π- and π^*-orbitals of CH_2O increase in importance.

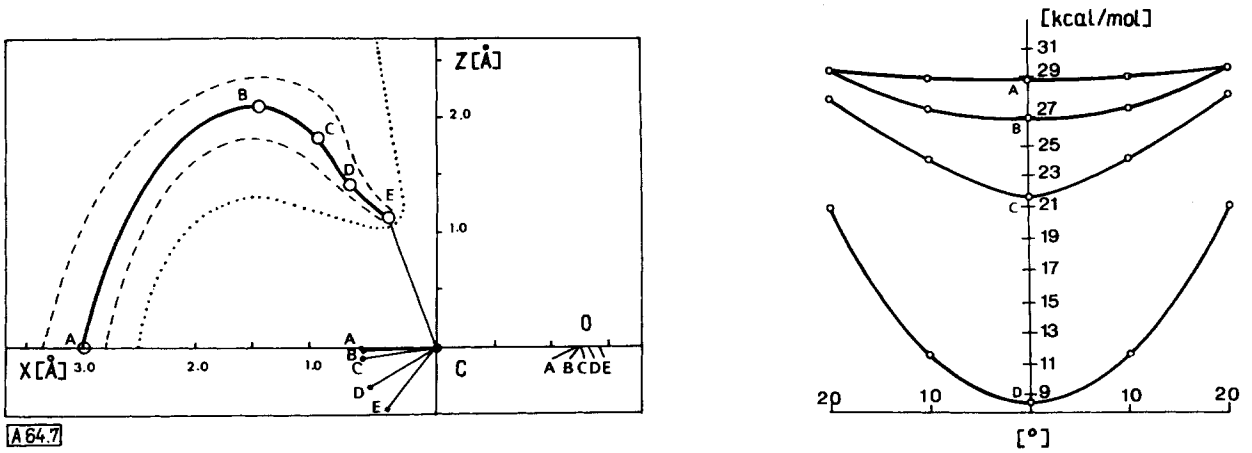


Fig. 7. Computed reaction path for nucleophilic addition of H^- to CH_2O. Points A—E correspond to $H^- \cdots C$ distances of 3.0, 2.5, 2.0, 1.5 and 1.12 Å. Stabilization energies relative to the separated reactants are 19.4, 21.2, 26.7, 39.9 and 48.4 kcal/mol. The dashed and dotted curves show paths that are 0.6 and 6.0 kcal/mol higher than the minimum energy path (left). Energy profiles for lateral angular displacements out of the XZ plane (right).

The agreement between structural, kinetic and quantum chemical results seems to justify the conclusion that the reaction path of Fig. 6 pictures the essential stereochemical characteristics of nucleophilic addition. The formation and hydrolysis of acetals, ketals, esters, amides, anhydrides *etc.* should proceed along similar pathways[37] even though the exact direction of nucleophilic attack and the degree of pyramidalization at carbonyl carbon will depend on the type of nucleophile carbonyl interaction[33], on stereoelectronic factors[37, 39-42] and on nonbonded interactions between the substituents of the reactive groups.

The carbonyl group plays a central role in chemistry and biochemistry: It is an important constituent of many natural and synthetic molecules, it undergoes many reactions and may serve as a starting point for generating molecular asymmetry. The results discussed here may be combined with others obtained from further investigations of the structure and energy of transition states in order to achieve a more detailed understanding of enzymatic reactivity and specificity; the crystal structures of complexes between the proteolytic enzymes chymotrypsin[43a] or trypsin[44] and some natural inhibitors indeed represent intermediate points on the reaction path leading to the tetrahedral intermediate of amide hydrolysis; the structural data are in accord with the stereochemical course outlined in this section for such a reaction[43b].

6.3. Nucleophilic Substitution at Tetrahedral Molecules

This type of reaction is especially well investigated for carbon chemistry. The rate limiting step is either bimolecular (S_N2) or unimolecular (S_N1). Hypotheses concerning the structural course of S_N2 reactions require the breaking of the bond between central atom and leaving group to be simultaneous with the formation of the bond between central atom and entering nucleophile. The energy profile shows a single maximum (transition state) situated between two minima (starting materials and products). During an S_N1 reaction, however, the leaving group dissociates and a planar tricoordinated, solvated intermediate is formed. After a certain time the intermediate forms a bond to the entering nucleophile. The kinetic or mechanistic classification used above seems meaningless in the context of correlations among structural parameters; nevertheless, we have retained the nomenclature of *Hughes* and *Ingold*[45] in order to indicate that for S_N2 reactions all bond lengths and angles of the entity "tetrahedral molecule—entering nucleophile" have to be correlated, whereas for S_N1 reactions only the structural parameters of the tetrahedral molecule have to be taken into account.

S_N2 Reactions

Crystal structure data of a variety of different cadmium complexes may be ordered in such a way as to describe the structural changes typical of an S_N2 reaction at a tetrahedrally coordinated atom[16].

The complexes under consideration all contain Cd^{II}-ions in a distorted trigonal bipyramidal environment [*(4)*]. The three equatorial ligands are bonded to cadmium *via* sulfur atoms. The axial ligands X and Y are bonded *via* iodine, sulfur or oxygen atoms. The different types of axial metal-to-ligand distances are transformed into comparable distance increments Δx and Δy by subtracting the appropriate sum of covalent radii from the observed distances $d(Cd \cdots X)$ and $d(Cd \cdots Y)$[14]. In general the cadmium atom does not lie in the plane of the three equatorial sulfur atoms. Its deviation out of this plane towards the axial ligand X is given by the parameter Δz. For $\Delta z > 0$ the average angle $\alpha_X = \langle \alpha(X \cdots Cd{-}S) \rangle_3$ is larger, the average angle $\alpha_Y = \langle \alpha(Y \cdots Cd{-}S_3) \rangle_3$ is smaller than 90°[46].

From a scatter-plot of Δx, Δy and Δz the following trends may be seen (Fig. 8): If Δx is small, Δy and Δz are large; as Δx increases, Δy and Δz decrease. If $\Delta x \approx \Delta y \approx 0.32$ Å, then $\Delta z \approx 0$ Å, *i.e.* the coordination of the cadmium atom

is trigonal bipyramidal, the two axial distances are about 0.3 Å larger than the sum of covalent radii and about equal to the sum of ionic radii. The changes of the equatorial Cd—S distances do not seem to correlate with changes in axial distances[16].

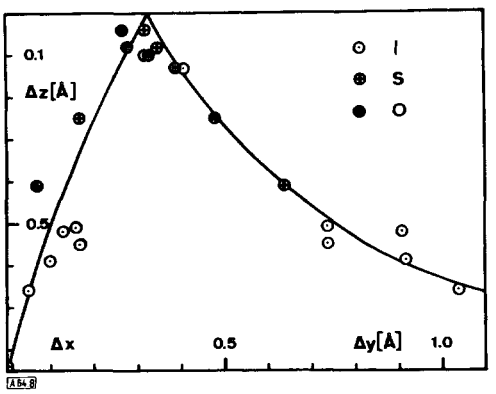


Fig. 8. Nucleophilic substitution at Cd^{II}: Scatter plot of Δz *versus* the distance increments Δx, Δy [14]. (Compare text and eq. (13).)

The experimental results of Figure 8 may be represented by equations (11)[46]

$$\begin{aligned}\Delta x &= -1.05\log(\tfrac{1}{2}+\tfrac{3}{2}\cos\alpha_X)\\ \Delta y &= -1.05\log(\tfrac{1}{2}+\tfrac{3}{2}\cos\alpha_Y)\end{aligned} \qquad (11)$$

The numerical constants are chosen such that the function passes through the points [$\Delta x=0$, $\alpha_X=109.47°$] and [$\Delta y=\infty$, $\alpha_Y=70.53°$]. Identification of $(\frac{1}{2}+\frac{3}{2}\cos\alpha_X)$ and $(\frac{1}{2}+\frac{3}{2}\cos\alpha_Y)$ with *Pauling*'s bond numbers n_X and n_Y leads to an invariance similar to the one used in the case of nucleophilic addition to carbonyl:

$$n_X+n_Y=1 \qquad (12)$$

This relation holds at any point along the reaction path. The mutual dependence of Δx and Δy is thus obtained from equations (11) and (12) to be

$$10^{-(\Delta x/1.05)}+10^{-(\Delta y/1.05)}=1 \qquad (13)$$

This function shows a hyperbolic shape. It describes the distribution of distances not only in the fragment X—CdS_3···Y, but also in the linear, triatomic fragments discussed earlier and shown in Figure 1: I_3^-, S···S—S, Cl···Sb—Cl, Mo···O—Mo, O···H—O. Most of these triatomic molecular fragments may be considered as three-center four-electron systems. The corresponding similarity in electronic structure may thus be responsible in part for the similarity in scatterplots over wide ranges of distances (compare section 7.3).

The correlations observed in the case of the cadmium complexes describe the structural course of the reaction

$$Y + CdS_3X \rightarrow Y\cdots CdS_3\cdots X \rightarrow YCdS_3 + X \qquad (14)$$

The reaction starts from a tetrahedral CdS_3X complex with a potential, fifth ligand Y on the face of the tetrahedron opposite X. As Y approaches Cd, the CdS_3-pyramid flattens and X moves away from Cd. Once the distance increments Δx and Δy are equal, Cd is coplanar with its three sulfur atoms. As Y moves closer to Cd, X moves further away from it and the reaction terminates with a $YCdS_3$ complex (showing an inverted CdS_3 pyramid) and a ligand X.

The same sequence of structural changes has been postulated to occur during S_N2 reactions at carbon. For lack of data this hypothesis cannot be tested by means of structural correlations[47]. The hypothesis is in general agreement, however, with results obtained from *ab initio* calculations[48] on the reactions

$$\begin{aligned}FCH_3 + F^- &\rightarrow [F\cdots CH_3\cdots F^-] \rightarrow F^- + CH_3\\ FCH_3 + H^- &\rightarrow [F\cdots CH_3\cdots H^-] \rightarrow F^- + CH_4\end{aligned} \qquad (15)$$

The axial bonds in the trigonal bipyramidal transition state (or intermediate) are clearly longer than the corresponding bonds in the tetrahedral molecules (by 0.85 Å for C—H; by 0.5 Å for C—F; by 0.3 Å for Cd—X and Cd—Y)[49]. Analyses of calculated electron distributions in trigonal bipyramidal molecules and transition states[48, 50] reveal strong ionic character of the axial bonds and increased covalent character of the equatorial bonds. This is in qualitative agreement with the picture obtained from bond distances.

S_Ni Reactions

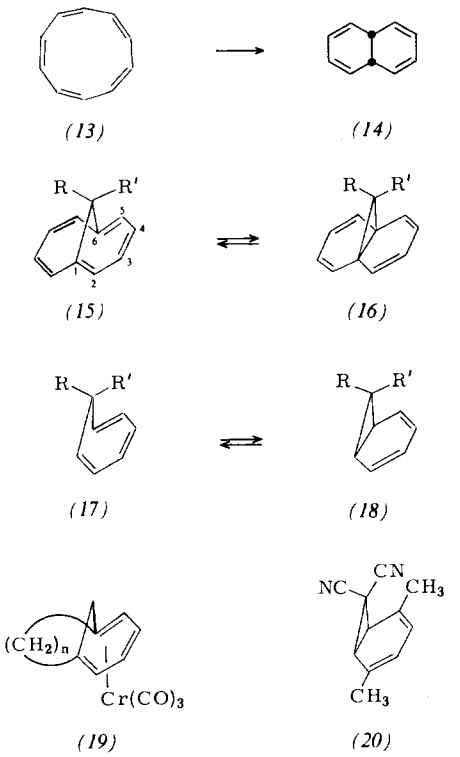
In Section 4 we discussed some similarities in the distortion patterns of $AlCl_4^-$-, PO_4^{3-}- and SO_4^{2-}-tetrahedra of approximate C_{3v} symmetry. As the axial bond length r_2 increases, $\langle r_1\rangle$ decreases and the central atom approaches the plane of the three equivalent ligands (Fig. 4). The observed structural correlations correspond to the distortions of a T_d symmetric molecule during an S_Ni reaction: The axial bond is cleaved and planar trigonal molecules such as $AlCl_3$ and SO_3 are formed. Detailed information on corresponding deformations of four-coordinated carbon atoms is sparse. However, the relevant parameters of *tert*-butyl chloride[51], the prototype of a molecule with S_Ni reactivity, are close to our curves. This may be an indication that they are an acceptable approximation for the S_Ni reaction path of *tert*-butyl chloride.

The correlation between $\langle r_1\rangle$ and $\langle\theta_1\rangle$ obtained from molecules of the type MSO_3 and $MSnCl_3$ also describes the removal of an electron pair from a tricoordinated pyramidal fragment, *e.g.* $SO_3^{2-}\rightarrow SO_3+2e^-$. The points mapping this oxidation process lie on the same curve as those mapping the S_Ni dissociation of a four-coordinated tetrahedral fragment (Fig. 3b, d).

6.4. Electrocyclic Reaction: A Disrotatory Ring Closure

According to orbital symmetry considerations[52] a chemical reaction should proceed with low activation energy and in a concerted manner when all occupied orbitals remain bonding during the entire reaction. The electrocyclic ring closure cyclodecapentaene (*13*) → *cis*-4a,8a-dihydronaphthalene (*14*) is a thermally allowed process and seems to occur at about −10 °C[53]. The course of the reaction path will be determined by changes in conformation, π-conjugation, hybridization and by changes in bonding interactions between C(1) and C(6) as well as in nonbonding interactions between H(1) and H(6).

Molecules suitable to map part of such a reaction path include 1,6-methano[10]annulene (*15*), R=R′=H) and its substituted derivatives. In this survey, substituted cycloheptatrienes and norcaradienes are also included because they pertain to the related reaction: hexatriene→cyclohexadiene. The



(13) (14) (15) (16) (17) (18) (19) (20)

barrier for the process (15)→(16) (R=R′=CH_3) has been measured by ^{13}C-NMR experiments and was found to be smaller than 6.6 kcal/mol[54]. 11,11-Dimethyl-1,6-methano-[10]annulene ((15), R=R′=CH_3) is more stable (by 0.2 kcal/mol!), 11-cyano-11-methyl-1,6-methano[10]annulene ((15), R=CN, R′=CH_3) is less stable than the corresponding tricyclic tetraene (16). The barrier between 7,7-dimethoxycarbonylnorcaradiene and the corresponding cycloheptatriene is about 7 kcal/mol, the former being more stable by 0.25 kcal/mol[55]. The results show that the structure of these compounds is very dependent on perturbations. In the crystalline state the distance between the bridgehead atoms C(1) and C(6) of (15) (R=R′=CH_3) has been determined to be 1.78 Å and 1.83 Å from two symmetry-independent molecules. The lengthening relative to a C—C bond in cyclopropane is 0.3 Å. Corresponding C···C distances in cycloheptatriene derivatives (19), coordinated to $Cr(CO)_3$ are 1.65 Å (n=3)[57] and 1.72 Å (n=4)[58]. In all four molecules mentioned C(1) deviates by an amount Δ from the plane defined by its three carbon ligands. The deviation is towards C(6). The corresponding deviation of C(6) is towards C(1). The differences between C···C bond lengths of the perimeter are large and significant for cyclopropane derivatives (≈0.13 Å) but small and partly insignificant for open compounds (≈0.03 Å, Table 4)[59].

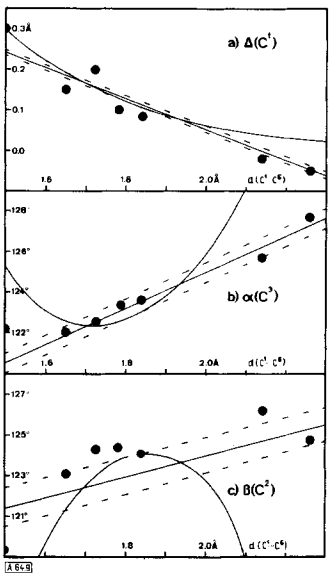


Fig. 9. Electrocyclic ring closure reaction. Experimental data from Table 4. The curve represents a computed reaction path based on eq. (16), the straight lines represent a reaction path showing minimum angle strain at C(2) and C(3) with reference angles of 125° (top line, dashed), 122.5° (middle line, solid), 120° (bottom line, dashed).

In order to discern the minimum energy pathway for the electrocyclic reaction from intramolecular strain in the polycyclic skeletons we have analyzed two models, both of which are based on an idealized molecule. This molecule is assumed to have C_{2v} symmetry and to show a coplanar arrangement of atoms C(1) to C(6). The bond lengths are assumed to be 1.4 Å in the perimeter and 1.5 Å in the methano bridge with an angle of 110° between the six-membered and the three-membered ring fragment. The structure of this molecular model is entirely determined by only two additional variables.

Table 4. Distances [Å] and angles [°] in derivatives of [10]annulene (15) and cycloheptatriene [(19), (20)] (averages).

	⟨Δ⟩	⟨α(C(3))⟩	⟨β(C(2))⟩	⟨β(C(2))corr.⟩ [a]	d(C(1)···C(6))	⟨d(C(1)—C(2))⟩	⟨d(C(2)—C(3))⟩	⟨d(C(3)—C(4))⟩
2,5-Dimethyl-7,7-dicyanonorcaradiene (20) [103]	0.32 [b]	122.2	118.8	119.3	1.501	1.480	1.351	1.452
(Bicyclo[4.3.1]deca-1,3,5-triene)tricarbonylchromium ((19), n=3) [57]	0.15	122.0	119.4	123.0	1.65	1.47	1.38	1.43
(Bicyclo[4.4.1]undeca-1,3,5-triene)tricarbonylchromium ((19), n=4) [58]	0.20	122.5	121.0	124.3	1.72	1.47	1.37	1.41
11,11-Dimethyltricyclo[4.4.1.0^{1,6}]undeca-2,4,7,9-tetraene ((16), R=R′=CH_3) [56]	0.102	123.3	123.9	124.5	1.780	1.458	1.335	1.419
(1,6-Methanocyclodecapentaene)tricarbonylchromium [(15)-$Cr(CO)_3$] [104]	0.083	123.6	123.8	124.1	1.836	1.453	1.348	1.431
11,11-Difluoro-1,6-methanocyclodecapentaene ((15), R=R′=F) [105] [c]	−0.02	125.7	122.0	126.2	2.14	1.44	1.39	1.41
1,6-Methanocyclodecapentaene-2-carboxylic acid ((15), R=R′=H) [106]	−0.08	128.8	122.5	124.0	2.25	1.44	1.38	1.37
	−0.053	127.7	122.3	124.8	2.257	1.409	1.383	1.415

[a] The observed angles between the best planes through atoms C(2)—C(5) and through atoms C(1), C(2), C(5), C(6) amount to as much as 20°. Corrected β(C(2)) values were calculated from the observed ones for coplanar atoms C(1)—C(6). These are comparable with the molecular model (compare text).
[b] Calculated assuming three carbon atoms at a distance of 1.49 Å from C(1).
[c] Disordered crystal structure.

One of our models assumes as an additional constraint that the minimum energy pathway is determined by the condition of minimum angle strain at C(2) and C(3) for any distance C(1)···C(6). The reaction paths, calculated for zero strain angles of 120°, 122.5° and 125°, are shown as three straight lines in Fig. 9. The other model assumes a reaction path determined by a logarithmic dependence of d(C···C) on Δ (similar to eq. (6)):

$$d(C(1)\cdots C(6)) = -0.71\log(\Delta/\Delta_{max}) + d(C{-}C) \qquad (16)$$

The prelogarithmic constant is the same as the one chosen by *Pauling* for C—C bonds; $\Delta_{max} \approx 0.31$ Å and d(C—C) ≈ 1.50 Å (from (20)). The corresponding, calculated reaction path is shown as curves in Figure 9. A comparison of the experimental structures with the calculated pathways indicates that the bonding interaction between atoms C(1) and C(6), expressed in equation (16), does influence the course of the pathway at short C(1)···C(6) distances (1.5—1.7 Å). Between 1.7 and 2.0 Å both models yield the same path, which agrees reasonably well with the experimental data. For long C(1)···C(6) distances (>2.0 Å) the condition of minimum angle strain seems to fit the experimental values best. These observations indicate that observed structural correlations are a result of all intra- (and inter-)molecular interactions. If their individual contributions to the observed structure cannot be separated, structural correlations should be interpreted with caution (compare Section 6.2).

6.5. Intramolecular Processes with Small Energy Barriers: Pseudorotation of Cyclopentane

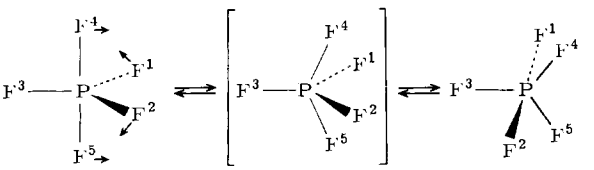
The conformation of the nonplanar cyclopentane molecule is indeterminate because the maximum torsion angle ω_0 may travel from one bond to the next at practically no cost in energy[61]. The C_s- and the C_2-conformation are special only because of their symmetries but not because of their energies which are the same within a few wave numbers as those of all nonsymmetric conformations. The five torsion angles ω_i describing an arbitrary conformation of the ring are obtained from the relationship[62, 63]:

$$\omega_i = \omega_0 \cdot \cos\left(\frac{4\pi i}{5} + \varphi\right) \quad (i = 1, 2, \ldots 5) \qquad (17)$$

The phase angle φ is a cyclic coordinate describing a path of practically constant energy, the pseudorotation pathway. The maximum torsion angle is given by ω_0. The change in energy due to changes in ω_0 is quadratic in $\Delta\omega_0$ as long as $\Delta\omega_0$ is small. For $\Delta\omega_0 = -\omega_0$ the ring is planar and the energy corresponds to a local maximum. Substituents on the five-membered ring hinder free pseudorotation[62] and may thus freeze in any conformation of the ring. Ring D of steroids may serve as an example. The average of ω_0, determined from 11 different structures, is 46.7 ± 2.6°; the phase angle φ, however, takes any value within the asymmetric unit of the pseudorotation pathway ($0° < \varphi < 18°$)[63]. In furanose rings of β-purine or β-pyrimidine glycosides ω_0 averages 38—40° with standard deviation of 3—4°. The phase angles φ are distributed uniformly between 0 and 18°. There is no obvious correlation between ω_0 and φ[64].

6.6. Intramolecular Processes with Low Activation Energy: The Berry Mechanism

The NMR spectrum of the trigonal bipyramidal molecule PF_5 shows only one kind of fluorine nucleus, even at low temperature[65]. This was interpreted by *Berry* in terms of a rapid intramolecular exchange between axial and equatorial fluorine atoms. The reaction path proposed by *Berry* starts at the D_{3h}-symmetric PF_5 molecule *(21)*, passes through a tetragonal-pyramidal C_{4v}-symmetric transition state *(22)* and ends at the D_{3h}-symmetric product molecule *(23)*. All nuclear configurations along the minimum energy pathway retain at least C_{2v} symmetry. Empirical force-field calculations[67, 68], semiempirical[50] and nonempirical[70] quantum mechanical calculations have helped this mechanism to widespread recognition. Its energy barrier is estimated to be <6 kcal/mol.



(21) *(22)* *(23)*

The coordination polyhedra of MX_5-type molecules have been described as trigonal bipyramids, tetragonal pyramids

Table 5. Selected bond angles (α_{ij}) for ML_5 complexes of the type *(21)* and selected dihedral angles (φ_{ij}) between adjacent faces of the corresponding coordination polyhedra [71] in [°].

Compound	α_{13}	α_{23}	α_{34}	α_{35}	φ_{13}	φ_{23}	φ_{34}	φ_{35}
$CdCl_5^{3-}$ [107]	120	120	90	90	53.8	53.8	101.1	101.1
$Ni[P(OC_2H_5)_3]_5^{2+}$ [108]	119.3	117.5	91.5	90.1	54.2	57.3	98.0	98.9
$Mn(CO)_5^-$ [109]	118.5	118.0	89.4	89.8	—	—	—	—
	117.6	117.5	90.3	91.5	—	—	—	—
$Co(CNCH_3)_5^+$ [110]	115.9	115.9	89.2	89.2	—	—	—	—
$Fe(CO)_5$ [111]	116	116	90	90	—	—	—	—
$Ni(CN)_5^{3-}$ [112]	111.5	107.4	92.3	94.4	62.7	68.6	87.4	88.2
	100.9	99.4	96.8	103.9	75.0	79.4	78.2	78.5
$Ni(CN)_5^{3-}$ [113]	99.2	99.2	99.0	99.0	—	—	—	—
$Nb(NC_5H_{10})_5$ [114]	112.0	109.0	97.3	99.5	65.4	67.0	85.7	87.0
	110.1	106.6	100.5	100.2	68.2	70.6	82.6	82.8
$Nb(N(CH_3)_2)_5$ [114]	109.1	109.1	101.5	101.5	70.2	70.2	83.0	83.0
$Fe(N_3)_5^{2-}$ [115]	118.3	118.3	93.1	93.1	—	—	—	—
$Co(C_6H_7NO)_5^{2+}$ [116]	115.4	113.7	94.7	91.4	54.5	58.5	93.4	98.6
$P(C_6H_5)_5$ [117]	119.6	117.8	91.9	91.1	51.8	52.3	101.3	101.4
$Sb(C_6H_5)_5$ [118]	106.0	104.8	99.6	96.4	68.5	69.2	79.7	82.0

or distorted variants of these forms. *Muetterties* and *Guggenberger*[71] have characterized the polyhedra in terms of the dihedral angles defined by two neighboring polyhedral faces. They found that these angles show very closely C_{2v} symmetry, *i.e.* the polyhedra fulfill the condition to lie on the Berry reaction path. The scatter plot of average dihedral angles, $(\varphi_{13}+\varphi_{23})/2$ *versus* $(\varphi_{34}+\varphi_{35})/2$ (Table 5, Fig. 10), is the basis of a continuous curve (Fig. 10a) and has been interpreted in terms of the reaction path of the Berry mechanism[71]. In an alternative representation, averages of bond angles, $(\alpha_{34}+\alpha_{35})/2$ *versus* $(\alpha_{13}+\alpha_{23})/2$ (Table 5) are plotted. This representation shows that the angle between axial and basal ligands of the tetragonal pyramid determines the details of the reaction path. The angle is between 99° (d^8 cations) and 105° (d^0 cations).

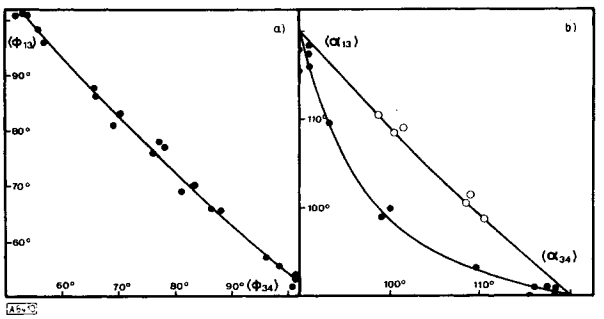


Fig. 10. Berry mechanism (Table 5): a) Scatter plot of $\langle\varphi_{13}\rangle=(\varphi_{13}+\varphi_{23})/2$ *versus* $\langle\varphi_{14}\rangle=(\varphi_{34}+\varphi_{35})/2$. b) Scatter plot $(\alpha_{13}+\alpha_{23})/2$ *vs.* $(\alpha_{34}+\alpha_{35}/2$ for d^0 cations (○) and d^8 cations (●).

7. Energy Hypersurfaces

7.1. Working Hypothesis

In Section 6 we have interpreted crystal structure data in terms of the detailed reaction paths for nucleophilic addition, nucleophilic substitution and electrocyclic ring closure reactions as well as for pseudorotations. Such interpretations implicitly contain statements about the corresponding energy hypersurfaces. The hypotheses and assumptions underlying our procedure will therefore be reviewed in some detail.

In any crystal or molecular structure all atoms, including those of the fragment under investigation, occupy an equilibrium position. The interplay of forces responsible for the equilibrium is hardly ever known in detail. If, in spite of varying environments, structures of a molecular fragment may be ordered in a continuous sequence, we assume that a property which is inherent to the structural fragment is responsible for this behavior. This property, the characteristic energy hypersurface of the fragment, is taken as equal for equal fragments. The interactions between a fragment and its environment are superimposed on the characteristic surface and will in general tend to deform the fragment along a path of minimum resistance. We therefore conclude that a continuous sequence of structural changes describes a valley in the energy surface of the fragment.

The scatter of observed data with respect to the correlation curves may be due, in part, to experimental inaccuracy. It will also be due, however, to the influence of the perturbing forces from the environment which will distort the structural fragment in directions perpendicular to the minimum energy path as well, although to a lesser extent.

If we accept the interpretation of the correlations in terms of prototype reaction paths, we have to accept also that the underlying energy surface of a fragment rises in all directions perpendicular to the path. We don't know how steep the energy rises in these directions nor do we have information about the changes in energy along the reaction pathway. The lacking information has to be obtained from different sources.

7.2. Test of the Working Hypothesis

In order to test the working hypothesis and to get the lacking information energy surfaces of fragments have to be derived by methods independent of structural correlations. The reaction paths derived from such surfaces may then be compared with those obtained from structural data. The results of the comparison may be summarized as follows: The reaction path for nucleophilic addition of a tertiary amine to a carbonyl group is very similar to the path calculated by nonempirical methods for the addition of H^- to CH_2O[38] (Section 6.2). Qualitative agreement is found between the S_N2 reaction paths determined for tetrahedrally coordinated Cd^{II} ions from structural data and the path calculated by *ab initio* methods for CH_3F[48] (Section 6.3). Structure correlations[63, 64] on the one hand and spectroscopic data[62] or force field calculations[72] on the other hand are consistent with the model of free pseudorotations in five-membered rings (Section 6.5). EH-[50] and nonempirical calculations[70] for PH_5 as well as a mechanical model (five points on a sphere repelling each other[67, 68]) yield a reaction path of the Berry mechanism which is compatible with results of structure correlations (Section 6.6)[71].

The qualitative agreement found between results from independent sources lends support to our working hypothesis according to which the structure of a distorted molecular fragment is the result of adding perturbations to its intrinsic energy surface. This conclusion is not new, and may be taken as a further indication that model molecular force fields, which are based on pairwise additive atomic interactions, are suitable for simulating extended parts of energy hypersurfaces (molecular mechanics)[73].

7.3. Two Marginal Notes

1. The change in molecular energy in the immediate neighborhood of a minimum may be investigated experimentally by means of vibrational spectroscopy and force-field analysis[74]. The number of force constants needed is usually larger than the number of observable normal vibrations. In order to obtain a physically realistic force field, additional observations (Coriolis coupling constants, amplitudes of thermal vibration, isotopic substitution data[75], Raman intensities[76], *etc.*) have to be taken into account.

Under suitable conditions, ratios of force constants may be obtained from structural correlations[16, 33, 37, 59, 78]. Consider a quadratic energy surface of the form

$$2V = k_{ii}S_i^2 + k_{jj}S_j^2 + 2k_{ij}S_iS_j \qquad (18)$$

The angle α_i between the minimum energy pathway and the coordinate S_i, which may be an internal or symmetry displacement coordinate, is obtained from

$$\tan 2\alpha_i = \frac{2k_{ij}}{k_{ii}-k_{jj}} \quad (19)$$

(see Refs. [16, 33, 37]). If one variable, S_i say, is fixed by a constraint, the minimum energy pathway is subject to the conditions

$$(dV/dS_j)_{S_i} = 0 \quad (20)$$
$$k_{ij}/k_{jj} = -S_j/S_i \quad (21)$$

(see Refs. [59, 78]). Ratios of force constants may be included in force field analyses. Thus structural correlations may represent a source of additional information for molecules in condensed phases where neither Coriolis coupling constants nor amplitudes of vibration can be measured directly. The feasibility of incorporating ratios of force constants into force field analyses is a subject for future investigations[77].

2. The approximate constancy of sums of structurally defined bond numbers may be taken as a basis for a coherent description of the changes in bonding during a chemical reaction. The three-center four-electron system X—Y···X and its description in terms of a simple Hückel-model are a simple, maybe naive example. The reaction

$$X^1 - Y + X^2 \rightarrow X^1\cdots Y\cdots X^2 \rightarrow X^1 + Y - X^2 \quad (22)$$

is described by the Hückel-determinant

$$\begin{bmatrix} -x & 0 & \sin^m\varphi \\ 0 & -x & \cos^m\varphi \\ \sin^m\varphi\cos^m\varphi & h_y & -x \end{bmatrix} = 0 \quad (23)$$

The variable φ is a measure of the reaction coordinate: $\varphi=0°$ at the beginning of the reaction, $\varphi=45°$ at the transition state and $\varphi=90°$ at the end point of the reaction. The solutions of the eigenvalue problem (23) yield bond orders $p(X^1\cdots Y)$ and $p(Y\cdots X^2)$[79]. The sum of their squares is independent of φ and equals 1 if $m=1$ and $-\infty<h_y<\infty$ or if $h_y=0$ and $-\infty<m<\infty$. This constancy of squares of bond orders suggests a relationship between Hückel bond orders p and Pauling bond numbers n which, in turn, are expressed in terms of distances and angles and whose sum is also constant (Section 5). More accurate calculations, namely Hartree-Fock-SCF calculations have been performed for the hydrogen bridged species $(H_3N{-}H\cdots NH_3)^+$[80] and Hartree-Fock-SCF calculations with limited configuration interaction for the linear H_3 species (not H_3^-)[81]. In both cases the calculated reaction path for hydrogen transfer may be approximated by a hyperbolic curve of the analytical form (15). The deviations of the calculated points from these curves are smaller than the scatter of the experimental observations in Fig. 1. It seems an open question whether the corresponding wave functions or overlap populations along the calculated reaction path show invariance properties similar to those of the Hückel-model or the structural correlations.

8. Conclusions

Most conclusions have been given in the summary at the beginning of this contribution. At its end we cite *Woodward* and *Hoffmann*. On the last page of their book on "The Conservation of Orbital Symmetry"[52] the authors state that "a chemical reaction will proceed the more readily, the more bonding may be maintained throughout the transformation". This statement which summarizes a lot of chemical experience seems a logical extension of the older principle according to which each atom tries to form its characteristic number of bonds. This principle and its extension should also apply to our findings and interpretations. Translated into the language of structural correlations one might say that molecular fragments show maximal distortions at minimum costs in energy only in those directions which allow the fragment to maintain a maximum of bonding.

This contribution has been accepted as "Habilitationsschrift" by the Swiss Federal Institute of Technology (ETH), Zürich. The author thanks Prof. J. D. Dunitz, E. Shefter and P. Murray-Rust for many discussions.

Received: November 8, 1974 [A 64 IE]
German version: Angew. Chem. *87*, 461 (1975)

[1] a) *L. Pauling:* The Nature of the Chemical Bond, 3rd Edition. Cornell University Press, Ithaca, N. Y. 1960; Die Natur der chemischen Bindung, 3. Aufl. Verlag Chemie, Weinheim 1968; b) all standard distances cited in this contribution are taken from [1a].
[2] *A. Bondi*, J. Phys. Chem. *68*, 441 (1964).
[3] *V. Schomaker* and *D. P. Stevenson*, J. Amer. Chem. Soc. *63*, 37 (1941).
[4] *J. H. van't Hoff*, Arch. Neer. Sci. Exactes Natur. *9*, 445 (1874); *J. A. Le Bel*, Bull. Soc. Chim. Fr. *22*, 337 (1874).
[5] *A. v. Baeyer*, Ber. Deut. Chem. Ges. *18*, 2268 (1885).
[6] Review: *J. D. Dunitz*, Perspect. Struct. Chem. *2*, 1 (1968).
[7] *K. S. Pitzer*, Science *101*, 672 (1945).
[8] *R. B. Corey* and *L. Pauling*, Proc. Roy. Soc. London *B141*, 10 (1953); *R. E. Marsh* and *J. Donohue*, Advan. Protein Chem. *22*, 235 (1967); *G. N. Ramachandran* and *V. Sasisekharan*, *ibid. 23*, 283 (1968).
[9] *S. Arnott*, *S. D. Dover*, and *A. J. Wonacott*, Acta Crystallogr. *B 25*, 2192 (1969).
[10] *K. O. Stromme*, Acta Chem. Scand. *13*, 268 (1959).
[11] *H. A. Bent*, Chem. Rev. *68*, 587 (1968).
[12] *F. W. B. Einstein* and *A. C. MacGregor*, J. C. S. Dalton *1974*, 778.
[13] The author thanks Prof. *I. C. Paul* for a list of published and unpublished data.
[14] This somewhat arbitrary procedure to compare incomparable distances was used first for Cd—I, Cd—S and Cd—O distances [16] (Section 6.3). Its success seems to be related to the fact that many bonds elongate by 0.2—0.3 Å when their bond number is halved: d(C=C)=1.34, d(C—C)=1.54, Δ=0.20 A; d(O—H)=0.98, d(O···H···O)=1.21, Δ=0.23 Å; d(I—I)=2.67, d(I···I···I$^-$)=2.90, Δ=0.23 Å; d(S—S)=2.08, d(S···S···S)=2.35, Δ=0.27 Å.
[15] *W. C. Hamilton* and *J. A. Ibers:* Hydrogen Bonding in Solids, W. A. Benjamin, New York 1968, p. 54.
[16] *H. B. Bürgi*, Inorg. Chem. *12*, 2321 (1973).
[17] *J. C. Speakman* in *G. A. Sim* and *L. E. Sutton:* Molecular Structure by Diffraction Methods. The Chemical Society, London 1973, p. 209.
[18] *L. Kihlborg*, Ark. Kemi *21*, 471 (1963).
[19] *P. Murray-Rust*, *H. B. Bürgi*, and *J. D. Dunitz*, J. Amer. Chem. Soc. *97*, 921 (1975).
[20] Structures of distorted tetrahedra may be expressed in terms of linear combinations of internal coordinates transforming as irreducible representations of the point group of the undistorted tetrahedron (T_d). Criteria may be defined in terms of these symmetry coordinates in order to discern distorted tetrahedra with approximate C_{3v} symmetry from those with other approximate symmetries [16, 21].
[21] *P. Murray-Rust*, unpublished results.
[22] If M stands for a lone pair of electrons, $\langle\theta_1\rangle$ may be estimated from $\langle\theta_2\rangle$ using the relationship: $\sin(\langle\theta_1\rangle)=\frac{2}{3}\cdot\sqrt{3}\sin(\langle\theta_2\rangle 2)$.
[23] The monotonous curve is another illustration of VSEPR rules (Valence Shell Electron Pair Repulsion) [24]. According to these rules a lone pair of electrons occupies more space than a bonding pair. As a consequence the angles θ_2 in $SnCl_3^-$ are smaller and the distances r_1 are larger than those in $SnCl_4$.
[24] *R. J. Gillespie:* Molecular Geometry. Van Nostrand Reinhold, London 1972, Chapt. III; Molekülgeometrie. Verlag Chemie, Weinheim 1975, Chapt. 3.
[25] Cf. [1a], English version pp. 239, 255.
[26] *L. Pauling*, J. Amer. Chem. Soc. *69*, 542 (1947). *Pauling* justifies the analytical form of equation (1) in one sentence: "This logarithmic relation is, of course, to be expected in consequence of the exponential character of interatomic forces"!

[27] The constant c for C—H bonds is about 0.18 Å. *H. B. Bürgi*, unpublished results.

[28] *E.g.: I. D. Brown* and *R. D. Shannon*, Acta Crystallogr. *A 29*, 266 (1973); *W. H. Baur*, *ibid. B 30*, 1195 (1974); *G. A. Lager* and *G. V. Gibbs*, Amer. Mineral. *58*, 756 (1973).

[29] *L. E. Sutton*: Interatomic distances. Special Publications *18*, *(18a)*. The Chemical Society, London 1958 (1965).

[30] *H. Eyring* and *M. Polanyi*, Z. Phys. Chem. *B 12*, 279 (1931).

[31] *K. Fukui*, J. Phys. Chem. *74*, 4161 (1970).

[32] *H. B. Bürgi*, *J. D. Dunitz*, and *E. Shefter*, J. Amer. Chem. Soc. *95*, 5065 (1973).

[33] *H. B. Bürgi*, *J. D. Dunitz*, and *E. Shefter*, Acta Crystallogr. *B30*, 1517 (1974).

[34] We have accepted the challenge: In our laboratories the crystal structures of naphthalene derivatives with electrophilic substituents in position 1 and nucleophilic substituents in position 8 are being investigated.

[35] Proton transfer as well as acid- and base-catalysis, which are also part of the reaction, have not been taken into account.

[36] *D. R. Storm* and *D. E. Koshland*, J. Amer. Chem. Soc. *94*, 5805, 5815 (1972); *R. M. Moriarty* and *T. Adams*, *ibid. 95*, 4070 (1973).

[37] *H. B. Bürgi*, *J. D. Dunitz*, *J. M. Lehn*, and *G. Wipff*, Tetrahedron *30*, 1563 (1974).

[38] *H. B. Bürgi*, *J. M. Lehn*, and *G. Wipff*, J. Amer. Chem. Soc. *96*, 1956 (1974).

[39] Differences in reactivity within a given class of compounds (acetals, ketals, orthoesters, amides, *etc.*) may often be predicted on the basis of differences in conformation [40, 41], bond lengths [33, 41, 42] or overlap populations [41, 42]. Details are given in [37].

[40] *P. Deslongchamps*, *C. Moreau*, *D. Fréhel*, and *P. Atlani*, Can. J. Chem. *50*, 3402 (1972); *P. Deslongchamps*, *P. Atlani*, *D. Frehel*, and *A. Malaval*, *ibid. 50*, 3405 (1972); *P. Deslongchamps*, *C. Lebreux*, and *R. Taillefer*, *ibid. 51*, 1665 (1973).

[41] *G. A. Jeffrey*, *J. A. Pople*, and *L. Radom*, Carbohyd. Res. *25*, 117 (1972).

[42] *J. M. Lehn*, *G. Wipff*, and *H. B. Bürgi*, Helv. Chim. Acta *57*, 493 (1974); *J. M. Lehn* and *G. Wipff*, J. Amer. Chem. Soc. *96*, 4048 (1974).

[43] a) *A. Rühlmann*, *D. Kukla*, *P. Schwager*, *K. Bartels*, and *R. Huber*, J. Mol. Biol. *77*, 417 (1973); b) *R. Huber*, private communication (1973).

[44] *D. M. Blow*, *J. Janin*, and *R. M. Sweet*, Nature *249*, 54 (1974).

[45] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press. Ithaca, N. Y., 1953, Chapt. V.

[46] The following relationships apply: $\langle a_X(X{-}Cd{-}S)\rangle = \arccos(-\Delta z \langle d(Cd{-}S)\rangle)$, $\langle a_Y(Y{\cdots}Cd{-}S)\rangle = \arccos(\Delta z/\langle d(Cd{-}S)\rangle)$. For a tetrahedron with T_d symmetry $\Delta z = d(Cd{-}S)/3$.

[47] Activation energies for these reactions seem to be higher than the intra- or intermolecular strain energies attainable in such systems. As a consequence it is very difficult to freeze-in a nuclear configuration resembling a transition state.

[48] *A. Dedieu* and *A. Veillard*, J. Amer. Chem. Soc. *94*, 6730 (1972); *A. J. Duke* and *R. F. W. Bader*, Chem. Phys. Lett. *10*, 631 (1971).

[49] *Ab initio* calculations for reaction (12) ($FCH_3 + F^- \rightarrow F^- + CH_3F$) yield absolute minima in energy for the monopole dipole complex $F^-\cdots CH_3F$ and a maximum for the transition state ($F\cdots CH_3\cdots F^-$). Bond lengths and angles describing nuclear configurations between the two minima are approximately related by equations of the type (13), (14) and (15).

[50] *R. Hoffmann*, *J. M. Howell*, and *E. L. Muetterties*, J. Amer. Chem. Soc. *94*, 3047 (1972).

[51] *R. L. Hildebrandt* and *J. D. Wieser*, J. Chem. Phys. *55*, 4648 (1971).

[52] *R. B. Woodward* and *R. Hoffmann*: The Conservation of Orbital Symmetry. Verlag Chemie, Weinheim, and Academic Press, New York 1970.

[53] *E. E. van Tamelen* and *T. L. Burkoth*, J. Amer. Chem. Soc. *89*, 151 (1967); *S. Masamune* and *R. T. Seidner*, Chem. Commun. *1969*, 542.

[54] *H. Günther*, *H. Schmickler*, *W. Bremser*, *F. A. Straube*, and *E. Vogel*, Angew. Chem. *85*, 585 (1973); Angew. Chem. internat. Edit. *12*, 570 (1973).

[55] *M. Görlitz* and *H. Günther*, Tetrahedron *25*, 4467 (1969).

[56] *R. Bianchi*, *G. Morosi*, *A. Mugnoli*, and *M. Simonetta*, Acta Crystallogr. *B 29*, 1196 (1973).

[57] *R. L. Beddoes*, *P. F. Lindley*, and *O. S. Mills*, Angew. Chem. *82*, 293 (1970); Angew. Chem. internat. Edit. *9*, 304 (1970).

[58] *M. J. Barrow* and *O. S. Mills*, J. Chem. Soc. *A 1971*, 1982.

[59] *H. B. Bürgi*, *J. D. Dunitz*, and *E. Shefter*, unpulished results.

[60] The observed angles β at C(2) where corrected for the observed non-planarity of the six-membered ring fragment. The corrected angles β are comparable with those of the molecular model which is assumed to have planar six-membered ring fragments.

[61] *J. E. Kilpatrick*, *K. S. Pitzer*, and *R. Spitzer*, J. Amer. Chem. Soc. *69*, 2483 (1947).

[62] *K. S. Pitzer* and *W. E. Donath*, J. Amer. Chem. Soc. *81*, 3213 (1959).

[63] *C. Altona*, *H. J. Geise*, and *C. Romers*, Tetrahedron *24*, 13 (1968).

[64] *C. Altona* and *M. Sundaralingam*, J. Amer. Chem. Soc. *94*, 8205 (1972); *ibid. 95*, 2333 (1973).

[65] Review on experimental investigations of five coordinate molecules: *R. R. Holmes*, Accounts Chem. Res. *5*, 296 (1972).

[66] *R. S. Berry*, J. Chem. Phys. *32*, 933 (1960).

[67] *D. L. Kepert*, Inorg. Chem. *12*, 1938 (1973).

[68] *L. S. Bartell* and *V. Plato*, J. Amer. Chem. Soc. *95*, 3097 (1973).

[69] *B. Beagley* and *K. T. McAloon*, Trans. Faraday Soc. *67*, 3216 (1971).

[70] *A. Rauk*, *L. C. Allen*, and *K. Mislow*, J. Amer. Chem. Soc. *94*, 3035 (1972).

[71] *E. L. Muetterties* and *L. J. Guggenberger*, J. Amer. Chem. Soc. *96*, 1748 (1974).

[72] *S. Lifson* and *A. Warshel*, J. Chem. Phys. *49*, 5116 (1968).

[73] Reviews: *E. M. Engler*, *J. D. Andose*, and *P. v. R. Schleyer*, J. Amer. Chem. Soc. *95*, 8005 (1973); *C. Altona* and *D. H. Faber*, Fortschr. Chem. Forsch. *45*, 1 (1974); *J. D. Dunitz* and *H. B. Bürgi*, MTP Int. Rev. Sci., in print.

[74] *E.g. E. B. Wilson, Jr.*, *J. C. Decius*, and *P. C. Cross*: Molecular Vibrations. McGraw Hill, New York 1955.

[75] *H. Fujii* and *M. Kimura*, J. Mol. Spectrosc. *37*, 517 (1971). Example: $SnCl_4$.

[76] *H. Schulze*, *N. Weinstock*, *A. Müller*, and *G. Vandrish*, Spectrochim. Acta *29 A*, 1705 (1973). Examples: PO_4^{3-}, SO_4^{2-}.

[77] This problem is currently under investigation ([19], footnotes 13 and 14).

[78] *O. Ermer*, Tetrahedron *30*, 3103 (1974).

[79] *E. Heilbronner* and *H. Bock*: Das HMO-Modell und seine Anwendung, Vol. I. Verlag Chemie, Weinheim 1968.

[80] *P. Merlet*, *S. D. Peyerimhoff*, and *R. J. Buenker*, J. Amer. Chem. Soc. *94*, 8301 (1972).

[81] *B. Liu*, J. Chem. Phys. *58*, 1925 (1973).

[82] Review: *A. Hordvik* and *L. J. Saethre*, Isr. J. Chem. *10*, 239 (1972).

[83] *I. L. Karle*, J. Chem. Phys. *23*, 1739 (1955).

[84] *A. I. Kitaigorodski*, *T. L. Khotsyanova*, and *Y. T. Struchkov*, Zh. Fiz. Khim. *27*, 780 (1953).

[85] *E. E. Havinga* and *E. H. Wiebenga*, Acta Crystallogr. *11*, 733 (1958).

[86] *G. H. Cheesman* and *A. J. T. Finney*, Acta Crystallogr. *B 26*, 904 (1970).

[87] *J. Broekema*, *E. E. Havinga*, and *E. H. Wiebenga*, Acta Crystallogr. *10*, 596 (1957); *R. J. Hach* and *R. E. Rundle*, J. Amer. Chem. Soc. *73*, 4321 (1951).

[88] *E. E. Havinga*, *K. H. Boswijk*, and *E. H. Wiebenga*, Acta Crystallogr. *7*, 487 (1954).

[89] *J. Runsink*, *S. Swen-Walstra*, and *T. Migchelsen*, Acta Crystallogr. *B 28*, 1331 (1972).

[90] *H. A. Tasman* and *K. H. Boswijk*, Acta Crystallogr. *8*, 59 (1955).

[91] *J. W. Bats*, *J. J. de Boer*, and *D. Bright*, Inorg. Chim. Acta *5*, 605 (1971).

[92] *T. Migchelsen* and *A. Vos*, Acta Crystallogr. *23*, 796 (1967).

[93] *R. C. L. Mooney Slater*, Acta Crystallogr. *12*, 187 (1959).

[94] *T. Bernstein* and *F. H. Herbstein*, Acta Crystallogr. *B 24*, 1640 (1968).

[95] Methadone: *H. B. Bürgi*, *J. D. Dunitz*, and *E. Shefter*, Cryst. Struct. Commun. *2*, 667 (1973).

[96] *N*-Methyl-11-azabicyclo[5.3.1]undecan-4-one: *M. Kaftory* and *B. Schweizer*, private communication.

[97] Cryptopine: *S. R. Hall* and *F. R. Ahmed*, Acta Crystallogr. *B24*, 346 (1968).

[98] Protopine: *S. R. Hall* and *F. R. Ahmed*, Acta Crystallogr. *B24*, 337 (1968).

[99] Senkrikine: *G. I. Birnbaum*, J. Amer. Chem. Soc. *96*, 6165 (1974).

[100] Clivorine: *K. B. Birnbaum*, Acta Crystallogr. *B28*, 2825 (1972).

[101] Retusamine: *J. A. Wunderlich*, Acta Crystallogr. *B23*, 846 (1967).

[102] Mitomycine A: *A. Tulinsky* and *J. H. van der Hende*, J. Amer. Chem. Soc. *89*, 2905 (1967).

[103] *C. J. Fritchie*, Acta Crystallogr. *20*, 27 (1966).

[104] *P. E. Baikie* and *O. S. Mills*, J. Chem. Soc. *A 1969*, 328.

[105] *C. M. Gramaccioli* and *M. Simonetta*, Acta Crystallogr. *B28*, 2231 (1972).

[106] *M. Dobler* and *J. D. Dunitz*, Helv. Chim. Acta *48*, 1429 (1965).

[107] *E. F. Epstein* and *I. Bernal*, J. Chem. Soc. *A 1971*, 3628.

[108] *E. F. Riedel* and *R. A. Jacobson*, Inorg. Chim. Acta *4*, 407 (1970).

[109] *B. A. Brenz* and *J. A. Ibers*, Inorg. Chem. *11*, 1109 (1972).

[110] *F. A. Cotton*, *T. G. Dunne*, and *J. S. Wood*, Inorg. Chem. *4*, 318 (1965).

[111] *J. Donohue* and *A. Caron*, Acta Crystallogr. *17*, 663 (1964).

[112] *K. N. Raymond*, *P. W. R. Corfield*, and *J. A. Ibers*, Inorg. Chem. *7*, 1362 (1968).

[113] *A. Terzis*, *K. N. Raymond*, and *T. G. Spiro*, Inorg. Chem. *9*, 2415 (1970).

[114] *C. Heath* and *M. B. Hursthouse*, Chem. Commun. *1971*, 143.

[115] *J. Drummond* and *J. S. Wood*, Chem. Commun. *1969*, 1373.

[116] *B. A. Coyle* and *J. A. Ibers*, Inorg. Chem. *9*, 767 (1970).

[117] *P. J. Wheatley*, J. Chem. Soc. *1964*, 2206.

[118] *A. L. Beauchamp*, *M. J. Benett*, and *F. A. Cotton*, J. Amer. Chem. Soc. *90*, 6675 (1968).

[119] Cf. [19], footnote 12.

[120] L. K. Hansen and A. Hordvik, Acta Chem. Scand. 27, 411 (1973).
[121] S. Bezzi, M. Mammi, and C. Garbuglio, Nature 182, 247 (1958); F. Leung and S. C. Nyburg, Chem. Commun. 1969, 137.
[122] B. Birknes, A. Hordvik, and L. J. Saethre, Acta Chem. Scand. 27, 382 (1973).
[123] O. Hjellum and A. Hordvik, Acta Chem. Scand. 27, 2666 (1973).
[124] A. Hordvik, O. Sjolset, and L. J. Saethre, Acta Chem. Scand. 27, 379 (1973).
[125] A. Hordvik and L. J. Saethre, Acta Chem. Scand. 26, 3114 (1972).
[126] A. Hordvik and L. M. Milje, Acta Chem. Scand. 27, 510 (1973).
[127] A. Hordvik, Acta Chem. Scand. 25, 1583 (1971).
[128] A. Hordvik, Acta Chem. Scand. 25, 1822 (1971).
[129] A. Hordvik, O. Sjolset, and L. J. Saethre, Acta Chem. Scand. 26, 1297 (1972).
[130] B. Birknes, A. Hordvik, and L. J. Saethre, Acta Chem. Scand. 26, 2140 (1972).
[131] A. Hordvik and L. J. Saethre, Acta Chem. Scand. 26, 1729 (1972).
[132] A. J. Barnett, R. J. S. Beer, B. V. Karaoghlanian, E. C. Llaguno, and I. C. Paul, J. C. S. Chem. Comm. 1972, 836.
[133] A. Hordvik and P. Oftedal, J. C. S. Chem. Comm. 1972, 543.
[134] P. L. Johnson and I. C. Paul, Chem. Commun. 1969, 1014.
[135] S. M. Johnson, M. G. Newton, and I. C. Paul, J. Chem. Soc. B 1969, 986.
[136] A. Hordvik and K. Julshamn, Acta Chem. Scand. 25, 1835 (1971).
[137] A. Hordvik, E. Sletten, and J. Sletten, Acta Chem. Scand. 23, 1852 (1969).
[138] J. Sletten, Acta Chem. Scand. 25, 3577 (1971).
[139] R. Kristensen and J. Sletten, Acta Chem. Scand. 27, 2517 (1973).
[140] J. Sletten, Acta Chem. Scand. 27, 229 (1973).
[141] K. I. G. Reid and I. C. Paul, J. Chem. Soc. B 1971, 952.
[142] P. L. Johnson, K. I. G. Reid, and I. C. Paul, J. Chem. Soc. B 1971, 946.
[143] R. Pinel, Y. Mollier, E. C. Llaguno, and I. C. Paul, Chem. Commun. 1971, 1353.
[144] A. Hordvik and L. J. Saethre, Acta Chem. Scand. 26, 849 (1972).
[145] A. Hordvik, E. Sletten, and J. Sletten, Acta Chem. Scand. 23, 1377 (1969).
[146] G. Eide, A. Hordvik, and L. J. Saethre, Acta Chem. Scand. 26, 2140 (1972).
[147] F. Leung and S. C. Nyburg, Chem. Commun. 1970, 707.
[148] Review: A. Hordvik and L. J. Saethre, Isr. J. Chem. 10, 239 (1972).

Ring Contractions and Expansions of Vicinally Disubstituted Cyclobutanes and Cyclopropylmethyl Compounds

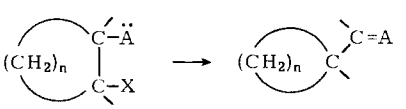
New synthetic methods (10)

By J. M. Conia and M. J. Robson[*]

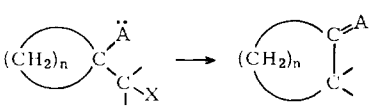
Cyclobutanes and cyclopropylmethyl compounds vicinally disubstituted in appropriate manner by one electron-donating group and one leaving or electron-receiving group undergo extremely facile ring contractions and expansions respectively. Unlike many rearrangements of small-ring compounds and most rearrangements of larger-ring compounds, these reactions usually give a single product in high yield and thus possess real synthetic interest. The subject matter of this progress report is classified according to the substituents in question since the nature of these groups largely determines the conditions under which rearrangement takes place.

1. Introduction

Among the many known carbocyclic ring expansions and contractions there is a particular class of reactions in which rearrangement is brought about by the presence of an electron-donating group (A) attached to one ring carbon atom and a leaving or electron-receiving group (X) on a vicinal carbon, either in the ring (giving rise to ring contraction) or outside it (leading to expansion).



(1)



(2)

Reactions in this category include, principally, the acyloin and pinacol rearrangements and related transformations such as the glycol monotosylate rearrangement, the benzilic acid rearrangement, the quasi-Favorskii rearrangement (*i.e.* proceeding *via* a semibenzilic mechanism), the Demjanov-Tiffeneau rearrangement and the reactions of ketones with diazoalkanes. Both ring expansions[1] and contractions[2] have been the subjects of excellent general reviews by *Gutsche* and *Redmore*.

Interconversions of normal and medium ring compounds *via* such reactions have been known for a long time, as have ring expansions of cyclobutanes to cyclopentanes, but the corresponding ring contractions are rare and proceed only with difficulty for obvious thermodynamic reasons[1, 2]. Ten years ago most of the known interconversions of three- and four-membered rings were of the Wagner-Meerwein type, involving monofunctionalized compounds reacting *via* carbenium ion intermediates[1–4].

However, since these reactions afford mixtures of cyclobutyl, cyclopropylmethyl, and 3-butenyl compounds they are of limited synthetic applicability; this is especially true of the contractions[2]. Since then, the respective ring contractions and ring enlargements of numerous vicinally-difunctionalized cyclobutanes and cyclopropylmethyl compounds have been described and it has become clear that the interconversion of these systems is altogether easier and more general than for the larger rings and does not necessarily require carbenium ion formation. Such reactions (eq. (1) and (2) with $n=2$), which may be thermal or acid- or base-catalyzed, normally give a single product in high yield, even when they certainly proceed *via* a carbenium ion intermediate.

[*] Prof. Dr. J. M. Conia [+] and Dr. M. J. Robson
Laboratoire des Carbocycles
Universite de Paris-Sud
91405 Orsay (France)
[+] To whom correspondence should be addressed.

A somewhat arbitrary classification has been made according to the nature of the electron-donating and leaving groups (Table 1). Both expansions and contractions are dealt with in each section (where applicable).

Table 1. A classification of ring contractions and ring expansions according to the nature of the electron-donating groups A and electron-receiving or leaving groups X.

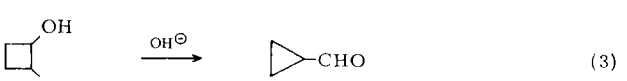
Section	Ring contraction		Ring expansion	
	—C—A	—C—X	C—A	>C—X
2	—C—OH	—C—Cl	C—OH	>C—Br
	—C—OH	—C—Br	C—OH	>C—OTs
	—C—OH	—C—OTs	C—OH	>C—OH
	—C—OH	CCl_2	C—OH	$>C—N_2^{\oplus}$
	—C—OH	CBr_2		
	—C—OH	—C—OH		
	—C—OH	$C(OCH_3)_2$		
3	C=O	—C—Cl		
	C=O	—C—Br		
	C=O	—C—OTs		
	C=O	CCl_2		
	C=O	CBr_2		
4	$C(OR)_2$	—C—Br	C—OR	—CH—OH
			C—OR	—CH—OCOAr
			C—OR	$—CH—N_2^{\oplus}$
			$C—OSi(CH_3)_3$	$>C—OSi(CH_3)_3$
			$C—OSi(CH_3)_3$	$—C(OCH_3)_2$
			C—SR	>C—OH
	$—C—NH_2$	—C—I	$C—NH_2$	$C(O)—C_6H_5$
5			and	
6	—C—OH	C=O	C—OH	—C=O
	—C—OH	$C(OH)—OCH_3$	$C—OCH_3$	—C=O
			$C—OSi(CH_3)_3$	—C=O
			$C—OCOCH_3$	—C=O
7	C=O	C=O		
8	—C—OH	C=C<	C—OH	C=C<
9	oxidative rearrangements of small ring systems			

2. α-Substituted Alcohols

The simplest systems that can react according to eqs. (1) and (2) are those in which an alcohol is α-substituted by a leaving group. In this category are found both ring expansions and ring contractions, which will now be considered according to the conditions under which they take place.

2.1. Base-Catalyzed Reactions

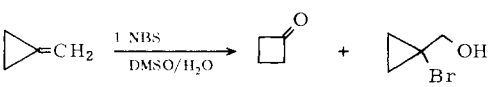
2-Bromo- and 2-tosyloxycyclobutanol, prepared by $LiAlH_4$ reduction of the ketones, undergo quantitative transformation to cyclopropanecarbaldehyde on treatment with aqueous sodium hydroxide [eq. (3)]. The same reaction is also induced by boiling water or on refluxing in a water-methanol mixture[5, 6].



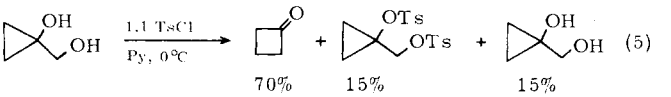
(3)

The corresponding ring expansion occurs on treating methylenecyclopropane with *N*-bromosuccinimide (NBS) [eq. (4)] or on reaction of α-hydroxycyclopropylmethanol with *p*-toluenesulfonyl chloride/pyridine [eq. (5)][7].

Methylenecyclopropane probably first yields a mixture of the two α-bromo alcohols, the cyclopropanol subsequently



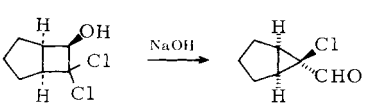
(4)



(5)

rearranging to cyclobutanone. In the case of the diol, the initially formed primary tosylate may undergo either ring contraction or a second tosylation. Use of the more basic lutidine as solvent increases the yield of cyclobutanone to 88%[7].

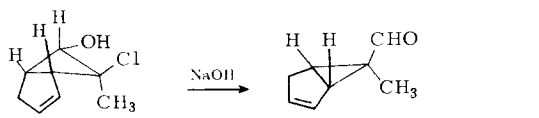
Several ring contractions of halocyclobutanols forming part of a bicyclic system have been reported. The earliest work concerned ring-contraction of 2,2-dihalocyclobutanols upon treatment with aqueous base [eq. (6)][8, 9]; the corresponding dihalo ketones (Section 3.3), undergo cleavage.



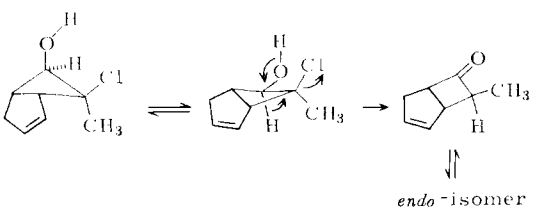
(6)

The reactions were shown to be stereospecific with respect to the configuration of the hydroxyl group, *exo*-alcohols giving *endo*-aldehydes and *vice versa*. Since, in related reactions (see Sections 3.1 and 3.2) contraction occurs with inversion of configuration at the halogen-bearing carbon, it is presumably the chlorine atom *trans* to the hydroxyl group that is displaced. The reaction is not promoted by silver salts, indicating that carbenium ions are not involved[8, 9].

Later work showed that the reactions of the corresponding monochloro alcohols are stereospecific with respect to the configuration of the halogen atom and that contraction can only occur if this atom is able to adopt a pseudo-equatorial conformation [(*e. g.* eq. (7)]. When this is sterically unfavorable, a 1,2-hydrogen shift can occur instead, provided that the necessary antiperiplanar arrangement of hydrogen and leaving group can be attained [eq. (8)][10].



(7)

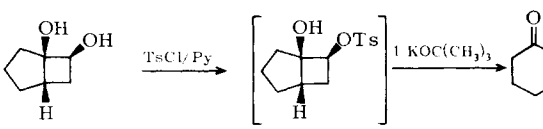


(8)

endo-isomer

Other examples of ring contractions of bicyclic[11, 12] and spiro-fused[13, 14] 2-halocyclobutanols have been reported.

The rearrangement of bicyclic 2-tosyloxycyclobutanols occurs in an analogous manner and has been shown to proceed with rigorous stereospecificity[15, 16]. The example shown in eq. (9) is particularly striking in this respect[16].



(9)

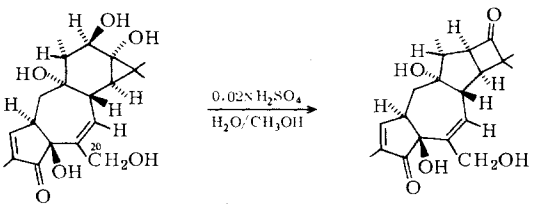
83%

An example of base-catalyzed ring expansion in a fused-ring system is the reaction of the 20-monoacetate of the naturally occurring diol phorbol [see eq. (10)] with $POCl_3$/pyridine to give phorbobutanone[17].

2.2. Acid-Catalyzed Reactions

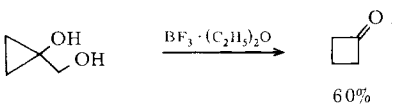
Ring contractions of 1,2-cyclobutanediols have been reported fairly widely, the first example being noted by *Criegee*[18]. Both *cis*-[6, 19] and *trans*-diols[6, 18–21] rearrange under the influence of acid to give the corresponding cyclopropanecarbaldehydes or ketones, usually in high yield (see Table 2). Particularly noteworthy, perhaps, are the contractions of the isomeric 1,2-diphenyl-1,2-diols since no products of migration of the normally fairly mobile phenyl group could be detected[19, 20]. In contrast, however, boron trifluoride-ether-catalyzed rearrangements of both the *cis*-1,2-diallyl- and *trans*-1,2-divinyldiols gave solely the products of allyl and vinyl migration[19]. In the cases of the 1,2-dialkylated diols the *trans* isomer was normally found to rearrange somewhat more easily than the *cis* compound[6, 19]; on reaction of the monoalkylated compounds the tertiary hydroxyl is the preferred or exclusive leaving group[19]. 1-Vinyl-*cis*-1,2-cyclobutanediol undergoes quantitative ring contraction, there being no competing vinyl migration[19]. All of these contractions presumably proceed *via* carbenium ion intermediates.

The corresponding ring expansion was first demonstrated in the conversion of phorbol to phorbobutanone [eq. (10)][22, 23].



(10)

The parent diol, 1-hydroxycyclopropylmethanol has similarly been rearranged using boron trifluoride-ether as the catalyst [eq. (11)][113].



(11)

60%

2.3. Thermal Rearrangements

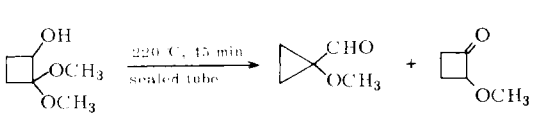
Only the 1,2-cyclobutanediols have been subjected to a thorough thermolysis study. The reaction is performed either in a sealed tube (almost certainly acid catalyzed) or in the gas phase (Table 2).

Under sealed-tube conditions ring contraction usually occurs in high yield at temperature of 230—270 °C, depending upon the starting compound. The simple mono- and dialkylated compounds give products which are the same as for the acid-catalyzed reactions. In cases where allyl, vinyl, or phenyl substituents are present, however, a ring-contracted product could be isolated in only one case (Table 2, example 4). As with acid catalysis, the *trans* diols were found to rearrange more easily than their *cis* counterparts.

In the gas phase three *trans* diols were found to undergo quantitative ring-contraction at 310 °C, whereas two of the corresponding *cis* isomers remained unchanged at this temperature[19].

Interestingly, on simple distillation at atmospheric pressure, several 1,2-dialkyl-*cis*-1,2-cyclobutanediols undergo alkyl migration rather than ring contraction, giving 2,2-dialkylcyclobutanones in high yield[19, 24].

The thermolysis of 2,2-dimethoxycyclobutanol has also been carried out [eq. (12)][25]. The resulting methoxycyclobutanone

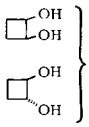
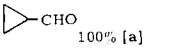
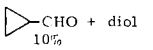
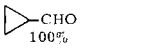
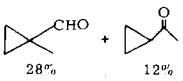
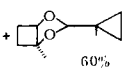
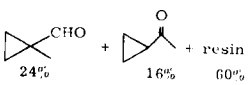
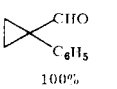
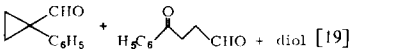
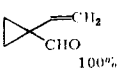
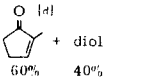
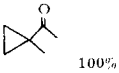
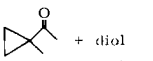
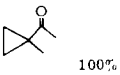
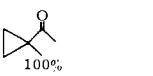
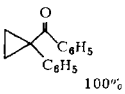
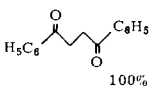
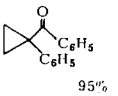
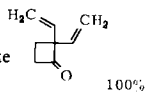
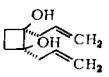
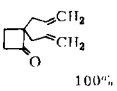
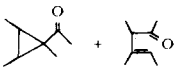
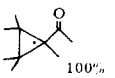


(12)

+ CH_3OH

is most probably formed by acid-catalyzed rearrangement of the methoxycyclopropanecarbaldehyde product (cf. Section 6). The ambivalent nature of the ketal function should be mentioned, since this group may equally act as the electron-donating substituent (see Section 4.1).

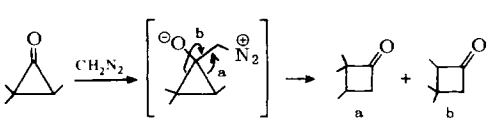
Table 2. Ring contractions of 1,2-cyclobutanediols.

No.	Diol	Acid catalyzed		Thermal (sealed tube)		Ref.
		Conditions	Products	Conditions	Products	
1		distillation from $BF_3{\cdot}(C_2H_5)O$	 100% [a]	230 °C, 1 h [b]	 10% + unidentified products	[19, 24]
2				230 °C, 1 h [b]	 100%	[19, 24]
3		$TsOH/C_6H_6$ 1.5 h reflux	 28% 12%  60%	230 °C, 12 h [b]	 24% 16% 60%	[24]
4		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, 70 °C, 2 h	 100%	230 °C	 50% 30% 20%	[19]
5		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, 70 °C, 5 min	 100%	230 °C	 [d] 60% + diol 40%	[19]
6		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, 70 °C, 5 h	 100%	265 °C, 1 h [b]	 70% + diol 30%	[19, 24]
7		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, RT, immediate	 100%	230 °C, 2 h [b]	 100%	[19]
8		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, 70 °C, 1.5 h	 100%	205 °C, 30 min	 100%	[19]
9		20% aq. H_2SO_4, reflux, 3 h	 95%			[20]
10		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, RT, immediate	 100%	230 °C	resin	[19]
11		$BF_3{\cdot}(C_2H_5)_2O$/ $CHCl_3$, RT, immediate	 100%	230 °C	resin	[19]
12		H_2SO_4/aq. acetone				[18]
13		$TsOH{\cdot}C_6H_6$ 4 h, reflux [c]	 100%			[19]

[a] One of the best preparative routes to cyclopropanecarbaldehyde.
[b] Gas phase thermolyses gave the following results: No. 1, 400 °C, 5 h, 100% diol; No. 2, 400 °C, 5 h, 100% aldehyde; No. 3, 325 °C, 4 h, 100% diol; No. 6, 310 °C, 3 h, 100% diol; No. 7, 310 °C, 2 h, 100% ketone.
[c] With azeotropic removal of water.
[d] Enone formed *via* ring-opened product $C_2H_5{-}CO{-}(CH_2)_2{-}CHO$, isolable in gas-phase experiment.

2.4. Ylide-Induced Reactions

A simple way of forming a cyclopropylmethyl system set up for rearrangement consists in addition of an ylide to a cyclopropanone. Thus the addition of diazomethane and diazoethane to various cyclopropanones leads directly to cyclobutanones [*e.g.* eq. (13)][26].

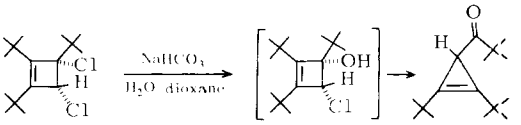


(13)

An analogous cyclobutanone-forming ring enlargement has been postulated to occur in the reaction of dimethylsulfoxonium methylide with 17-halogeno-16α-methyl-20-oxosteroids[27].

2.5. Unsaturated Systems

One well-defined example of a cyclobutene to cyclopropene ring contraction has been reported [eq. (14)]. Although the starting material is a dichloride, it has been proposed that the species effectively undergoing contraction is an α-chlorocyclobutenol[28].

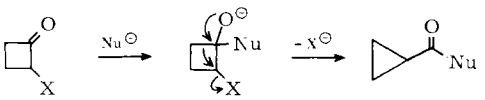


(14)

Corresponding ring expansions have only been reported as steps in postulated pathways for the formation of cyclobutenones from alkynes and dichlorocarbene precursors[29, 30].

3. α-Substituted Cyclobutanones

Closely related to the ring contractions of α-substituted cyclobutanols and actually longer known are those of the analogous ketones. These reactions are effected by nucleophiles, the species undergoing contraction being a cyclobutoxide formed by the addition of the nucleophile ($Nu^{\ominus}$) to the carbonyl carbon atom [eq. (15)]. Many aspects of the subject

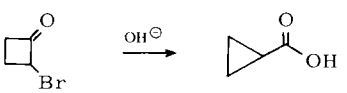


(15)

have already been dealt with at length[31] and will be treated only briefly here.

3.1. Monocyclic Compounds

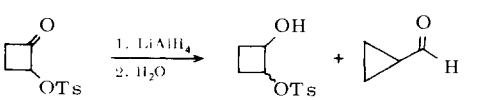
The first reactions to be reported in this category were ring contractions of 2-bromocyclobutanone to give cyclopropanecarboxylic acid or derivatives thereof in excellent yields [*e.g.* eq. (16)]. Reagents shown to be effective include aqueous sodium carbonate, sodium ethoxide in ethanol or ether (ester formation), liquid ammonia (amide formation), and even boiling water[32, 33].



(16)

Of the four mechanisms initially considered possible for this reaction only the semibenzilic acid mechanism [*i.e.*, as in eq. (15)] was found to be consistent with stereochemical, kinetic, and labeling evidence. The reaction proceeds, even in water alone, without the intermediacy of a carbenium ion. Additionally, evidence was adduced to show that such contractions take place stereospecifically with inversion of configuration at the C-2[31].

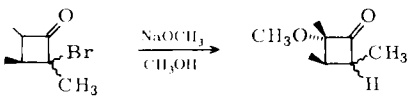
Later work showed that the contraction of 2-tosyloxy- or 2-bromocyclobutanone may equally be effected by $LiAlH_4$ or methylmagnesium iodide, though in the former case a certain amount of the cyclobutanol intermediate can be isolated [*e.g.* eq. (17), cf. Section 2.1][5, 6]. By contrast, $NaBH_4$ reduction of analogous bicyclic chloroketones gives the pure alcohol[10].



(17)

The presence of other substituents on the ring does not normally affect the reaction course[34–37]. Exceptions occur, however, when position 2 is substituted by a second halogen (see Section 3.3) or by a *tert*-butyl group. In the latter case the reaction is inhibited completely[37], which could be either due to simple steric inhibition of attack on the carbonyl group or to the fact that the *tert*-butyl group prevents the halogen from adopting a pseudo-equatorial conformation (see Section 3.2).

One anomalous result has been reported [eq. (18)], the observed reaction being apparently interpreted in terms of *cine*-substitution[38], although strictly speaking it is not possible to distinguish between *cine* and normal substitution from the data given[39]. However, in view of several reported *cine*-substitutions[14, 40–42], this interpretation seems reasonable and it even seems possible that some "simple substitutions" of 2-bromocyclobutanone itself[33, 43] could in fact proceed *via* a *cine*-substitution mechanism.

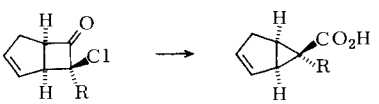


(18)

3.2. Bicyclic Compounds

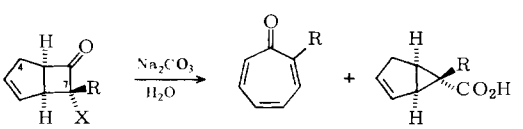
The nucleophile-induced reactions of 7-halobicyclo[3.2.0]-hept-2-en-6-ones and related ketones have been thoroughly studied, mainly because these compounds are easily prepared from halo ketenes and cyclopentadienes[44].

The reactions of the *endo*-halo ketones are simple, leading exclusively to the ring-contracted acids, or derivatives thereof. As with the simpler systems, the rearrangements occur stereospecifically with inversion of configuration at the halogen-bearing carbon [*e.g.* eq. (19)][41, 45–47].



(19)

The situation for the *exo*-halogeno isomers is, however, more complicated [eq. (20)] since two other types of reaction can occur; *viz.*, tropone formation[48, 49] and *cine*-substitution[40, 41] [as in eq. (18)].

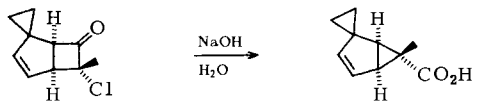


(20)

cine-Substitution seems either to be the sole reaction or not to occur at all[40, 41], the reasons underlying this behavior being rather obscure. It appears, however, that alkali metal methoxides in methanol tend to favor *cine*-substitution in general[14, 39, 42]. In the other cases, the product is normally a tropone and/or a bicyclo[3.1.0]hexane derivative[41, 49]. The composition of the product seems to be governed in the following manner: strong bases favor ring contraction and weak ones tropone formation[41, 49]; the extent of ring contraction depends on the halogen in the following order of preference Cl < Br < I[49]; the proportion of ring contraction decreases as the size of the substituent geminal to the halogen increases[44, 49].

This last factor has been explained in terms of a strong, unfavorable steric interaction between the pseudo-axial 7-alkyl group and the 4-*endo*-hydrogen[44], it being assumed that the halogen must adopt the pseudo-equatorial conformation in order for ring contraction to take place[31].

The presence of substituents on the five-membered ring can also affect the outcome of the reaction. In certain obvious cases only ring contraction occurs, simply because tropone formation is impossible[47, 51] [*e.g.* eq. (21)[47]].



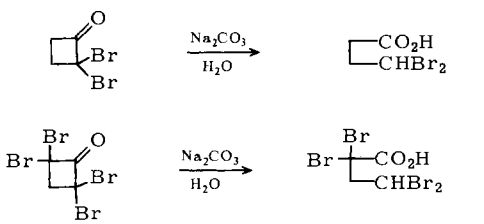
(21)

98%

In other instances, however, tropone formation, while remaining possible, occurs to a much smaller extent[49].

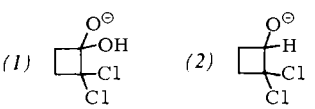
3.3. Dihalo- and Polyhalocyclobutanones

In contrast to the monosubstituted derivatives, α,α-dihalocyclobutanones do not generally undergo ring contraction in the presence of nucleophiles but suffer cleavage instead. This was initially demonstrated for 2,2-dibromo- and 2,2,4,4-tetrabromocyclobutanone[34] [eq. (22)], and has since been reported in several other cases[47, 52–56].

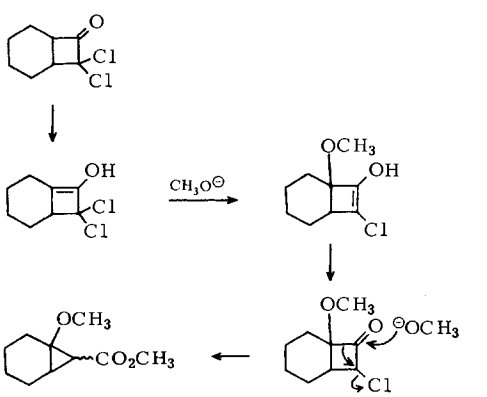


(22)

Worthy of particular attention is the pronounced disparity between the nucleophile-induced reactions of the 2,2-dihalocyclobutanones and the base-catalyzed reactions of the corresponding alcohols (see Section 2.1) which should proceed *via* intermediates that are closely similar, *e.g. (1)* and *(2)*. The difference in behavior has been put down to weakening of the C^1—C^2 bond by the additional electron-withdrawing substituent in the ketones[56].



The action of weak nucleophiles on 7,7-dihalobicyclo[3.2.0]-hept-2-en-6-ones can lead to tropolones[49, 54, 55, 57, 58], the reaction apparently occurring *via* initial *cine*-substitution[38, 54]. The latter process is also involved as the first step of a single outstanding reaction leading to ring contraction, the species effectively undergoing rearrangement being the intermediate α-monohalo-α′-methoxy compound [eq. (23)][59].

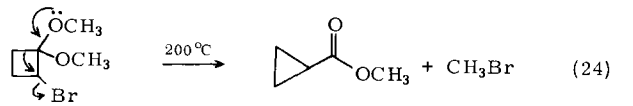


(23)

4. α-Substituted Ketals, Ethers, Thioethers, and Amines

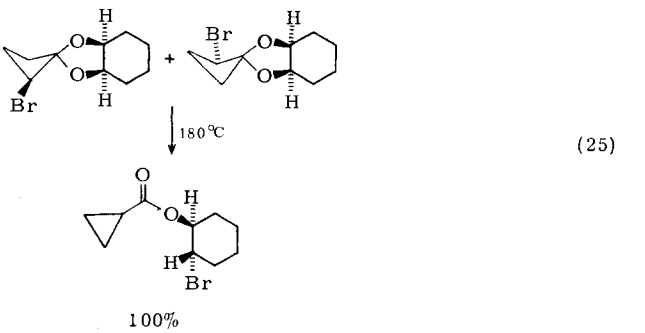
4.1. α-Substituted Ketals

The thermal ring contractions of α-bromocyclobutanone ketals have been well investigated and found to lead to cyclopropanecarboxylic esters and alkyl bromides in the case of simple ketals [*e.g.* eq. (24)] and to bromo esters in the case of cyclic ketals [*e.g.* eq. (25)][60–62].



(24)

100%



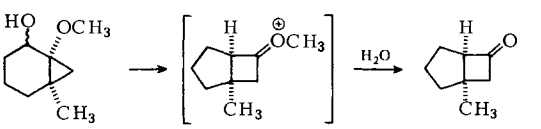
(25)

100%

This quantitative reaction is bimolecular, non-ionic, and proceeds with inversion of configuration at the halogen-receiving carbon atom[61, 62].

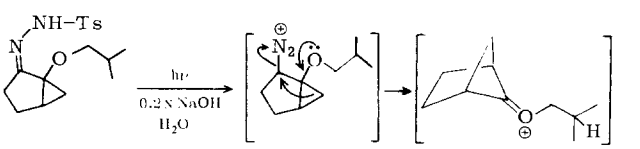
4.2. α-Substituted Ethers

Only expansions have been observed in this category, the first being the simple acid-catalyzed rearrangement of a methoxybicyclo[4.1.0]heptanol [eq. (26)][63].

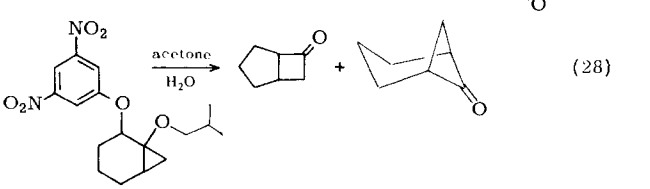


(26)

70–85%



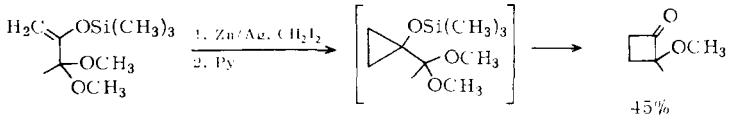
(27)



(28)

Two other reactions proceeding under somewhat different conditions and again involving bicyclic molecules have since been reported [*e.g.* eq. (27) and (28)][64].

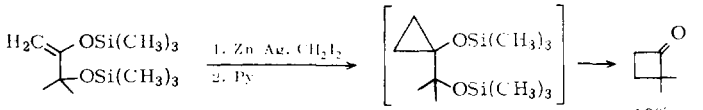
Finally, two trimethylsilyl enol ethers give cyclobutanones under the conditions of the modified Simmons-Smith reaction[109]. The reaction probably proceeds *via* the corresponding siloxycyclopropanes, the ring expansions of which may possibly be catalyzed by the zinc iodide formed on cyclopropanation [eq. (29) and (30)][66].



(29)

45%

+ $CH_3OSi(CH_3)_3$



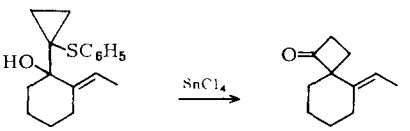
(30)

40%

+ $(CH_3)_3SiOSi(CH_3)_3$

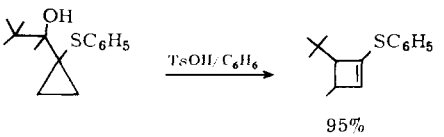
4.3. α-Substituted Thioethers

Phenylthiocyclopropylmethanols have been shown to rearrange in high yield to cyclobutanone derivatives. The use of a Lewis acid catalyst followed by hydrolysis (preferred), or of aqueous acid, leads to the cyclobutanone [*e.g.* eq. (31)], whilst *p*-toluenesulfonic acid in dry benzene gives the cyclobutenyl sulfide [eq. (32)][67–69].



(31)

84%

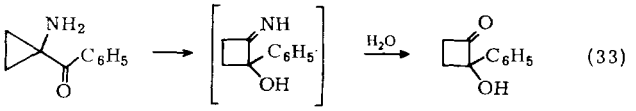


(32)

95%

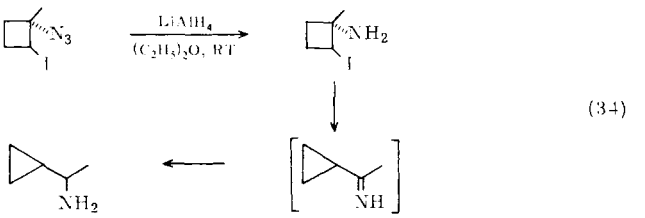
4.4. α-Substituted Amines

The earliest reported ring expansion of such compounds was the thermolysis of 1-aminocyclopropyl phenyl ketone which leads, after hydrolysis, to 2-hydroxy-2-phenylcyclobutanone[70] [eq. (33)]. There appear to be no other clear-cut instances involving ring expansion (cf., however, ref.[71]).



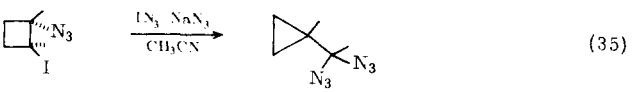
(33)

There are, however, several examples of the corresponding ring contraction. Thus 2-iodocyclobutyl azides have been converted into cyclopropylmethylamines by treatment with $LiAlH_4$ [*e.g.* eq. (34)]. The intermediacy of the iodo amine seems almost certain as this compound has been prepared and shown to give the same product on treatment with $LiAlH_4$[72].



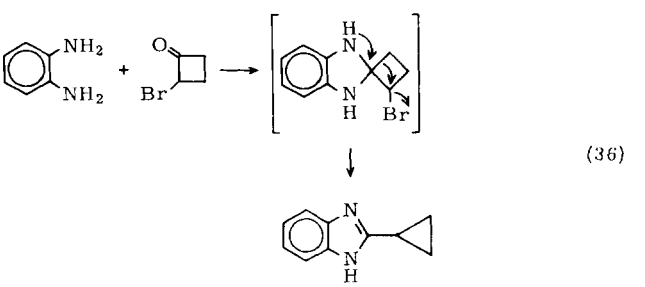
(34)

Interestingly, in one case the rearrangement could also be effected by the action of sodium azide/iodine azide in acetonitrile [eq. (35)]. The mechanism of this reaction was not established, and in particular it was not shown whether the iodine azide is necessary[72].



(35)

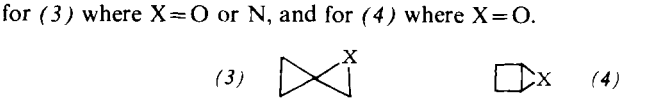
A 2-bromocyclobutylamine has been reasonably postulated as an intermediate in the reaction of *o*-phenylenediamine with 2-bromocyclobutanone to give 2-cyclopropylbenzimidazole [eq. (36)][73].



(36)

5. Epoxides and Aziridines

Systems of types *(3)* and *(4)*, where X can act as both electron donor and electron acceptor and/or where the C—X bond is susceptible to heterolysis, would be expected to rearrange under appropriate conditions. Examples are known for *(3)* where X=O or N, and for *(4)* where X=O.



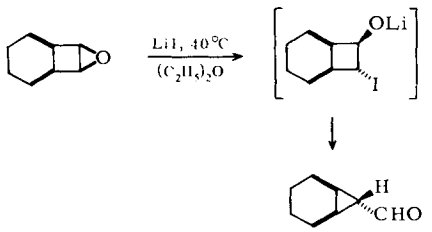
(3) *(4)*

5.1. 1,2-Epoxycyclobutanes

The first ring contraction of a 1,2-epoxycyclobutane was reported by *Criegee et al.*; however, the conditions used also led to ring opening [eq. (37)][18].

(37)

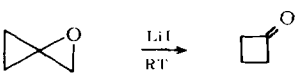
More extensive studies have since been carried out, showing that while the careful use of protic acids gives cyclopropyl products exclusively and in good yield, the employment of aluminum chloride leads to some concomitant cyclobutanone formation, except when this is impossible[74, 75]. Lithium iodide and lithium thiocyanate have also been used as catalysts, and in these cases the reaction occurs stereospecifically with retention of configuration at C-2; according to the proposed addition-elimination mechanism the contraction is really that of a 2-halocyclobutoxide [eq. (38)][111].



(38)

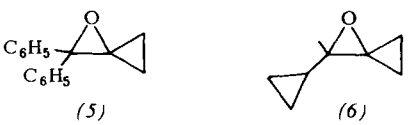
5.2. Oxaspiropentanes

Oxaspiropentanes undergo facile thermal or catalyzed rearrangement to cyclobutanones [*e.g.* eq. (39)]; the best presently available preparative route to cyclobutanone leads from methallyl chloride *via* methylenecyclopropane and oxaspiropentane[7, 76].



(39)

Yields are very often quantitative, though certain oxaspiropentanes give a significant proportion of ring cleavage products[7, 76-78]. Attempts to isolate compounds *(5)* and *(6)* have not been successful because they rearrange so easily[79].

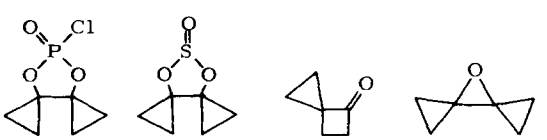


(40)

(5) *(6)*

The "thermal" reaction proceeds in either the liquid or the gas phase, the temperature required depending on the conditions used and on the compound in question. Where no activating substituents are present, liquid-phase reactions occur at temperatures upwards of about 100 °C[7, 76, 80] and are in reality almost certainly acid catalyzed. Under such conditions oxaspiropentane itself gives a high proportion (60 %) of ring-cleavage products[7, 76]. Gas-phase rearrangements have been effected either on a GLC column (effectively an acid catalyst) at temperatures of around 150 °C[80, 82] or at higher temperatures[77, 78] (see also ref.[81]).

The thermal (130 °C) reactions of the cyclic phosphoric acid derivative *(7)* and the sulfite *(8)* to give the cyclobutanone



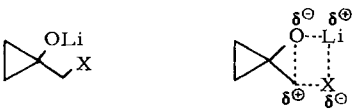
(41)

(7) *(8)* *(9)* *(10)*

(9) probably proceed *via* an oxaspiropentane intermediate *(10)*[83].

Catalysts which have been used to promote this type of rearrangement include protic acids[77-79, 84, 85], lithium halides[7, 76, 84], lithium salts with non-nucleophilic counterions[84, 86], a europium complex $Eu(fod)_3$[84], and trimethylchlorosilane[7].

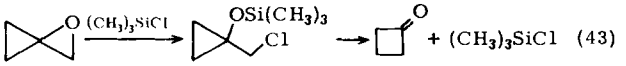
The reactions catalyzed by protic acids appear to involve carbenium ions[84], with the diol also being a potential intermediate in aqueous media. The lithium halide-catalyzed rearrangements probably proceed *via* the lithium salts *(11)* whilst when lithium salts with non-nucleophilic counterions are employed a more loosely bond intermediate *(12)* seems more probable[7].



(42)

(11) *(12)*

The trimethylchlorosilane-catalyzed reaction has been shown to proceed *via* an intermediate adduct [eq. (43)][7].



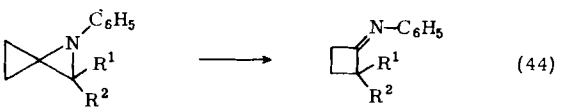
(43)

Finally, owing their preparative significance, it should be emphasized that oxaspiropentanes are readily accessible by condensation of diphenylsulfonium cyclopropylide with aldehydes and ketones, and can be converted into cyclobutanones by treatment with acids[79, 84].

Another recent route to cyclobutanones *via* oxaspiropentanes uses bromine-lithium exchange on *gem*-dibromocyclopropanes, followed by reaction with aldehydes and ketones at −90 °C, warming to room temperature, and acidification[85].

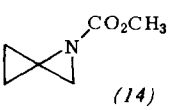
5.3. Azaspiropentanes

Azaspiropentanes react in the same manner as oxaspiropentanes, though only the four compounds *(13a)*—*(13c)* and *(14)* appear to have been studied [eq. (44)].



(44)

(13a), $R^1 = R^2 = H$
(13b), $R^1 = H$, $R^2 = C_6H_5$
(13c), $R^1 = R^2 = C_6H_5$

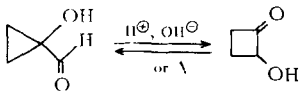


(14)

Of these, the most easily rearranged is the triphenyl compound *(13c)*. It may be prepared at −78 °C, but spontaneously gives the corresponding cyclobutanimine on warming to room temperature[87]. The diphenyl compound *(13b)* can be rearranged either by heating to 100 °C[87, 88], by treatment with hydrogen chloride in benzene[87], or by prolonged irradiation in methylene dichloride[88]. By contrast, the monophenyl derivative *(13a)* gives only ring-opening products on treatment with hydrogen chloride, though its rearrangement can be effected either by prolonged irradiation in benzene[87] or by gas-phase thermolysis[87, 89]. Compound *(14)* does not rearrange, either on thermolysis or on acid treatment[89].

6. Acyloins

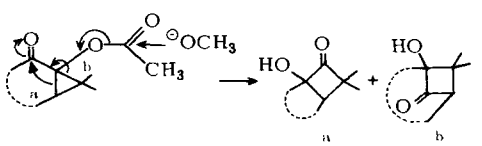
The acyloins are unique among the systems under discussion in that, at least theoretically, the starting cyclopropylmethyl and cyclobutyl compounds can be interconverted by respective ring expansion and ring contraction [eq. (45)].



(45)

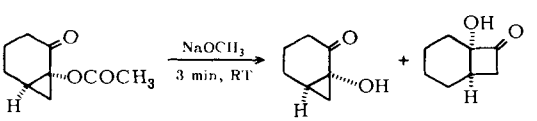
6.1. Ring Expansion

The earliest example of such a ring expansion seems to be the methoxide-induced rearrangement of a phorbol derivative. Ring expansion of an α-acetoxycyclopropyl ketone moiety follows upon liberation of the free hydroxyl group by the action of methoxide ion [eq. (46)][90].



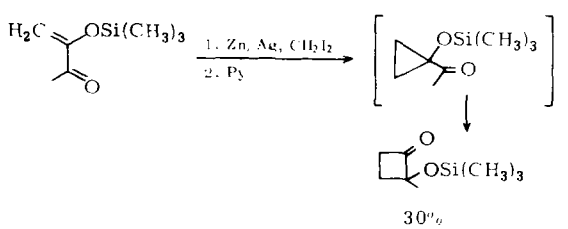
(46)

In a similar reaction, only one of the two possible ring-expansion products was observed, in addition to a little unrearranged acyloin [eq. (47)][16]. In view of all the other results it seems probable that the latter could only be isolated on account of the short reaction time.

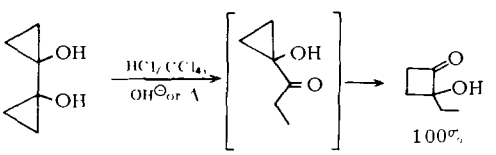


(47)

In two more complex transformations, the ring-expansion of a hydroxycyclopropyl ketone (or ether derivative thereof) has been proposed as part of the mechanism [eq. (48)][66] and (49)[83]. Reaction (49) can also be performed with base catalysis at 100 °C or in the gas phase at 230 °C (5 min).

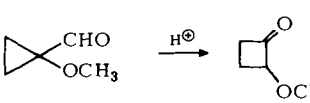


(48)



(49)

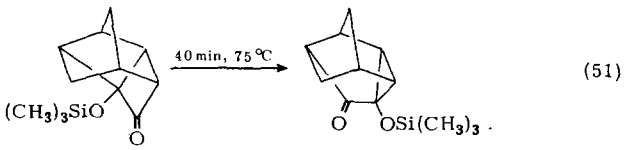
Attempts to prepare the simplest possible starting compound, α-hydroxycyclopropanecarbaldehyde, were unsuccessful[91]. However, the methyl ether thereof was found to undergo very rapid rearrangement upon treatment with a trace of acid (*e. g.* by dissolution in "spectrograde" CCl_4)[25] [eq. (50)].



(50)

6.2. Ring Contraction

Apparently the only clear-cut example of a ring contraction in this category, although involving a silyl ether rather than a free acyloin, is the thermal rearrangement of the tetracyclic molecule *(15)* [eq. (51)][92].

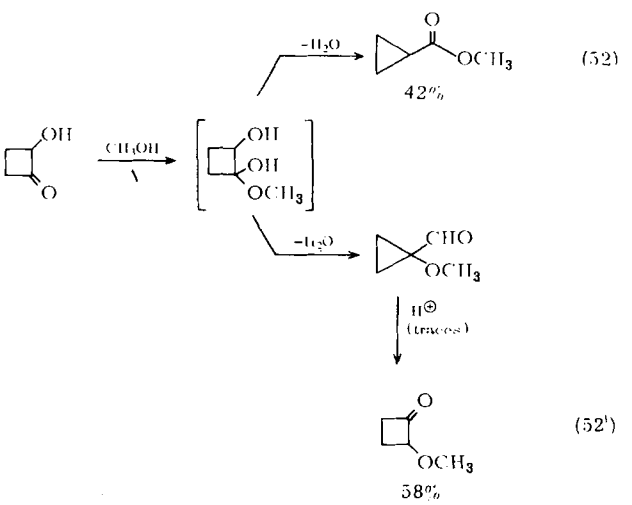


(51)

(15)

Attempts to effect the contraction of the simplest case, that of 2-hydroxycyclobutanone, by heating it in a sealed tube either alone (210 °C) or with water (230 °C) failed to bring about any reaction at all. The conclusion drawn was that while contraction almost certainly occurs, the equilibrium [eq. (45)] lies heavily on the side of the four-membered ring[25]. The facile reaction of the tetracyclic compound *(15)* shows however that this equilibrium may be markedly shifted when other factors, such as additional ring strain, come into play.

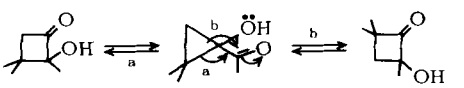
Heating 2-hydroxycyclobutanone with methanol leads, by contrast, to partial rearrangement, though in the alternative sense[25]. Two ring-contracted products are formed: the methyl cyclopropanecarboxylate [eq. (52)] and α-methoxycyclopropanecarbaldehyde [eq. (52')], both of them probably *via* the 1-methoxy-1,2-diol; the methoxyaldehyde, as shown independently (see above), undergoes rapid ring expansion.



(52)

(52')

The ring-contractions of α-hydroxycyclobutanones forming part of a bicyclic system have been postulated as steps in mechanistic schemes, in the conversion of phenylcyclobutenedione to a quinone derivative[93], and more recently in the hydroxide-ion-induced reaction of an α-chloro ketone[40].



(53)

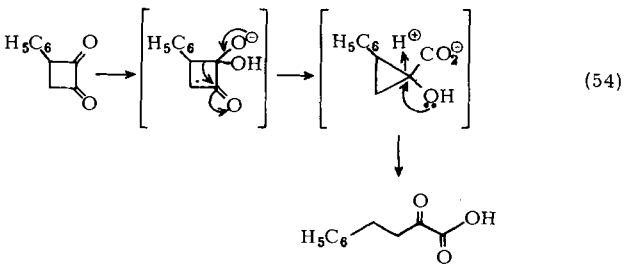
(16) *(17)*

Finally an intriguing interconversion of two hydroxytrimethylcyclobutanones *(16)* and *(17)* has been described[94]. A simple methyl migration was suggested by the claimed—but not proved—stereospecificity of the reaction. Actually such

a rearrangement [eq. (53)] appears to illustrate the equilibrium of eq. (45).

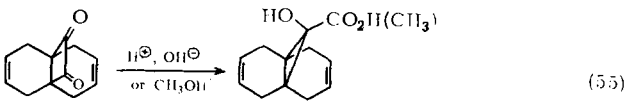
7. 1,2-Cyclobutanediones

A ring contraction of 1,2-cyclobutanediones was first postulated in order to account for the formation of an α-keto acid from phenylcyclobutanedione [eq. (54)][95].

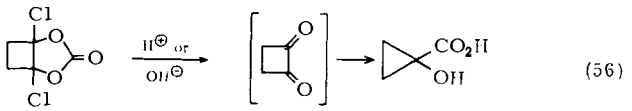


(54)

It was only ten years later that a clear-cut example of such a rearrangement was reported [eq. (55)][96], although a slightly earlier report had proposed cyclobutanedione itself as an intermediate in the acid- or base-catalyzed ring contraction of a dichlorocarbonate [eq. (56)][97]. (For more recent examples of the latter type of reaction, see ref.[98].)

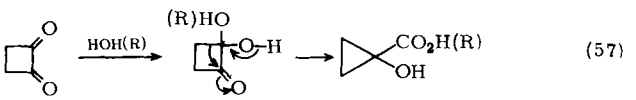


(55)



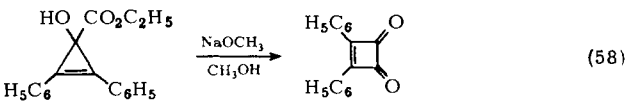
(56)

Cyclobutanedione has now been prepared and shown to undergo ring contraction to hydroxycyclopropanecarboxylic acid[25, 99, 100]. The reaction may be catalyzed by aqueous acid or base, but even takes place, though more slowly, in pure water or methanol [eq. (57)][25, 99]. 3,4-Di-*tert*-butyl-1,2-cyclobutanedione and the 3,4-diphenyldione undergo ring contraction in the presence of methoxide ion and amines or hydrazines, respectively[101, 102]. (Concerning a photochemical ring contraction of a 1,2-cyclobutanedione, see ref.[117].)



(57)

Interestingly, when there is a double bond in the ring reaction proceeds in the reverse sense [eq. (58)][103].



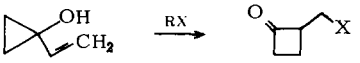
(58)

8. 1-Vinylcyclopropanols and 2-Alkylidenecyclobutanols

Both expansions and contractions have been observed in this category of 2,3-unsaturated alcohols, the former being more numerous. Reaction proceeds thermally or under catalysis by acids or other electrophilic reagents.

8.1. Ring Expansion

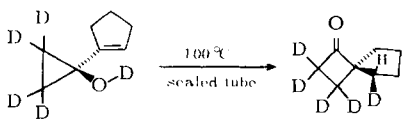
The earliest studies on ring expansion were carried out with simple molecules, using acids or electrophiles such as *tert*-butyl hypochlorite as catalyst [*e.g.* eq. (59)][104, 105, 116]. With the latter reagent it was also possible to effect expansion of an alkynylcyclopropanol[105]. A later report indicates that for highly substituted vinylcyclopropanols a significant amount of ring cleavage can occur when acid catalysts are used[106].



(59)

R = Br, X = H; R = $C_6H_5CO_2$, X = OH;
R = $(CH_3)_3CO$, X = Cl

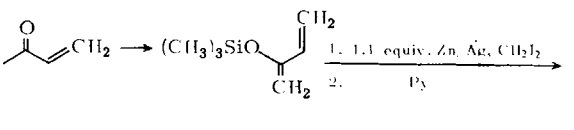
Vinylcyclopropanols also undergo thermal rearrangement, either in the liquid or the gas phase, at temperatures of 100 °C or more. A deuterium labeling study has shown that under sealed-tube conditions the new carbon-carbon and carbon-hydrogen bonds are formed stereospecifically *cis* to one another [eq. (60)]. The result has been interpreted in terms of a non-con-

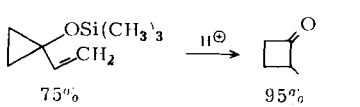


(60)

certed mechanism involving an intramolecular proton transfer[7, 109]. One vinylcyclopropanol has been shown to rearrange even at room temperature, apparently in the absence of catalysts[110].

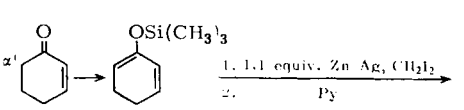
The reaction may be carried out as easily, starting from the corresponding trimethylsilyl derivatives, using aqueous acid as the catalyst[79, 107]. These compounds are readily prepared by cyclopropanation of silyl enol ethers derived from α-ethylenic ketones, by Simmons-Smith reaction with a Zn/Ag couple and pyridine work-up[65], and their acid or thermal treatment constitutes an excellent route to cyclobutanones[107]. Yields are high, but only when the siloxy group is able to adopt a cisoid configuration with respect to the double bond [*e.g.* eq. (61)][107]. In the case of cyclic systems where this is impossible, no ring expansion occurs and only



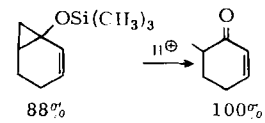


75% 95%

(61)



(62)

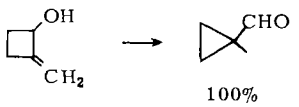


88% 100%

opening of the cyclopropane ring is observed with formation of the α′-methylation product [*e.g.* eq. (62)][108].

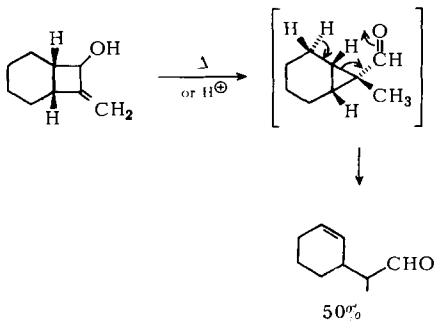
8.2. Ring Contraction

The corresponding ring contractions proceed with greater difficulty. Thus the rearrangement of 2-methylenecyclobutanol occurs thermally only at 245 °C (sealed tube, 4 h), and with acid catalysis (5 % aqueous sulfuric acid, 30 min) only at 100 °C [eq. (63)][25, 111].



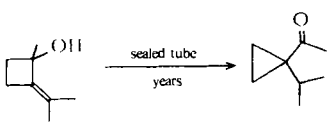
(63)

In certain cases the aldehydic product may undergo ring opening during the reaction, and thus prove difficult to isolate [*e.g.* eq. (64)][25, 111].



(64)

If the hydroxyl group is tertiary, it appears impossible to effect the ring contraction thermally or with acid, on account of the extreme facility of the competing dehydration reaction; however, after standing at room temperature for seven years in a sealed tube, 2-isopropylidene-1-methylcyclobutanol had rearranged to the extent of 60 % [eq. (65)][25, 111].

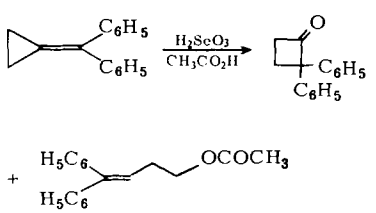


(65)

9. Miscellaneous Oxidative Rearrangements

On oxidative expansion and/or contraction of small ring compounds, olefins and ketones react in analogous manner to α-substituted alcohols and acyloins, respectively.

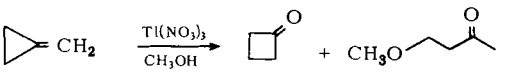
The earliest such reaction entailed ring expansion of a substituted methylenecyclopropane by the action of selenious acid [eq. (66)][112].



(66)

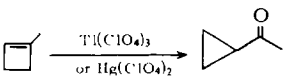
The rearrangement of methylenecyclopropane itself has since been performed with thallic nitrate; the yield of cyclobutanone was low [eq. (67)][113].

The ring-contractions of cyclobutene and 1-methylcyclobutene form part of a study of the mercury(II) and thallium(III)



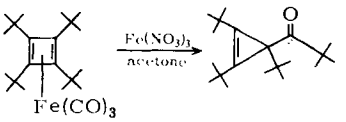
(67)

oxidations of a series of (mainly cyclic) alkenes [*e.g.* eq. (68)][114].



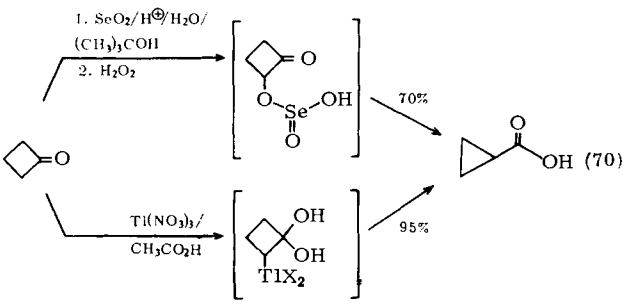
(68)

The analogous rearrangement of a cyclobutadiene complex has been effected using cerium(IV) or iron(III) reagents [eq. (69)][115].



(69)

Treatment of cyclobutanone under aqueous acidic conditions with either hydrogen peroxide/selenium dioxide or thallium(III) salts gives cyclopropanecarboxylic acid in good yield [eq. (70)][113].



(70)

10. Conclusion

The present article has reviewed recent work on a hitherto neglected class of carbocyclic ring rearrangements, namely interconversions of cyclobutane and cyclopropylmethyl systems. The material considered suggests that such rearrangements are actually more numerous and often more versatile, because more specific, than those of corresponding larger rings.

The very facile interconversion of such systems can be explained by the generally small difference (≈ 1.5 kcal/mol) between their ring strain energies. Moreover, formation of a cyclopropylcarbonyl compound from a cyclobutane and of a cyclobutanone from a cyclopropylmethyl compound are favored by a powerful driving force. These reactions, which may be thermal or acid- or base-catalyzed, normally give a single product, even when involving a carbenium ion intermediate.

Many of these ring contractions and expansions possess a real synthetic interest. For instance, an excellent preparative pathway to cyclopropanecarbaldehyde uses ring contraction of 1,2-cyclobutanediol and a very good route to cyclobutanone uses ring expansion of oxaspiropentane, two starting materials which, like many other small ring compounds, are now readily available. Likewise it has been seen that a given cyclobutanone can be prepared by expansion reactions of six or seven appropriate cyclopropylmethyl compounds, and a given cyclopropylcarbonyl compound by contraction reactions of an even greater number of appropriate cyclobutanes.

We thank the Centre National de la Recherche Scientifique (Paris) for enabling us and the Laboratoire des Carbocycles to participate to the development in the field reviewed in this article, and the Royal Society (London) for the award of a European Fellowship to one of us (M. J. R.).

Received: December 9, 1974 [A 66 IE]
German version: Angew. Chem. *87*, 505 (1975)

[1] *C. D. Gutsche* and *D. Redmore* in *H. Hart* and *G. J. Karabatsos*: Carbocyclic Ring Expansion Reactions. (Advan. Alicyclic Chem. Suppl. 1). Academic Press, New York 1968.
[2] *D. Redmore* and *C. D. Gutsche* in *H. Hart* and *G. J. Karabatsos*: Carbocyclic Ring Contraction Reactions. (Advan. Alicyclic Chem. Vol. 3, pp. 1–138). Academic Press, New York 1971.
[3] *R. Breslow* in *P. de Mayo*: Molecular Rearrangements. Academic Press, New York 1968, p. 245.
[4] a) *H. G. Richey* in *G. A. Olah* and *P. v. R. Schleyer*: Carbonium Ions. Wiley-Interscience, New York 1972, Vol. 2, p. 1201; b) *K. B. Wiberg, B. A. Hess, Jr.*, and *A. J. Ashe*, *ibid.* p. 1295.
[5] *J. R. Salaun* and *J. M. Conia*, Chem. Commun. *1970*, 1358.
[6] *J. P. Barnier, J. M. Denis, J. R. Salaun*, and *J. M. Conia*, Tetrahedron *30*, 1405 (1974).
[7] *J. R. Salaun, B. Garnier*, and *J. M. Conia*, Tetrahedron *30*, 1413 (1974).
[8] *P. R. Brook*, Chem. Commun. *1968*, 565.
[9] *P. R. Brook* and *A. J. Duke*, J. C. S. Perkin I, *1973*, 1013.
[10] *P. R. Brook* and *A. J. Duke*, Chem. Commun. *1970*, 652.
[11] *D. L. Garin*, J. Org. Chem. *36*, 1697 (1971).
[12] *M. Rey* and *A. S. Dreiding*, Helv. Chim. Acta *57*, 734 (1974).
[13] *P. R. Brook* and *A. J. Duke*, Chem. Commun. *1970*, 1344.
[14] *W. T. Brady* and *A. D. Patel*, J. Org. Chem. *38*, 4106 (1973).
[15] *J. V. Paukstelis* and *J. L. Kao*, Tetrahedron Lett. *1970*, 3691.
[16] *J. V. Paukstelis* and *J. L. Kao*, J. Amer. Chem. Soc. *94*, 4783 (1972).
[17] *H. Bartsch* and *E. Hecker*, Liebigs Ann. Chem. *725*, 142 (1969).
[18] *R. Criegee* and *K. Knoll*, Liebigs Ann. Chem. *627*, 1 (1959).
[19] *J. P. Barnier* and *J. M. Conia*, to be published.
[20] *G. W. Griffin* and *R. B. Hager*, J. Org. Chem. *28*, 599 (1963).
[21] *C. Buchanan* and *B. R. Davis*, J. Chem. Soc. *C 1967*, 1340.
[22] *L. Crombie, M. L. Games*, and *D. J. Pointer*, J. Chem. Soc. *C 1968*, 1347.
[23] *H. W. Thielmann* and *E. Hecker*, Liebigs Ann. Chem. *728*, 158 (1969).
[24] *J. M. Conia* and *J. P. Barnier*, Tetrahedron Lett. *1971*, 4981.
[25] *J. P. Barnier, J. M. Denis, J. R. Salaun*, and *J. M. Conia*, Tetrahedron *30*, 1405 (1974).
[26] *N. J. Turro* and *R. B. Gagosian*, J. Amer. Chem. Soc. *92*, 2036 (1970).
[27] *R. Wiechert*, Angew. Chem. *82*, 219 (1970); Angew. Chem. internat. Edit. 9, 237 (1970).
[28] *A. E. Feiring* and *J. Ciabattoni*, J. Amer. Chem. Soc. *95*, 5266 (1973).
[29] *R. Breslow, L. J. Altman, A. Krebs, E. Mohacsi, I. Murata, R. A. Peterson*, and *J. Posner*, J. Amer. Chem. Soc. *87*, 1326 (1965).
[30] *E. V. Dehmlow*, Tetrahedron Lett. *1965*, 4003.
[31] *J. M. Conia* and *J. R. Salaun*, Accounts Chem. Res. *5*, 33 (1972), and references cited therein.
[32] *J. M. Conia* and *J. L. Ripoll*, C. R. Acad. Sci. *251*, 1071 (1960).
[33] *J. M. Conia* and *J. L. Ripoll*, Bull. Soc. Chim. Fr. *1963*, 755.
[34] *J. M. Conia* and *J. L. Ripoll*, Bull. Soc. Chim. Fr. *1963*, 763.
[35] *J. M. Conia* and *J. L. Ripoll*, Bull. Soc. Chim. Fr. *1963*, 773.
[36] *J. M. Conia* and *J. R. Salaun*, Bull. Soc. Chim. Fr. *1964*, 1957; Tetrahedron Lett. *1963*, 1175.
[37] *J. R. Salaun* and *J. M. Conia*, Bull. Soc. Chim. Fr. *1968*, 3735.
[38] The term *cine*-substitution is used here to mean the replacement of a group in the position α to a carbonyl group by a substituent entering at the α'-position, the reaction occurring *via* the enol.
[39] *W. T. Brady* and *J. P. Hieble*, J. Org. Chem. *36*, 2033 (1971).
[40] *P. R. Brook* and *J. M. Harrison*, J. C. S. Chem. Comm. *1972*, 997.
[41] *D. L. Garin* and *K. L. Cammack*, J. C. S. Chem. Comm. *1972*, 333.
[42] *W. D. Brady* and *A. D. Patel*, J. Org. Chem. *39*, 1949 (1974).
[43] *J. M. Conia* and *J. L. Ripoll*, C. R. Acad. Sci. *252*, 423 (1961).
[44] *P. R. Brook, A. J. Duke, J. M. Harrison*, and *K. Hunt*, J. C. S. Perkin I, *1974*, 927.
[45] With one exception: the bicycloheptenone in eq. (19) with R = H does not react *via* ring contraction.
[46] *P. R. Brook, J. M. Harrison*, and *A. J. Duke*, Chem. Commun. *1970*, 589.
[47] *P. R. Brook* and *J. M. Harrison*, J. C. S. Perkin I, *1974*, 779.
[48] *W. T. Brady* and *J. P. Hieble*, Tetrahedron Lett. *1970*, 3205.
[49] *W. T. Brady* and *J. P. Hieble*, J. Amer. Chem. Soc. *94*, 4278 (1972).
[50] Cf. *K. B. Wiberg* and *A. J. Ashe*, J. Amer. Chem. Soc. *90*, 63 (1968).
[51] *E. Wenkert, P. Bakuzis, R. J. Baumgarten, C. L. Leicht*, and *H. P. Schenk*, J. Amer. Chem. Soc. *93*, 3208 (1971).
[52] *L. Ghosez, R. Montaigne*, and *P. Mollet*, Tetrahedron Lett. *1966*, 135.
[53] *T. R. Potts* and *R. E. Harmon*, J. Org. Chem. *34*, 2792 (1969).
[54] *P. D. Bartlett* and *T. Ando*, J. Amer. Chem. Soc. *92*, 7518 (1970).
[55] *H. C. Stevens, J. K. Rinehart, J. M. Lavanish*, and *G. M. Trenta*, J. Org. Chem. *36*, 2780 (1971).
[56] *P. R. Brook* and *A. J. Duke*, J. Chem. Soc. *C 1971*, 1764.
[57] *H. C. Stevens, D. A. Reich, D. R. Brandt, K. R. Fountain*, and *E. J. Gaughan*, J. Amer. Chem. Soc. *87*, 5257 (1965).
[58] *R. W. Turner* and *T. Seden*, Chem. Commun. *1966*, 399.
[59] *V. R. Fletcher* and *A. Hassner*, Tetrahedron Lett. *1970*, 1071.
[60] *J. R. Salaun* and *J. M. Conia*, Tetrahedron Lett. *1968*, 4545.
[61] *J. R. Salaun* and *J. M. Conia*, Tetrahedron Lett. *1971*, 4023.
[62] *J. R. Salaun, B. Garnier*, and *J. M. Conia*, Tetrahedron *29*, 2895 (1973).
[63] *E. Wenkert, R. A. Muller, E. J. Reardon Jr., S. S. Sathe, D. J. Sharf*, and *G. Tosi*, J. Amer. Chem. Soc. *92*, 7428 (1970).
[64] *W. Kirmse* and *J. Alberti*, Chem. Ber. *106*, 236 (1973).
[65] *J. M. Denis* and *J. M. Conia*, Tetrahedron Lett. *1972*, 4593; *J. M. Denis, C. Girard*, and *J. M. Conia*, Synthesis *1972*, 549.
[66] *J. P. Barnier, B. Garnier, C. Girard, J. M. Denis, J. R. Salaun*, and *J. M. Conia*, Tetrahedron Lett. *1973*, 1747.
[67] *B. M. Trost, D. Keeley*, and *M. J. Bogdanowicz*, J. Amer. Chem. Soc. *95*, 3068 (1973).
[68] *B. M. Trost* and *D. E. Keeley*, J. Amer. Chem. Soc. *96*, 1252 (1974).
[69] *B. M. Trost*, Accounts Chem. Res. *7*, 85 (1974).
[70] *C. L. Stevens, R. M. Weier*, and *K. G. Taylor*, 152nd Nat. Meeting, Amer. Chem. Soc., New York, Sept. 1966, Abstr. S-101.
[71] *J. K. Crandall* and *L. C. Crawley*, J. Org. Chem. *39*, 489 (1974).
[72] *M. J. O'House* and *D. Swern*, Tetrahedron Lett. *1973*, 1607.
[73] *R. C. De Selms*, Tetrahedron Lett. *1970*, 3001.
[74] *J. L. Ripoll* and *J. M. Conia*, Tetrahedron Lett. *1965*, 979.
[75] *J. L. Ripoll* and *J. M. Conia*, Bull. Soc. Chim. Fr. *1965*, 2755.
[76] *J. R. Salaun* and *J. M. Conia*, Chem. Commun. *1971*, 1579.
[77] *J. K. Crandall* and *D. R. Paulson*, J. Org. Chem. *33*, 991 (1968).
[78] *J. K. Crandall* and *D. R. Paulson*, J. Org. Chem. *33*, 3291 (1968).
[79] *B. M. Trost* and *M. J. Bogdanowicz*, J. Amer. Chem. Soc. *95*, 5311 (1973).
[80] *J. R. Wiseman* and *H. F. Chan*, J. Amer. Chem. Soc. *92*, 4749 (1970).
[81] *D. H. Aue, M. Mestishnak*, and *D. F. Shellhamer*, Tetrahedron Lett. *1973*, 4799.
[82] *C. R. Johnson, G. F. Katelkar, R. F. Huxol*, and *E. R. Janiga*, J. Amer. Chem. Soc. *93*, 3771 (1971).
[83] *J. M. Denis* and *J. M. Conia*, Tetrahedron Lett. *1972*, 4593.
[84] *B. M. Trost* and *M. J. Bogdanowicz*, J. Amer. Chem. Soc. *95*, 5321 (1973).
[85] *M. Braun* and *D. Seebach*, Angew. Chem. *86*, 279 (1974); Angew. Chem. internat. Edit. *13*, 277 (1974).
[86] *B. M. Trost* and *M. J. Bogdanowicz*, J. Amer. Chem. Soc. *95*, 5298 (1973).
[87] *J. K. Crandall* and *W. W. Conover*, J. Org. Chem. *39*, 63 (1974).
[88] *J. K. Crandall* and *W. W. Conover*, J. C. S. Chem. Comm. *1973*, 33.
[89] *D. H. Aue, R. B. Louns*, and *G. S. Helwig*, Tetrahedron Lett. *1973*, 4795.
[90] *H. Bartsch* and *E. Hecker*, Liebigs Ann. Chem. *725*, 142 (1969).
[91] *J. M. Conia, J. M. Denis*, and *J. R. Salaun*, unpublished results.
[92] *R. D. Miller* and *D. L. Dolce*, Tetrahedron Lett. *1973*, 5217.
[93] *W. Ried* and *W. Kunkel*, Liebigs Ann. Chem. *717*, 54 (1968).
[94] *W. H. Urry, J. C. Duggan*, and *M. H. Pai*, J. Amer. Chem. Soc. *91*, 5785 (1970).
[95] *L. Skattebol* and *J. D. Roberts*, J. Amer. Chem. Soc. *80*, 4085 (1958).
[96] *J. J. Bloomfield, J. R. S. Ireland*, and *A. B. Marchand*, Tetrahedron Lett. *1968*, 5647.
[97] *H. D. Scharf, W. Droste*, and *R. Liebigs*, Angew. Chem. *80*, 194 (1968); Angew. Chem. internat. Edit. 7, 215 (1968).
[98] *H. D. Scharf*, Angew. Chem. *86*, 567 (1974); Angew. Chem. internat. Edit. *13*, 520 (1974); Sections 6.4 and 6.5.
[99] *J. M. Conia* and *J. M. Denis*, Tetrahedron Lett. *1971*, 2845.
[100] *H. G. Heine*, Chem. Ber. *104*, 2869 (1971).
[101] *A. de Groot, D. Oudman*, and *H. Wynberg*, Tetrahedron Lett. *1969*, 1529.
[102] *W. Ried, A. H. Schmidt*, and *H. Medem*, Liebigs Ann. Chem. *1973*, 1530.
[103] *C. D. de Boer*, J. C. S. Chem. Comm. *1972*, 377.
[104] *H. H. Wasserman* and *D. C. Clagett*, J. Amer. Chem. Soc. *88*, 5368 (1966).
[105] *H. H. Wasserman, R. E. Cochoy*, and *M. S. Baird*, J. Amer. Chem. Soc. *91*, 2375 (1969).
[106] *F. Bourelle-Wargnier*, Tetrahedron Lett. *1974*, 1591.
[107] *C. Girard, P. Amice, J. P. Barnier*, and *J. M. Conia*, Tetrahedron Lett. *1974*, 3329.
[108] *C. Girard* and *J. M. Conia*, Tetrahedron Lett. *1974*, 3327.
[109] *J. R. Salaun* and *J. M. Conia*, Tetrahedron Lett. *1972*, 2849.

[110] C. R. Johnson and R. W. Herr, J. Org. Chem. 38, 3153 (1973).
[111] J. P. Barnier, J. M. Denis, J. R. Salaun, and J. M. Conia, J. C. S. Chem. Comm. 1973, 103.
[112] E. V. Dehmlow, Z. Naturforsch. 24b, 1197 (1969).
[113] J. R. Salaun, B. Garnier, and J. M. Conia, Tetrahedron 30, 1413 (1974).
[114] P. A. Abley, J. E. Byrd, and J. Halpern, J. Amer. Chem. Soc. 95, 2591 (1973).
[115] J. Ciabattoni and A. E. Feiring, J. Amer. Chem. Soc. 94, 5113 (1972).
[116] H. H. Wasserman, H. Adickes, and O. E. de Ochoa, J. Amer. Chem. Soc. 93, 5586 (1971).
[117] J. M. Denis and J. M. Conia, Tetrahedron Lett. 1973, 461.

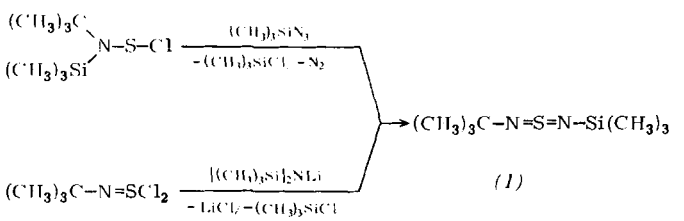
COMMUNICATIONS

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

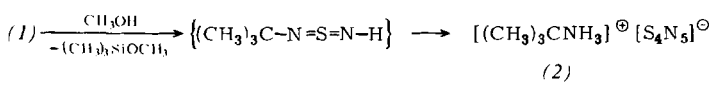
Synthesis of the Tetrasulfur Pentanitride Anion

By *Otto J. Scherer* and *Gotthelf Wolmershäuser*[*]

In contrast to the well studied neutral and cationic binary sulfur-nitrogen compounds[1] the corresponding anionic species have been hardly investigated[1, 2]. Starting from *N*-trimethylsilyl-*N'*-*tert*-butylsulfur(IV) diimide *(1)*, obtainable as follows,



methanolysis according to[5]



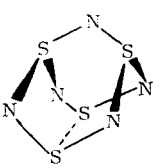
affords the tetrasulfur pentanitride anion as the *tert*-butylammonium salt *(2)*.

(1): yellow liquid; ^{1}H-NMR (10% solution in CCl_4, TMS internal standard): $\delta CH_3Si = -0.20$ (s), $\delta CH_3C = -1.47$ ppm (s); IR (film): $\nu NSN = 1105$ and 1035 cm^{-1}.

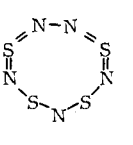
(2) forms yellow crystals that are insoluble in apolar organic solvents, soluble in dimethyl sulfoxide, and very soluble in methanol[6]. It was characterized by complete elemental analysis, conductivity measurements, and mass, ^{1}H-NMR and ^{14}N-NMR spectra. In methanol and in dimethyl sulfoxide the salt *(2)* displays a somewhat higher conductivity than $[(CH_3)_3CNH_3]^+Cl^-$. Molecular weight (osmometric in methanol): 172. Mass spectrum (70 eV): $m/e = 199$ (0.5%, S_4N_5H), 198 (1.5, S_4N_5), 184 (1), 138 (6), 92 (18), 78 (9), 76 (18), 64 (30), 62 (11), 59 (5), 58 (99), 57 (7), 48 (5), 47 (9), 46 (75), 44 (14), 42 (16), 41 (25), 39 (7), 35 (8), 32 (19), 30 (9), 29 (6), 28 (100), 27 (12), 18 (17), 17 (9), 16 (6), 15 (9), 14 (5); all other peaks <(5). The ^{1}H-NMR spectrum (measured in [D$_5$]DMSO) contains two signals, area ratio 1:3. The ^{14}N-NMR spectrum (in DMSO, NO_3^- as external standard)[9] exhibits a broad signal ($\Delta h_{1/2} \approx 1600$ Hz) at $\delta = -306$ ppm.

Treatment of an ethanolic solution of *(2)* with $NaOC_2H_5/C_2H_5OH$ precipitates $Na^+[S_4N_5]^-$ as a yellow powder in about 80% yield. The soldium salt, characterized by complete elemental analysis, IR and mass spectra, is slightly soluble in dimethyl sulfoxide, methanol, and ethanol. The substance explodes at about 180 °C (dark coloration and partial sintering starts above about 150 °C) and under the influence of pressure[15]. IR spectrum (KBr, 4000–300 cm^{-1}): 1040 m, 950 vs, 915 vs, 885 sh, 745 s, 725 w, 700 s, 665 vs, 635 w, 600 vs, 530 vs, 505 s, 440 vs, 410 s, 335 w, 305 m. Mass spectrum (70 eV): $m/e = 92$ (2.5%, S_2N_2), 78 (2, S_2N), 64 (100, S_2), 46 (7, SN), 32 (16, S), 28 (36, N_2).

Of the most probable structural alternatives *(A)* and *(B)* for the anion, we prefer *(A)*[10].



(A)



(B)

This structural type[11] would formally correspond to an S_4N_4 molecule after insertion of an additional N atom into a transannular S—S bond[13].

Procedure:

(1): $[(CH_3)_3Si]_2NH$ (134.9 g, 0.836 mol) in pentane (800 ml) is metalated with *n*-C_4H_9Li/hexane solution (513 ml, 0.836 mol), and then directly added dropwise to a vigorously stirred solution of $(CH_3)_3CNSCl_2$ (145.5 g, 0.836 mol) in pentane (1500 ml) at −78 °C. After warming up to room temperature (*ca.* 12 h) the mixture is filtered through a G3 frit. The filtrate is concentrated in a water-pump vacuum and fractionated over a Vigreux column. Yield 131 g (82%); b.p. 47 to 50 °C/5 torr.

(2): Methanol (6.4 g, 0.2 mol) is added to a solution of *(1)* (38.0 g, 0.2 mol) in benzene (50 ml) and the mixture slowly stirred for 14 days at room temperature (nitrogen is evolved). After filtration (G3 frit) the solid product is washed with benzene until the filtrate is colorless. The yellow crystals[14]

[*] Prof. Dr. O. J. Scherer and Dipl.-Chem. G. Wolmershäuser
Fachbereich Chemie der Universität
675 Kaiserslautern, Postfach 3049 (Germany)

are dried in an oil-pump vacuum. Yield 6.2 g (65% based on the stoichiometry given in ref.[5]).

Received: March 10, 1975;
supplemented: March 17, 1975 [Z 217 IE]
German version: Angew. Chem. 87, 485 (1975)

[1] Cf. *H. G. Heal*, Adv. Inorg. Chem. Radiochem. *15*, 375 (1972); *H. J. Emeléus*, Endeavour *32*, 76 (1973); *H. W. Roesky*, Chem. Ztg. *98*, 121 (1974).
[2] While the existence of $[S_4N_4]^-$ has only been established below 0 °C [3], that of $[S_4N_4]^{4-}$ has not been confirmed beyond doubt [4].
[3] *R. A. Meinzer, D. W. Pratt*, and *R. J. Myers*, J. Am. Chem. Soc. *91*, 6623 (1969).
[4] *A. J. Banister* and *D. Younger*, J. Inorg. Nucl. Chem. *32*, 3763 (1970); *M. Becke-Goehring* and *R. Schwarz*, Z. Anorg. Allg. Chem. *296*, 3 (1958).
[5] The mass balance indicates the following overall equation:

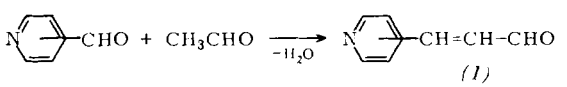
$$17(CH_3)_3CNSNH \rightarrow 3[(CH_3)_3CNH_3]^+[S_4N_5]^- + 5[(CH_3)_3CN]_2S + 4(CH_3)_3CNH_2 + N_2$$

$(CH_3)_3CNSNH$, which can readily be enriched in highly dilute solution, can be detected by ^{1}H-NMR spectroscopy.
[6] Slow deposition of S_4N_4 from the solutions, which are always red at high concentration [7], begins after several hours in methanol. So far S_4N_4 is also the sole product isolated on thermolysis (decomposition of *(2)* begins at about 70 °C).
[7] It remains to be established whether radical species, *e.g.* $[SN_2]^{\cdot}$ [8], are also formed in the process.
[8] *I. Ruppert, V. Bastian*, and *R. Appel*, Chem. Ber. *107*, 3426 (1974).
[9] We are grateful to Prof. Dr. *W. Beck*, Munich, for carrying out the measurement.
[10] Supported by the alkaline hydrolysis of the two salts, which gives no indication of an N—N bond (hydrazine). A final decision can only be based on an X-ray structure analysis to be performed by Prof. Dr. *J. Weiss*, Heidelberg.
[11] Just as S_4N_4 and As_4S_4 represent a molecular pair with inverse structure, $[S_4N_5]^-$, which possesses the same number of electrons as the still unknown species S_5N_4, and As_4S_5[12] would be the second such example.
[12] *T. J. Bastow* and *H. J. Whitfield*, J. Chem. Soc. Dalton Trans. *1973*, 1740.
[13] Cf. also the proposed structure for the hypothetical $[S_4N_4]^{2-}$: *R. Gleiter*, J. Chem. Soc. *A1970*, 3174, and the structure of $[S_4N_5O]^-$: *R. Steudel, P. Luger*, and *H. Bradaczek*, Angew. Chem. *85*, 307 (1973); Angew. Chem. internat. Edit. *12*, 316 (1973).
[14] Somewhat larger crystals are formed with no stirring; however, they are sometimes orange-yellow in color.
[15] These data should be viewed with reservation since the removal of small amounts of substance from the frit with a spatula led to a *violent explosion*!

Vinylogous Pyridinecarbaldehydes by Wittig Reaction

By *Ilse Hagedorn* and *Wolfram Hohler*[*]

Condensation of aromatic aldehydes of the pyridine series with acetaldehyde leads to only very small yields of the pyridineacrylaldehydes *(1)*.



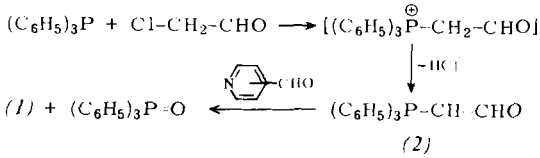
(1)

2-*(1)*: 11 σ_0[1]; 3-*(1)*: 0.8 σ_0[2]; 4-*(1)*: 0.6 σ_0[3]

According to a Japanese report[1] 2-*(1)* can be prepared in 44% yield with the aid of Amberlite IR-4B; however, on trying out this procedure only 10% was obtained[4]. 3-*(1)* is also formed by decarboxylation of β-picolylidenepyruvic acid (4.5%)[2]. Hydrolysis of the corresponding substituted tetrahydro-1,3-oxazine affords 14% 3-*(1)* or 23% 4-*(1)*[4].

[*] Prof. Dr. I. Hagedorn and Dr. W. Hohler
Chemisches Laboratorium der Universität
78 Freiburg, Albertstrasse 21 (Germany)

All three isomeric aldehydes *(1)* can be obtained more conveniently and in improved yields by Wittig reaction[5]. The reactions leading to the phosphorane *(2)* are described in the literature[6].



(2)

Pyridineacrylaldehyde (1)[7]

A mixture of freshly distilled pyridinecarbaldehyde (1.71 g; 15 mmol) and *(2)* (4.90 g; 16 mmol) in anhydrous benzene (100 ml) is heated under reflux for 24 h. The reaction is preferably carried out under nitrogen; in the case of the 4-isomers this is essential. After removal of solvent the solidified residue is extracted with ice-cooled ether; $(C_6H_5)_3P{=}O$ remains behind. The extract is concentrated and the resulting brown oil vacuum-sublimed in a small apparatus (oil pump). At first unreacted pyridinecarbaldehyde condenses on the cool finger; this is followed, at higher temperatures, by sublimation of the reaction product [2-*(1)* and 4-*(1)* at 60 °C/0.3 torr, 3-*(1)* at 80 °C/0.3 torr]. Yields: 2-*(1)* 21%, 3-*(1)* 56%, and 4-*(1)* 62%; m. p.: 2-*(1)* 39—40 °C (43 °C[11]), 3-*(1)* 65—66 °C (66—67 °C[4]) and 4-*(1)* 35—36 °C (36—37 °C[4]), all from petroleum ether; semicarbazone of 4-*(1)* 211.5 °C, phenylhydrazone of 4-*(1)* 199 °C, both from ethanol/water; oxime of 4-*(1)* 148–150 °C, from benzene.

Received: March 3, 1975;
supplemented: April 1, 1975 [Z 224 IE]
German version: Angew. Chem. 87, 486 (1975)

CAS Registry numbers:
2-*(1)*, 51689-49-7; 3-*(1)*, 28447-15-6; 4-*(1)*, 26505-36-2;
(2), 2136-75-6; 2-pyridinecarbaldehyde, 1121-60-4;
3-pyrridinecarbaldehyde, 500-22-1; 4-pyridinecarbaldehyde, 872-85-5

[1] *M. Ohta* and *Y. Isowa*, Nippon Kagaku Zasshi *80*, 688, 1198 (1959); Chem. Abstr. *55*, 3635a, 4505a (1961).
[2] *M. Strell* and *E. Kopp*, Chem. Ber. *91*, 2854 (1958).
[3] *G. B. Ellam* and *C. D. Johnson*, J. Org. Chem. *36*, 2284 (1971).
[4] *L. S. Davies* and *G. Jones*, J. Chem. Soc. *1971*, 2572.
[5] *S. Trippett*, Quart Rev. Chem. Soc. *17*, 406 (1963).
[6] *S. Trippett* and *D. M. Walker*, J. Chem. Soc. *1961*, 1266.
[7] *W. Hohler*, Dissertation, Universität Freiburg 1973.

1,2,3-Tri-*tert*-butyldiazaphosphiridine 3-Oxide[***]

By *Helmut Quast, Manfred Heuschmann*, and *Mohamed O. Abdel-Rahman*[*]

The chemistry of three-membered phosphorus heterocycles is still underdeveloped in comparison with that of the analo-

[*] Doz. Dr. H. Quast [+], Dipl.-Chem. M. Heuschmann, and Dr. M. O. Abdel-Rahman [**]
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

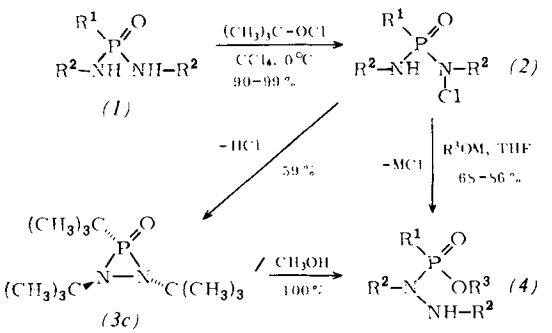
[+] To whom correspondence should be addressed.

[**] Present address: National Research Centre, Dokki, Cairo (Egypt)

[***] Three-Membered Heterocycles, Part 3. This work was supported by the Fonds der Chemischen Industrie. *M. O. A.-R.* is indebted to the Alexander von Humboldt-Stiftung for a research grant (1970—1972). The results are largely taken from the Diplomarbeit of *M. H.* Universität Würzburg 1974. Part 2: *H. Quast* and *F. Kees*, Angew. Chem. *86*, 816 (1974); Angew. Chem. internat. Edit. *13*, 742 (1974).

gous nitrogen and sulfur compounds. This applies particularly to phosphorus(v) heterocycles, since only two compounds have so far been isolated for which a phosphorus(v) three-membered ring structure has been postulated[1a, 1b]. In contrast, phosphorus(v) three-membered ring structures have frequently been assumed as reactive intermediates, and actually detected in some cases[1c]. We now report the isolation and structural proof of a diazaphosphiridine 3-oxide and a simple phosphonic ester hydrazide synthesis.

The phosphonic diamides *(1)*, which are readily accessible from phosphonic dichlorides and primary amines in acetonitrile, are smoothly converted into the stable crystalline *N*-chloro amides *(2)* by *tert*-butyl hypochlorite. Treatment of *(2)* with alkoxides in anhydrous THF affords the phosphonic ester hydrazides *(4)* in good yields. The N—N bond in *(4)* was established in the case of *(4c)*, $R^3=(CH_3)_3C$, by degradation with conc. hydrochloric acid to 1,2-di-*tert*-butylhydrazine, which was isolated as the perchlorate and as the 2,4,6-trinitrobenzenesulfonate.



(a), $R^1=CH_3$, $R^2=C(CH_3)_3$;
(b), $R^1=CH_3$, R^2 = 1-adamantyl;
(c), $R^1=R^2=C(CH_3)_3$;
(d), $R^1=C_6H_5$, $R^2=C(CH_3)_3$

$R^3OM = CH_3ONa$ or $(CH_3)_3COK$

Isolation of the diazaphosphoridine oxide *(3c)* can be accomplished by sublimation at 10^{-5} torr if the potassium salt of the non-nucleophilic, almost nonvolatile 3-*tert*-butyl-2,2-dimethyl-3-heneicosanol[2] is used as base under rigorous exclusion of moisture. *(3c)* forms colorless, extremely hygroscopic crystals which can be recrystallized from a small volume of *n*-hexane at −78 °C.

Elemental analysis and the high resolution mass spectrum indicated the expected molecular formula. The IR and NMR spectra as well as the reaction with methanol prove structure *(3c)*; IR (CCl_4): no NH, no OH; 1266, 1198 cm^{-1} (tBu, P=O); ^{1}H-NMR (90 MHz, [D$_8$]toluene): $\delta=1.21$ d, $^4J_{H\text{-}P}=0.4$ Hz, 2 tBu); 1.23 ppm (d, $^3J_{H-P}=17.9$ Hz, tBu). The ^{1}H-NMR spectrum is temperature dependent and on cooling of the sample it exhibits broadening and splitting of the *N*-*tert*-butyl doublet: $T_c=-38$ °C, $\Delta\nu(-73\,°C)=27.3$ Hz. Determination of the two long-range coupling constants at low temperature was unsuccessful owing to viscosity broadening of the signals. The low inversion barrier[5] ($\Delta G_c^{\neq}=11.7$ kcal mol^{-1}) is certainly attributable in part to steric interaction of the *cis*-*tert*-butyl groups in the ground state. ^{31}P-NMR (40.5 MHz, [D$_8$]toluene): $\delta_P=-2.35$ ppm[6]. The upfield shift of the ^{31}P-NMR signal of *(3c)* relative to that of *(1c)* [$\delta_P=-32.62$ ppm ($CDCl_3$)] and of *(2c)* [$\delta_P=-40.10$ ppm ($CDCl_3$)] indicates the special kind of bonding in the three-membered ring[7].

Further support for the structure *(3c)* comes from the immediate reaction with methanol, which quantitatively affords *(4c)*, $R^3=CH_3$, already obtained directly from *(2c)*. *(3c)* remains unchanged after 20 h at 90 °C in benzene. Complex decomposition yielding, *inter alia*, 2-methylpropene, only begins at 140 °C. A fragment C_4H_9OP corresponding to a cheletropic decomposition could not be detected in the high resolution mass spectrum.

1,2,3-Tri-tert-butyldiazaphosphiridine 3-oxide (3c)

tert-Butylphosphonic dichloride (0.2 mol) was heated to 150 °C with *tert*-butylamine (1.3 mol) in acetonitrile (135 ml) for 24 h. Yield: 97 % of *(1c)*, m. p. 181—182 °C (from ligroin). Compound *(1c)* (0.1 mol) and *tert*-butyl hypochlorite (0.12 mol) were reacted in CCl_4 at 0—20 °C to give *(2c)*, m. p. 110—111 °C, 95 % yield. A cooled solution of potassium 3-*tert*-butyl-2,2-dimethyl-3-heneicosanolate (10.5 mmol) in THF (25 ml) was added to a solution of *(2c)* (10 mmol) in THF (100 ml) at −30 °C under argon and with rigorous exclusion of moisture. The mixture was allowed to warm to −5 °C during 2 h, after which the solvent was distilled off at 10^{-3} torr. The residue was then sublimed at 35 °C/6×10^{-6} torr onto a cold finger at −30 °C; yield after resublimation 1.46 g (59 %) of *(3c)*, colorless crystals, m. p. 63.5—65 °C.

Received: March 27, 1975 [Z 229 IE]
German version: Angew. Chem. *87*, 487 (1975)

CAS Registry numbers:
(1c), 55702-27-7; *(2c)*, 55702-28-8; *(3c)*, 55702-29-9;
tert-butylphosphonic dichloride, 4707-95-3; *tert*-butylamine, 75-64-9

[1] a) *K.-D. Gundermann* and *A. Garming*, Chem. Ber. *102*, 3023 (1969); *E. W. Koos, J. P. Vander Kooi, E. E. Green*, and *J. K. Stille*, J. C. S. Chem. Comm. *1972*, 1085. b) *Note added in proof* (June 27, 1975): Recently a λ^5-phosphirane and a 1,2λ^5-azaphosphiridine have been obtained: *E. Niecke* and *W. Flick*, Angew. Chem. *87*, 355 (1975); Angew. Chem. internat. Edit. *14*, 363 (1975). c) *P. Burus, G. Capozzi*, and *P. Haake*, Tetrahedron Lett. *1972*, 975; *D. B. Denny* and *L. S. Shih*, J. Am. Chem. Soc. *96*, 317 (1974)
[2] The base was tailor-made for this purpose. The alcohol was prepared from 2,2,4,4-tetramethylpentanone [3] (yield 74 %, b.p. 1.5 to 142 °C/8×10^{-6} torr, m.p. 34—35 °C, from hexane) and reacted with KH in THF [4].
[3] *P. J. Pearce, D. H. Richards*, and *N. F. Scilly*, J. C. S. Perkin I *1972*, 1655.
[4] *C. A. Brown*, J. Org. Chem. *39*, 3913 (1974).
[5] *J. M. Lehn*, Fortschr. Chem. Forsch. *15*, 311 (1970); *J. B. Lambert*, Top. Stereochem. *6*, 19 (1971).
[6] $\delta_P<0$ indicates a downfield shift relative to 85 % phosphoric acid.
[7] *S. Chan, H. Goldwhite, H. Keyzer, D. G. Rowsell*, and *R. Tang*, Tetrahedron *25*, 1097 (1969).

Constitutional and Configurational Stability of a Carbamoyl-Tetracarbonyliron Anion Complex[1][**]

By *Johannes Schmetzer, Jörg Daub*, and *Peter Fischer*[*]

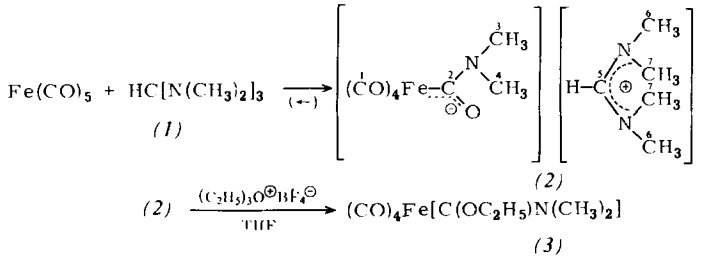
Acyl derivatives of transition metals may be synthesized from the corresponding carbonyl complexes with organoalkali metal compounds[2] as well as with aluminum and titanium amides[3, 4]. With hexamethylmethanetriamine *(1)*, we have now found another amide donor capable of transferring the $N(CH_3)_2$ moiety to transition metal carbonyl complexes.

Reaction of *(1)* with $Fe(CO)_5$ in a 1:10 molar ratio affords a red oil (94 % yield), sparingly soluble in apolar solvents and having the elementary composition $[C_7H_6FeNO_5][C_5H_{13}N_2]$. Alkylation yielding the known

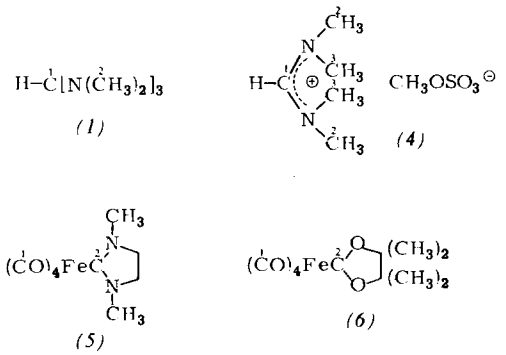
[*] Dipl.-Chem. J. Schmetzer and Prof. Dr. J. Daub
Chemisches Institut der Universität
84 Regensburg, Universitätsstrasse 31 (Germany)
Dr. P. Fischer
Institut für Organische Chemie der Universität
7 Stuttgart 80, Pfaffenwaldring 55 (Germany)

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

carbene complex *3*)[5] and spectroscopic evidence indicated structure *(2)* for this oil.



The ^{13}C-NMR data for the amidinium moiety of *(2)* are in close agreement, regarding both chemical shift and coupling constants, with those of tetramethylformamidinium methylsulfate *(4)* (Table 1). The resonance of the carbamoyl carbon



Fe(CO)$_5$/*(1)* since hexamethylmethanetriamine *(1)* can be extracted from the oil *(2)* with benzene. As shown by the well-resolved ^3J coupling between N-C^{3,4}H$_3$ protons and C^2, the rate of equilibration is fairly slow at room temperature; furthermore, the equilibrium must lie far on the side of the complex *(2)* because signals of *(1)* (see Table 1) cannot be detected in either the ^{1}H- or the ^{13}C-NMR spectrum. This extreme displacement of the equilibrium in favor of the carbamoyl complex—as compared with the Fe(CO)$_5$/amine system[4]—has to be accounted for in terms of the high amidinium cation stability[6].

Different activation barriers are found for the coalescence of the dimethylamino signals in the amidinium and carbamoyl part of *(2)*, the values from ^{1}H- and ^{13}C-NMR spectra, however, being comparable in each case (Table 2). This shows that the dynamic process responsible is indeed rotation of the N(CH$_3$)$_2$ groups about the C^2—N and C^5—N bond, respectively, for an amide exchange in the sense of the equilibrium discussed above would result in equilibration of all N-methyl protons.

The C—O stretching vibrations are displaced to increasingly lower wave numbers along the series *(6)* → *(5)* → *(2)*, corresponding to a decrease in C—O bond strength (Table 1); for the carbonyl ^{13}C resonance, there is a concomitant downfield shift[7]. Hence a distinctive gradation of ligand acceptor strength appears for the carbonyl iron complexes (CO)$_4$FeL:

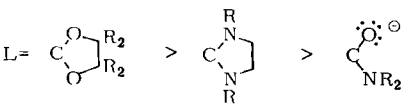


Table 1. ^{13}C-NMR and IR spetroscopic data of the carbonyliron complexes *(2)*, *(5)*, and *(6)*, of the compounds *(1)* and *(4)*, and of Fe(CO)$_5$.

(1)		*(4)*		*(2)*		*(5)*		*(6)*		(C^{1}O)$_5$Fe	
^{13}C-NMR [δ, ppm] [a]				C-1	221.10	C-1	217.4 [8]	C-1	215.33 [1]	C-1	209.6
				C-2	206.01	C-2	213.2	C-2	251.19	(neat)	
				C-3,4	~38						
C-1	101.66	C-1	157.65	C-5	156.98						
C-2	41.46	C-2,3	39.43 46.17	C-6,7	39.08 45.79						
IR [cm^{-1}]				$\nu_{C\equiv O}$ (THF)	2020 1947 1928 1890	$\nu_{C\equiv O}$ (hexane)	2044 [9] 1963 1938	$\nu_{C\equiv O}$ (KBr, high pressure)	2060 1979 1956 1937	$\nu_{C\equiv O}$	2022 2000

[a] Relative to TMS as internal standard, 30 °C, in CD$_3$CN.

C^2, on the other hand, is split into a heptuplet by long-range coupling to the six N-methyl protons ($^3J_{H_3C-N-C^2}$ = 3.3 Hz), thus providing direct evidence for the N(CH$_3$)$_2$ group being covalently bonded to one of the carbonyl functions. At 40 °C, two N—CH$_3$ signals in a 6:12 intensity ratio appear in the ^{1}H-NMR spectrum which, upon lowering the temperature, are successively resolved into two singlets each (Table 2).

Table 2. ^{1}H-NMR data [δ, ppm] of the complex *(2)* [a].

	−20 °C		+40 °C		T_c [°C]	$\Delta G_c^{\neq}$ [kcal/mol]
5-H	6.39	(1H)	6.56	(1H)		
3-H	3.25	(3H)	2.99	(6H)	+ 7	13.7
4-H	2.74	(9H)				
6-H	2.70		2.70	(12H)	≈40	15.3
7-H	2.33	(6H)				

[a] 100 MHz, in CD$_3$CN.

These findings provide unequivocal proof of the ionic structure *(2)*. At the same time, though, a dynamic equilibrium must exist between the carbamoyl complex *(2)* and

Received: April 8, 1975;
in abridged form: April 21, 1975 [Z 232 IE]
German version: Angew. Chem. *87*, 489 (1975)

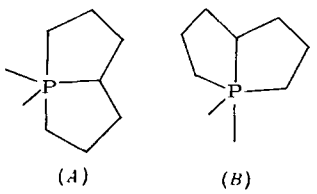
CAS Registry numbers:
Fe(CO)$_5$, 13463-40-6; *(1)*, 5762-56-1; *(2)*, 55658-17-8; *(4)*, 2013-91-4; *(5)*, 41755-21-9; *(6)*, 54854-43-2

[1] *J. Daub* and *J. Kappler*, J. Organometal. Chem. *80*, C5 (1974).
[2] *E. O. Fischer*, Angew. Chem. *86*, 651 (1974).
[3] a) *W. Petz* and *G. Schmid*, Angew. Chem. *84*, 997 (1972); Angew. Chem. internat. Edit. *11*, 934 (1972); b) *W. Petz*, J. Organometal. Chem. *72*, 369 (1974).
[4] *R. J. Angelici*, Accounts Chem. Res. *5*, 335 (1972).
[5] *E. O. Fischer, H.-J. Beck, C. G. Kreiter, J. Lynch, J. Müller*, and *E. Winkler*, Chem. Ber. *105*, 162 (1972).
[6] *W. Betz* and *J. Daub*, Chem. Ber. *107*, 2095 (1974).
[7] See also *G. M. Bodner* and *L. J. Todd*, Inorg. Chem. *13*, 1335 (1974).
[8] *D. J. Cardin, B. Cetinkaya, E. Cetinkaya, M. F. Lappert, E. W. Randall*, and *E. Rosenberg*, J. C. S. Dalton *1973*, 1982.
[9] *B. Cetinkaya, P. Dixneuf*, and *M. F. Lappert*, J. C. S. Dalton *1974*, 1827.

Synthesis of Oxazaphospholinobenzooxaazaphospholines and -oxadiazaphospholines—Compounds Having Pentacoordinated Phosphorus as Bridgehead of a Bicyclo[3.3.0]octane Skeleton[1]

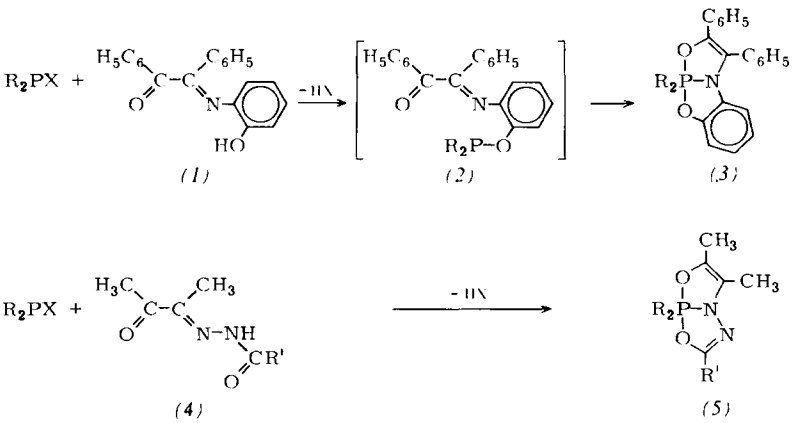
By *Alfred Schmidpeter* and *Josef Helmut Weinmaier*[*]

Incorporation into a small ring (four- or five-membered) modifies the reactivity of phosphorus in characteristic fashion; derivatives having coordination number 5 are considerably favored over those with coordination number 4 and also 3. When the phosphorus occurs as spiro juncture between two (axial-equatorial) five-membered rings, then the (trigonal-bipyramidal) pentacoordination is especially favorable. A similar, and possibly greater, stabilization is to be expected when the phosphorus forms a bridgehead of two condensed five-membered rings. Moreover, such systems can command greater interest as they possess two phosphorus functions not participating in ring formation for which the influence of structural parameters can be studied. Hence two alternative axial-equatorial arrangements of the five-membered rings can also be envisaged, *i.e.* with the common bond equatorial *(A)* or axial *(B)*.



(A) *(B)*

We now report the first examples of a facile route, which we have meanwhile found to be capable of generalization, leading to hetero-bicyclophosphoranes of the type shown[2]: A chlorophosphane (or another, at least monofunctional phosphorus(III) compound) is reacted under the conditions of its nucleophilic substitution with an ω-hydroxy compound having a seven-membered, α,γ doubly unsaturated chain. For instance, reaction with benzil mono-*o*-hydroxyanil *(1)* apparently proceeds *via* the unisolated substitutional intermediate *(2)* to give the 1,3,2λ⁵-oxazaphospholino[2,3-*b*]benzo[*d*][1,3,2λ⁵]oxazaphospholines *(3)* in an intramolecular [1+4]-cycloaddition[3]. Simple acylhydrazones of the biacetyl *(4)* afford the [1,3,2λ⁵]oxazaphospholino[2,3-*b*][1,3,4,2λ⁵]-oxadiazaphospholines *(5)*.



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

Table 1. [1,3,2λ⁵]Oxazaphospholino[2,3-*b*]benzo[*d*][1,3,2λ⁵]oxazaphospholines *(3)* and -[1,3,4,2λ⁵]oxadiazaphospholines *(5)*.

	R	X	R'	Color, m.p. [°C] (b.p. [°C/torr])	δ^{31}P [a] (in CH_2Cl_2)
(3a)	CH_3	Cl		colorless, 158—160	9.5
(3b)	C_6H_5	Cl		yellow, 177—178	33.4
(3c)	$N(CH_3)_2$	Cl		pale yellow, 134—135	36.0
(3d)	OCH_3	Cl, OCH_3		colorless, 148—150	41.0
(5a)	CH_3	Cl	CH_3	yellow oil	15.7
(5b)	CH_3	Cl	$CH_2C_6H_5$	yellow oil	14.4
(5c)	CH_3	Cl	C_6H_5	yellow, 68—70	14.8
(5d)	C_6H_5	Cl	CH_3	yellow, 104—105	38.0
(5e)	C_6H_5	Cl	$CH_2C_6H_5$	yellow, 140	38.8
(5f)	C_6H_5	Cl	C_6H_5	yellow, 130—132	39.0
(5g)	$N(CH_3)_2$	$N(CH_3)_2$	CH_3	yellow liquid ($44/10^{-3}$)	33.7
(5h)	$N(CH_3)_2$	$N(CH_3)_2$	$CH_2C_6H_5$	yellow liquid ($118/10^{-2}$)	34.2
(5i)	$N(CH_3)_2$	$N(CH_3)_2$	C_6H_5	pale yellow, 65	34.7
(5j)	OCH_3	OCH_3	C_6H_5	red liquid	43.7

[a] Upfield shifts (in ppm) relative to H_3PO_4.

The pronounced shielding of the phosphorus (Table 1) confirms the phosphorane structure for all products. In the ^{1}H-NMR spectrum the CH_3, $N(CH_3)_2$, or OCH_3 groups attached to phosphorus each give only a doublet. Their equivalence, as manifested by this observation, would indicate structure *(A)*, but could in principle also result from a mobile pseudorotational equilibrium between *(A)* and *(B)*.

Procedures:

a) X = Cl: R_2PCl (20 mmol) diluted with benzene is added dropwise to a solution of *(1)* or *(4)* (20 mmol) and triethylamine (20 mmol) in dry benzene (30 ml). The resulting suspension is stirred for 10 h at room temperature. Compound *(3)* or *(5)* is obtained crystalline or as an oil after the triethylammonium chloride has been filtered off and the solvent removed.

b) R = X = $N(CH_3)$: Compound *(4)* (20 mmol) and $P(N(CH_3)_2)_3$ (20 mmol) are heated to boiling in dry benzene (50 ml) for 24 h (until liberation of dimethylamine has ceased).

[*] Priv.-Doz. Dr. A. Schmidpeter and J. H. Weinmaier
Institut für Anorganische Chemie der Universität
8 München 2, Meiserstrasse 1 (Germany)

After removal of solvent, compounds *(5)* are vacuum-distilled or recrystallized.

c) R=X=OCH_3: Compound *(1)* or *(4)* is heated with an excess of $P(OCH_3)_3$ in the absence of a solvent to 100 °C and the methanol formed distilled off. On completion of reaction, the remaining $P(OCH_3)_3$ is also distilled off; compound *(3)* or *(5)* is obtained as residue.

The new compounds are readily soluble in benzene, $CHCl_3$, and CH_2Cl_2; acetonitrile proves suitable for recrystallization. The yields range between 50 and 90%.

Received: March 11, 1975 [Z 218a IE]
German version: Angew. Chem. 87, 517 (1975)

CAS Registry numbers:
(3a), 55590-36-8; *(3b)*, 55590-37-9; *(3c)*, 55590-38-0; *(3d)*, 55590-39-1; *(5a)*, 55590-40-4; *(5b)*, 55590-41-5; *(5c)*, 55590-42-6; *(5d)*, 55590-43-7; *(5e)*, 55590-44-8; *(5f)*, 55590-45-9; *(5g)*, 55590-46-0; *(5h)*, 55590-47-1; *(5i)*, 55590-48-2; *(5j)*, 55590-49-3; $(CH_3)_2PCl$, 811-62-1; $(C_6H_5)_2PCl$, 1079-66-9; $[N(CH_3)_2]_2PCl$, 3348-44-5; $(CH_3O)_2PCl$, 3743-07-5; $P(OCH_3)_3$, 121-45-9; $P[N(CH_3)_2]_3$, 1608-26-0 *(4)* (R=CH_3), 55590-51-7; *(4)* (R=CH_2Ph), 55590-52-8; *(4)*, (R=Ph), 55590-53-9; benzil-mono-*o*-hydroxyanil, 55590-50-6

[1] Four- and Five-Membered Phosphorus Heterocycles, Part 10. This work was supported by the Fonds der Chemischen Industrie.—Part 9: *A. Schmidpeter* and *J. Luber*, Chem. Ber. *108*, 820 (1975).

[2] So far three phosphoranes having a hetero-bicyclo[3.3.0]octane skeleton have been prepared by other routes: a) *D. B. Denney, D. Z. Denney, C. D. Hall*, and *K. L. Marsi*, J. Amer. Chem. Soc. *94*, 245 (1972); b) *D. Houalla, J. F. Brazier, M. Sanchez*, and *R. Wolf*, Tetrahedron Lett. *1972*, 2969; c) *D. Hellwinkel* and *W. Krapp*, Angew. Chem. *86*, 524 (1974); Angew. Chem. internat. Edit. *13*, 542 (1974).

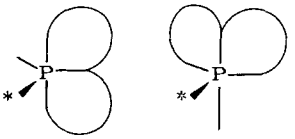
[3] *F. Ramirez*, Acc. Chem. Res. *1*, 168 (1968); Bull. Soc. Chim. Fr. *1970*, 3491; *D. Bernard* and *R. Burgada*, C. R. Acad. Sci. *272*, 2077 (1971).

Distortion of the Trigonal-Bipyramidal Ligand Arrangement in Bicyclophosphoranes—Structure of 2,3,8,8-Tetraphenyl[1,3,2λ^5]oxazaphospholino[2,3-*b*]benzo[*d*]-[1,3,2λ^5]oxazaphospholine[1]

By *William S. Sheldrick*, *Alfred Schmidpeter*, and *Josef Helmut Weinmaier*[*]

In recent years the number of known phosphoranes (compounds containing pentacovalent phosphorus) has increased considerably. Their stability is usually attributable to the incorporation of the phosphorus into one or two small rings, which inevitably leads, however, to some degree of distortion of the trigonal-bipyramidal arrangement of ligands coordinated to the phosphorus. Although the coplanarity of the phosphorus and the three equatorial ligands is always retained, this does not apply to their regular trigonal arrangement or to the linearity of the axis.

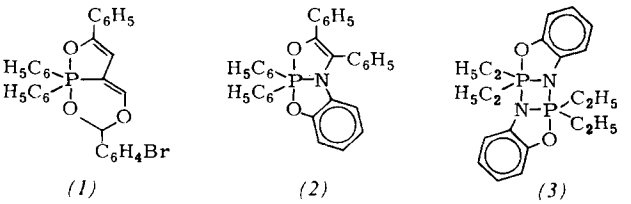
In these phosphoranes the small rings are always in an axial-equatorial arrangement; for the bicyclophosphoranes there exist two possibilities[2, 3], *(A)* and *(B)*, capable of interconversion by pseudorotation about the bond marked with an asterisk as a pivot:



(A) *(B)*

[*] Dr. W. S. Sheldrick
Gesellschaft für Molekularbiologische Forschung mbH
33 Braunschweig-Stöckheim, Mascheroder Weg 1 (Germany)
Priv.-Doz. Dr. A. Schmidpeter and J. H. Weinmaier
Institut für Anorganische Chemie der Universität
8 München 2, Meiserstrasse 1 (Germany)

The structure of a phosphorane bridgehead of fused five- and six-membered and fused five- and four-membered rings has been established for the examples *(1)*[3] and *(3)*[4, 5], respectively. We now report the structure of a phosphorane bridgehead of two fused five-membered rings for the example of the title compound *(2)*.



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

(2) forms monoclinic crystals, C2/c, with $a=24.556(5)$, $b=8.816(5)$, $c=23.220(4)$ Å; $\beta=97.22(2)°$; $Z=8$; $d_{calc}=1.29\ g\ cm^{-3}$. The structure was solved by direct methods and refined to $R=0.065$, $R_G=0.075$ for 2402 independent reflections (four-circle diffractometer, $F \geq 2.5\sigma(F)$). The positions of the hydrogen atoms could be localized in a Fourier difference synthesis and were then included in the final cycles of refinement with one common temperature factor each per benzene ring. All the other atoms were assigned anisotropic temperature factors.

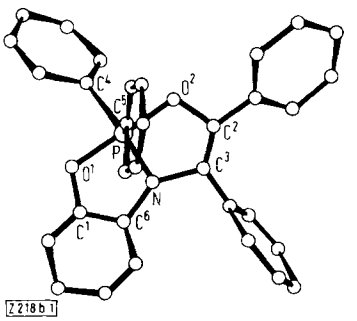


Fig. 1. Molecular structure of *(2)*. A selection of bond lengths [Å] with standard deviations:

P—O^1 = 1.763(5)	P—O^2 = 1.700(5)
P—C^4 = 1.818(5)	P—C^5 = 1.811(6)
P—N = 1.703(6)	

As for *(1)* and *(3)*, the structural alternative *(A)* with equatorial annelation is again approximately fulfilled in the case of *(2)*. Expectedly, the planarity of the equator is retained (deviation from the plane <0.001 Å); however, a striking and unexpected feature is the large difference in the two equatorial NPC angles (Table 1). The OPO axis is distinctly bent as a result of the small internal angle of the ring. Regarding its deviation from axial linearity, *(2)* assumes a position intermediate between the five/six- and the five/four-membered ring phosphoranes: *(1)* 3.1° < *(2)* 8.4° < *(3)* 15.6°. The overall distortion of the trigonal-bipyramidal ligand arrangement thus remains fairly small for *(1)*, while it is considerable for *(2)* and *(3)*; however, their structures differ fundamentally regarding the direction of bending of the axis.

In *(3)* the axis is bent in the direction of the equatorial bridge, *i.e.* the equatorial N atom lies in the OPN plane formed perpendicular to the equatorial plane by bending of the axis. The C_{2h} symmetry of *(3)* possible by virtue of the molecular skeleton is retained in this "eclipsed" arrangement.

In *(2)*, however, the two axial O atoms are "staggered", *i.e.* the axis is bent towards one of the two equatorial NPC angles. Hence this angle (N—P—C^4) becomes larger and the other (N—P—C^5) smaller than 120°. Furthermore, the two equatorial phenyl groups are no longer equivalent and *(2)*

no longer possesses any symmetry. The non-equivalence of the two exocyclic phosphorane bonds is characteristic of the structural alternative *(B)*, and the angles found for *(2)* can indeed be interpreted to a good approximation as an incipient transition *(A)* → *(B)* (Table 1). The pivot for this pseudorotational transition is C^5, which lies almost exactly in the OPO plane formed perpendicular to the equatorial plane by bending of the axis. Agreement between model and experimental values is at its weakest for the two OPN and the CPC angles. This is due to a certain degree of approach to the "eclipsed" arrangement: because of the small OPN angle arising from the ring the OPO plane does not exactly bisect the N—P—C^4 angle but lies closer to the PN bond. Thus the C^4—P—C^5 angle is "relieved" and decreases further. With regard to this angle too, compound *(2)* assumed a position between *(1)* and *(3)*: *(1)* 116.8° > *(2)* 112.8° > *(3)* 111.3°.

Table 1. Bond angles [°] at phosphorus in *(2)* according to the models *(A)* and *(B)*, for a 15% transformation *(A)* → *(B)*, and the experimental values with standard deviations.

	(A)	*(B)*	Transition	Experimental
O^1—P—O^2	180	120	171	171.6(3)
O^1—P—C^4	90	90	90	89.7(4)
O^2—P—C^4	90	90	90	89.4(4)
O^1—P—C^5	90	120	94.5	93.3(4)
O^2—P—C^5	90	120	94.5	94.7(4)
O^1—P—N	90	90	90	87.6(3)
O^2—P—N	90	90	90	86.6(3)
N—P—C^4	120	180	129	130.6(4)
N—P—C^5	120	90	115.5	116.5(4)
C^4—P—C^5	120	90	115.5	112.8(5)

Whereas P as one of the bridgeheads of the bicyclic is located far outside the plane of the surrounding ring members, the other bridgehead N is in a planar environment. This is possible because, while the benzooxazaphospholine ring P—O^1—C^1—C^6—N forms a good plane which also approximately contains C^3, the other five-membered ring is in the envelope configuration with the phosphorus lying 0.19 Å outside the plane O^2—C^2—C^3—N.

Among the bond lengths, a remarkable difference is observed between the phenolic PO^1 and enolic PO^2 bond. The relatively long PN bond length is significant for the structural discussion. It lies between the ranges commonly encountered for an equatorial and an axial PN bond of a phosphorane (1.62—1.68 Å and 1.73—1.78 Å respectively) and thus also corresponds to a transition from *(A)* with an equatorial and *(B)* with an axial PN bond.

With modified and in particular different occupations of its two exocyclic phosphorane positions, the structural type presented in this communication opens a new approach for determining fine differences in ligand apicophilic character on the basis of the *(A)* → *(B)* transition.

Received: March 11, 1975;
revised: March 18, 1975 [Z 218b IE]
German version: Angew. Chem. 87, 519 (1975)

CAS Registry numbers:
(2), 55590-37-9

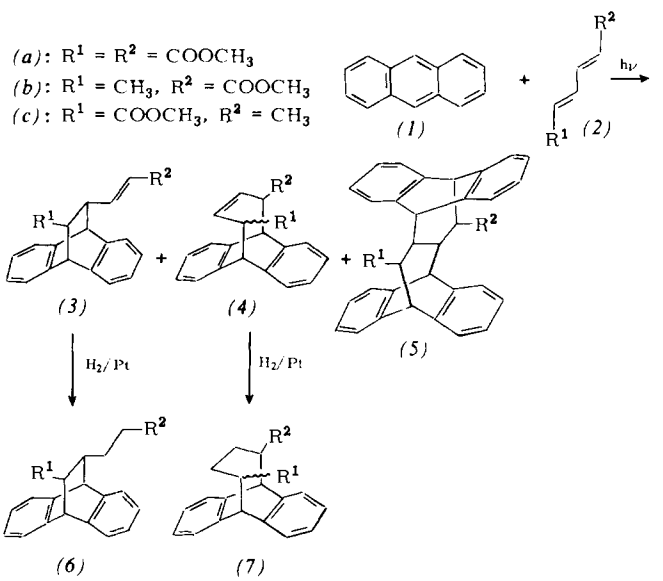
[1] Four- and Five-Membered Phosphorus Heterocycles, Part 11.—Part 10: ref. [2].
[2] *A. Schmidpeter* and *J. H. Weinmaier*, Angew. Chem. 87, 517 (1975); Angew. Chem. internat. Edit. 14, 489 (1975).
[3] *D. D. Swank, C. N. Caughlin, F. Ramirez*, and *J. F. Pilot*, J. Amer. Chem. Soc. 93, 5236 (1971).
[4] *A. Schmidpeter* and *J. Luber*, Phosphorus 5, 55 (1974).
[5] *M. I. Kabachnik, V. A. Gilyarov, N. A. Tikhonina, A. E. Kalinin, V. G. Andrianov, Yr. T. Struchkor*, and *G. I. Timofeera*, Phosphorus 5, 65 (1974).

Photo-Diels-Alder Reactions of Anthracene[**]

By *Gerd Kaupp, Rainer Dyllick-Brenzinger*, and *Inge Zimmermann*[*]

Preparative importance attaches to photochemical Diels-Alder reactions[1]. Since these appear to be "forbidden" by orbital-symmetry considerations[2, 3], antarafacial concerted mechanisms have been postulated[2]. For the geometrically more likely suprafacial course it has been predicted that short-wave or charge-transfer excitation (to exciplexes)[3] should "allow" the reactions[4]. Finally, one-stage stereospecific formation of cyclohexenes was expected from MO correlations between polar excited reaction complexes and products in the electronic ground state[5]. Irrespective of these theoretical positions, the experimental findings accord with non-concerted mechanisms *via* short-lived intermediates[1, 6]. We now report on [4+2]-photoadditions with dienophiles of various polarities which are open to choose formally "allowed" [4+4]-processes or (and) radical chain polymerizations as well.

Selective irradiation ($\lambda > 330$ nm) of anthracene *(1)* (0.75×10^{-2} mol/l) in the presence of the muconic ester *(2a)* (5.8×10^{-2} mol/l) in benzene leads to the *trans*-[4+2]-adduct *(3a)* (61%), along with sensitized isomerizations of *(2a)*, dimerization of *(1)* (13%) and copolymerization of *(1)* and *(2a)*. The adduct can be catalytically hydrogenated to give *(6a)*. Formation of *(4a)* or *(5a)* is not detectable by NMR spectroscopy. The photoreaction occurs with fluorescence quenching [55% quenching with 2.0×10^{-2} mol/l of *(2a)*], *i.e.* it follows a singlet mechanism. Long-wave exciplex fluorescence occurs simultaneously ($\lambda_{corr}^{max} = 525$ nm; $\phi_{fl} = 0.01$). The surprisingly slow disappearance of anthracene ($\phi = 0.0031$) is explained, at least in part, by non-productive exciplex formation. Thus the spectroscopic detection of exciplexes does not suffice to prove their intermediate role in photochemical reactions. The following experiments also fail to substantiate this postulate. The sorbic ester *(2b)* reacts with *(1)* ($\Phi = 0.015$) without detectable exciplex fluorescence and distinctly faster, although the fluorescence quenching is weaker (13%) than for *(2a)*. Even with a ten-fold increase in concentration of *(2b)*

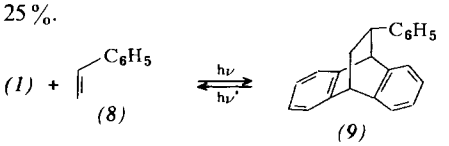


[*] Doz. Dr. G. Kaupp and I. Zimmermann
Chemisches Laboratorium der Universität
78 Freiburg, Albertstrasse 21 (Germany)
Dipl.-Chem. R. Dyllick-Brenzinger
Organisch-chemisches Laboratorium der Eidgenössischen Technischen Hochschule
CH-8006 Zürich, Universitätsstrasse 6 (Switzerland)

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

(59% quenching; $\Phi = 0.068$) no exciplex emission can be observed. Apart from stereoisomeric sorbic esters, dimerized anthracene (12%), and mainly copolymers of *(1)* and *(2b)*, chromatography of the reaction mixture indicated 19% of *(3b)*, 15% of *(5b)* (^{13}C-NMR in $CDCl_3$/TMS: 10 separate peaks in the aliphatic region between $\delta = 20.8$ and 56.4 ppm[7]) and 6% of *(4b)* (*cis-* and *trans- ca.* 1:1), all except *trans-(4b)* being obtained crystalline. *(3c)* and other products are formed in lower yields ($\leq 2\%$). The spectral data (cf. Table 1) prove the structures assigned. The vicinal $^1H/^1H$ coupling constants of the benzyhydrylic protons accord with expectation.

Also on selective irradiation of *(1)* in styrene *(8)*, with addition of some hydroquinone to prevent spontaneous polymerization, the photo-Diels-Alder reaction favorably competes with the copolymerization, although the reaction is slowed down by formation of a by-product (shoulder at $\lambda = 333$ nm) that regenerates *(1)* at 25°C. *(9)* can be distilled off from copolymers of *(1)* and *(8)* in a vacuum: reproducible yield 25%.



The fluorescence of *(1)* in *(8)* is 1.5 times weaker, displaced by 2.5 nm towards longer wavelengths, and slightly broader than in benzene. Exciplex fluorescence is not detectable.

Like the Diels-Alder photoadditions, [4+2]-photocleavage of *(3a, b, c)* and of *(9)* back to the components is especially favored; it can be achieved even at −196°C, *i.e.* without significant additional activation.

The results show that photochemical Diels-Alder reactions can easily be integrated into the cyclovinylogous series of two-step [2+2]-, [2+4]-, [4+4]-, *etc.*, four-center additions[6] and are not exceptional cases. Their limits apparently set by steric effects in intermediate formation (*e.g.* no significant quenching of fluorescence and no photoaddition between *(1)* and stilbene or 1,2-dichloroethylene)[1], and they require that the s-*cis*-conformation of the diene be present already before the light absorption. Electronic effects appear to play a subordinate role[1]. Thus 1,3-cyclohexadiene also photoadds to the 9,10-positions of *(1)*, giving the [4+2]- (19%; m.p. 155°C) and [4+4]-adduct (54%; m.p. 198°C) (cf., however, ref. [3]), and the electron-richer *p*-vinylanisole can be used instead of *(8)* [formation of *(9)* with a *p*-methoxyphenyl group in place of C_6H_5; m.p. 128°C].

Table 1. Melting points and characteristic ^{1}H-NMR data [a].

Compound	M.p. [°C]	Vinyl-H: τ (*J*)	Benzhydryl-H: τ (*J*)	Methoxy-H; Methyl-H: τ (*J*)
(3a)	154—156	3.62 (15.5, 8.3) 4.26 (15.5)	5.39 (2.2) 5.85 (2.2)	6.40; 6.44
(6a)	108—109	—	5.48 (2.1) 5.95 (1.8)	6.48; 6.52
(3b)	100—102	3.62 (15.5, 8.5) 4.32 (15.5)	5.95 (2.0) 6.07 (2.1)	6.38; 9.14 (6.8)
(3c)		4.8—4.65 (m)	5.96 (2.0) 6.12 (2.2)	6.36; 9.14 (6.8)
(6b)	93	—	6.01 (1.6) 6.15 (2.0)	6.42; 9.19 (6.0)
(4b) (cis-)	140—142	4.9—5.1 (m)	5.34 (3.5) 6.16 (3.5)	6.35; 8.77 (7.2)
(7b) (cis-)		—	5.38 (3.5) 6.19 (3.5)	6.34; 8.96 (7.0)
(5b)	288	—	5.82 (1.5) 6.01 (2.0) 6.1 (2.2) [b] 6.1 (1.5) [b]	6.09; 8.6 (6.0) [b]
(9)	99—100 [8]	—	5.70 (2.6) 5.92 (2.1)	— —

[a] τ-Values in CCl_4 with TMS as internal standard; coupling constants in Hz; all crystalline compounds gave satisfactory elemental analyses; the O/O transitions in the UV absorption lie without exception between 271 and 272 nm; IR, MS, and luminescence spectra provide further proof of structure.
[b] Coupling constants in $CDCl_3$ from decoupling and shift experiments with Eu(fod)$_3$ and Eu(dpm)$_3$.

Received: February 25, 1975;
revised: March 25, 1975 [Z 221 IE]
German version: Angew. Chem. *87*, 520 (1975)

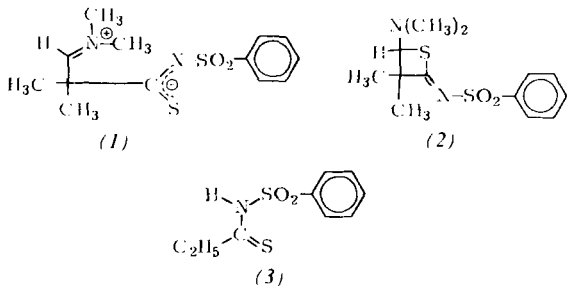
CAS Registry numbers:
(1), 120-12-7; *(2a)*, 1733-37-3; *(2b)*, 1515-80-6; *(3a)*, 55711-96-1; *(3b)*, 55711-97-2; *(3c)*, 55711-98-3; *cis-(4b)*, 55711-99-4; *trans-(4b)*, 55780-40-0; *(5b)*, 55712-00-0; *(6a)*, 55712-01-1; *(6b)*, 55712-02-2; *cis-(7b)*, 55712-03-3; *(8)*, 100-42-5; *(9)*, 22827-60-7;

[1] Lecture to the GDCh Photochemistry Group at Konstanz (Germany), Nov. 1974; *G. Kaupp* in Houben-Weyl: Methoden der Organischen Chemie, Thieme, Stuttgart, Vol. IV/5, in press; Angew. Chem. *84*, 718 (1972); Angew. Chem. internat. Edit. *11*, 718 (1972); Chimia *25*, 230 (1971); *G. O. Schenck, J. Kuhls*, and *C. H. Krauch*, Liebigs Ann. Chem. *693*, 20 (1966).
[2] *R. B. Woodward* and *R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969); *D. R. Arnold, L. B. Gillis*, and *E. B. Whipple*. Chem. Commun. *1969*, 918.
[3] *N. C. Yang* and *J. Libman*, J. Amer. Chem. Soc. *94*, 1405 (1972).
[4] *D. Bryce-Smith*, Chem. Commun. *1969*, 806.
[5] *N. D. Epiotis* and *R. L. Yates*, J. Org. Chem. *39*, 3150 (1974).
[6] *G. Kaupp*, Angew. Chem. *84*, 259 (1972); Angew. Chem. internat. Edit. *11*, 313 (1972); Liebigs Ann. Chem. *1973*, 884. Top. in Current Chem., in press.
[7] We thank Prof. *J. F. M. Oth* for recording the ^{13}C-NMR spectra.
[8] *W. E. Noland, M. S. Baker*, and *H. I. Freeman*, J. Amer. Chem. Soc. *78*, 2233 (1956).

X-Ray Structure Analysis of a Stable Dipole[1]

By *Ernst Schaumann, Armin Röhr, Stefan Sieveking*, and *Wolfgang Walter*[*]

The 1,4-dipoles often assumed[3] as intermediates of $[2\pi+2\pi]$-cycloadditions can be isolated in the reaction of sulfonylisocyanates or isothiocyanates with enamines[4, 5]. Thus, according to IR, NMR, and ESCA measurements the 1:1 adduct obtained from *N,N*-dimethyl-(2-methyl-1-propenyl)amine and benzenesulfonylisothiocyanate is present in the solid state as the dipole *(1)*, while in solution an equilibrium exists with the iminothiethane *(2)*[5]. We have now carried out an X-ray structure analysis of *(1)*.



(1) *(2)*

(3)

(1) crystallizes in the monoclinic space group $P2_1$ with $a=8.211$, $b=8.230$, $c=11.101$ Å, $\beta=104.35°$. A total of 1511 reflections were measured on a single crystal using a punched-tape controlled diffractometer. The structure was solved by the heavy atom method and refined using anisotropic temperature factors (H atoms isotropic) to an R value of 0.042 with the aid of the LSQ programm[6].

Besides the plane of the benzene ring (maximum deviation 0.01 Å) the molecule was shown to contain two further planes mutually twisted through 75.6° for the cation part (C^{11}—N^2—C^{12}—C^{13}; maximum deviation 0.01 Å) and the anion part (N^1—C^7—C^8—S^2; maximum deviation 0.011 Å) (Fig. 1). The anion part can be regarded as a *Z*-configurated thioamide anion.

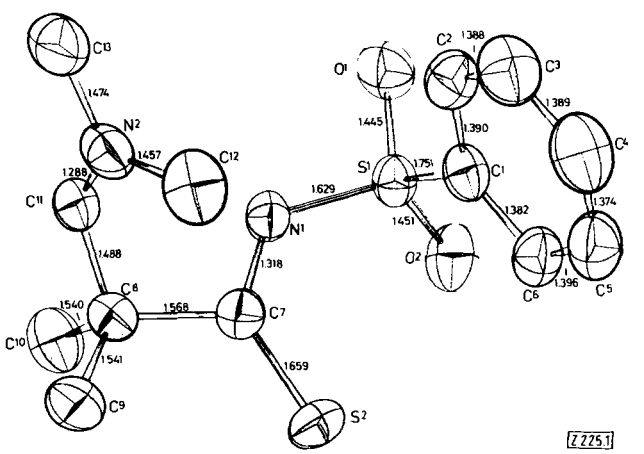


Fig. 1. Molecular structure of *(1)* showing ellipsoids of thermal motion and bond lengths [Å] (maximum standard deviation 0.006 Å).

The bond length $C^{11}-N^2$ (1.288 Å) corresponds to that of a double bond; *i.e.* the positive charge is essentially localized on the N^2 atom. In contrast to the bond lengths in the electron-deficient thioamide system of *N*-benzenesulfonylthiopropionamide *(3)* (C—N: 1.35, C—S: 1.62 Å[7]), the bond lengths in the anion portion proved to have values typical for thioamides (C—N: *ca.* 1.32, C—S: 1.65—1.69 Å[8]) owing to the additional electron. A further delocalization of the negative charge in the sulfonyl group follows from the shortened N^1—S^1 bond and the extended S^1—O bonds [respectively 1.63 and 1.45 Å each, instead of 1.65, 1.41, and 1.42 Å in *(3)*[7]].

The orientation of the negatively charged N^1 to the positively charged N^2 atom suggests an intramolecular interaction between the two charge centers. Unlike in the cycloadduct *(2)*, the S^2 atom is not oriented towards the cation part in the crystal. Besides a sterically more favorable arrangement this conformation makes interaction possible between the cation plane and the benzene ring oriented parallel to it. Further, the neighboring molecules are each so oriented that cation and benzene planes alternate. Thus the minimization of steric interactions, the electronic stabilization of the negative charge by the sulfonyl group and, at least in the solid state, electrostatic forces all participate in stabilization of the dipole *(1)*.

Received: April 1, 1975 [Z 225 IE]
German version: Angew. Chem. *87*, 486 (1975)

CAS Registry numbers:
(1), 55660-74-7; *N,N*-dimethyl-(2-methyl-1-propenyl)amine, 6906-32-7; benzenesulfonylisothiocyanate, 424-53-9

[1] Cycloaddition Reactions of Heterocumulenes, Part 5.—Part 4: ref. [2].
[2] *E. Schaumann, S. Sieveking*, and *W. Walter*, Chem. Ber. *107*, 3589 (1974).
[3] *R. Gompper*, Angew. Chem. *81*, 348 (1969); Angew. Chem. internat. Edit. *8*, 312 (1969); *R. Huisgen*, Z. Chem. *8*, 290 (1968); cf. also *N. D. Epiotis*, Angew. Chem. *86*, 825 (1974); Angew. Chem. internat. Edit. *13*, 751 (1974).
[4] *E. Schaumann, S. Sieveking*, and *W. Walter*, Tetrahedron Lett. *1974*, 209.
[5] *E. Schaumann, S. Sieveking*, and *W. Walter*, Tetrahedron *30*, 4147 (1974).
[6] *W. R. Busing, K. O. Martin*, and *H. A. Levy*, ORFLS a Fortran Crystallographic Program Oak Ridge 1962.
[7] *W. Walter, J. Holst*, and *A. Röhr*, Liebigs Ann. Chem., *1975*, 54.
[8] *W. Walter* and *J. Voss* in *J. Zabicki*: The Chemistry of Amides. Interscience, London 1970, p. 383.

[*] Dr. E. Schaumann [+], Dipl.-Chem. A. Röhr, Dr. S. Sieveking, and Prof. Dr. W. Walter
Institut für Organische Chemie und Biochemie der Universität
2 Hamburg 13, Papendamm 6 (Germany)
[+] To whom correspondence should be addressed.

Soluble Metal Complexes of Polymers for Catalysis

By *Ernst Bayer* and *Volker Schurig*[*]

Dedicated to Professor Eugen Müller on the occasion of his 70th birthday

In contrast to heterogeneous catalysts, homogeneous catalysts often exhibit higher substrate selectivity, better reproducibility, and reactivity under milder conditions. However, in many cases homogeneous catalysis presents problems, both in the laboratory and on an industrial scale as separation of low molecular reaction products from the low molecular homogeneous catalysts can be accomplished only with great expenditure of effort or with high losses, and continuous reaction is extremely difficult to achieve. These problems can be circumvented by "heterogenation" of the homogeneous catalyst, *i.e.* by binding the homogeneous catalyst to inorganic carrier material or organic polymers[1-4], *e.g.* to insoluble,

[*] Prof. Dr. E. Bayer and Priv.-Doz. V. Schurig
Lehrstuhl für Organische Chemie der Universität
74 Tübingen 1, Auf der Morgenstelle 18 (Germany)

[**] From a lecture at the Symposium on Metal Chemistry, Ettal (Germany), July 21—27, 1974.

crosslinked polystyrenes with functional phosphane groups. True, with these catalysts the starting material and reaction product can be separated, but the reactions involved are no longer homogeneous reactions. A disadvantage when using insoluble polymers as carriers is the differing accessibility of the catalytic functions.

It appeared appropriate to us, therefore, to use soluble metal complexes of polymers for the catalysis and to separate them from starting material and synthesis products on the basis of the difference in their molecular weight. Suitable methods of separation include precipitation, gel filtration, and membrane filtration.

As polymer we use functionalized soluble polystyrenes (abbreviation Ⓟ), polyethylene glycols, polyvinylpyrrolidinones, or polyvinyl chlorides[5].

Non-crosslinked linear polystyrene ($\overline{MW}$ *ca.* 100000) was chloromethylated and converted by treatment with potassium diphenylphosphide into the soluble polydiphenyl(styrylmethyl)phosphanes *(1a)*—*(1c)* (Table 1)[1-4]. The soluble macromolecular metal complexes *(2)*—*(7)*, which catalyze the homogeneous hydrogenation or hydroformylation of alkenes under mild conditions, were prepared by addition or ligand exchange reaction with transition metal derivatives (Table 1).

Table 1. Preparation and catalytic properties of soluble macromolecular transition-metal complexes *(2)*—*(7)*. Ⓟ = soluble, phosphane functionalized polystyrene.

Ⓟ [a]	Metal starting compound	Solvent, reaction conditions	Macromolecular *soluble* metal complex	Catalytic properties [b]
(1a)	$Rh(CO)_2(acac)$	benzene 24 h, 22 °C	*(2)*, $Rh(CO)Ⓟ(acac)$	H_2/CO (80 atm/80 °C)
(1c)	$Rh_2(CO)_4Cl_2$	benzene 24 h, 22 °C	*(3)*, $Rh(CO)_2ⓅCl$	H_2 (85 °C)
(1b)	$Rh(PPh_3)_3Cl$	benzene 24 h, 22 °C	*(4)*, $Rh(PPh_3)Ⓟ_2Cl$	H_2 (22 °C)
(1b)	$RhH(CO)(PPh_3)_3$	benzene 24 h, 22 °C	*(5)*, $RhH(CO)(PPh_3)Ⓟ_2$	H_2/CO (22 °C)
(1a)	$PdCl_2(PhCN)_2$	dioxane 24 h, 85 °C	*(6)*, $PdCl_2Ⓟ_2$	H_2 (22 °C)
(1c)	$PtCl_2(PhCN)_2$	dioxane 24 h, 85 °C	*(7)*, $PtCl_2Ⓟ_2$	H_2 (22 °C)

[a] *(1a)* contains 2.59 % Cl and 0.45 % P; *(1b)* contains <0.05 % Cl and 2.42 % P; *(1c)* contains 1.90 % P.
[b] H_2: homogeneous hydrogenation of monoalkenes, H_2/CO: homogeneous hydroformylation of monoalkenes.

Separation of the soluble macromolecular catalysts from low-molecular products was accomplished by continuous or batchwise membrane filtration. The soluble catalyst remains quantitatively in the membrane filtration cell and can be reused. The catalysts could also be separated by precipitation with *n*-hexane instead of by membrane filtration. The precipitates retained both their original solubility properties and after redissolution their catalytic activity.

Catalytic hydrogenation with $Rh(PPh_3)Ⓟ_2Cl$ (4)

128 mg *(1b)* and 15 mg $Rh(PPh_3)_3Cl$[6] (Rh: Ⓟ = 1 : 6) were stirred in 35 ml benzene for 24 h at 22 °C under N_2. The resulting yellowish brown solution was transferred to a membrane filtration cell (own construction from glass and Teflon) and subjected to membrane filtration for removal of the low-molecular fraction using 150 ml benzene (polyamide membrane[7] having cut-off limit MW 10000, ⌀ 75 mm, 85 ml/h at 2 atm N_2). Exchanged triphenylphosphane could be detected in the solution by mass spectrometry. 200 µl of 1-pentene was hydrogenated at 22 °C and 1 atm H_2 in the presence of the macromolecular catalyst *(4)* (50% conversion: 3 h). After 24 h the reaction solution was membrane-filtered with 150 ml benzene. *n*-Pentane could be determined gas-chromatographically as the sole product in the colorless filtrate. The catalyst retained quantitatively in the membrane filtration cell was recycled five times for the hydrogenation of 1-pentene. With prolonged reaction times the homogeneous catalytic hydrogenation of *cis*- and *trans*-2-pentene also led quantitatively to *n*-pentane.

Catalytic hydroformylation with $RhH(CO)(PPh_3)Ⓟ_2$ (5)

256 mg *(1b)* and 30 mg $RhH(CO)(PPh_3)_3$[8] (Rh: Ⓟ = 1 : 6) were stirred in 35 ml benzene under N_2 for 24 h at 22 °C. The deep yellow solution was membrane-filtered with 150 ml benzene. In the presence of the retained catalyst *(5)* 400 µl 1-pentene could be hydroformylated to C_6-aldehydes at 22 °C with 1 atm H_2/CO (1 : 1). After 72 h the reaction solution was membrane-filtered with 150 ml benzene. *n*-Hexanal (77 %) and methylpentanal (23 %) could be determined gas chromatographically in the colorless filtrate. Neither olefin hydrogenation or isomerization nor occurrence of C_6 alcohols could be detected. The retained catalyst was recycled twice (1-pentene, 24 h: *n*-hexanal (77 %) and methylpentanal (23 %); 1-hexene, 24 h: *n*-heptanal (78 %) and methylhexanal (22 %)).

Received: February 18, 1975;
revised: March 27, 1975 [Z 223 IE]
German version: Angew. Chem. 87, 484 (1975)

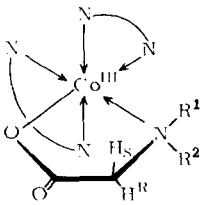
CAS Registry numbers:
polystyrene, 9003-53-6; rhodium, 7440-16-6; 1-pentene, 109-67-1; *cis*-2-pentene, 627-20-3; *trans*-2-pentene, 646-04-8; 1-heptene, 592-41-6; palladium, 7440-05-3; platinum, 7440-06-4

[1] *J. Manassen*, Chim. Ind. (Milan) *51*, 1058 (1969); Isr. J. Chem. Suppl. Proc. Isr. Chem. Soc. *8*, 5 (1970).
[2] *W. O. Haag* and *D. D. Whitehurst* in *J. W. Hightower*: Proc. 5th Internat. Congr. on Catalysis, 1972, Miami Beach, Florida. North-Holland Publ. Co., Amsterdam 1973, Abstract 29—465; Belg. Pat. 721686 (1969).
[3] *K. G. Allum, R. D. Hancock, S. McKenzie*, and *R. C. Pitkethly* in *J. W. Hightower*: Proc. 5th Internat. Congr. on Catalysis, 1972, Miami Beach, Florida. North-Holland Publ. Co., Amsterdam 1973, Abstract *30*—477; Belg. Pat. 739607 (1969).
[4] *R. H. Grubbs* and *L. C. Kroll*, J. Amer. Chem. Soc. *93*, 3062 (1971).
[5] *E. Bayer* and *V. Schurig*, DOS 2326489 (1974).
[6] *J. A. Osborn, F. H. Jardine, J. F. Young*, and *G. Wilkinson*, J. Chem. Soc. *A 1966*, 1711.
[7] Manufactured by Berghof GmbH, 7401 Tübingen-Lustnau.
[8] *C. K. Brown* and *G. Wilkinson*, J. Chem. Soc. *A 1970*, 2753.

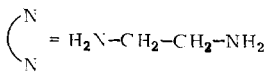
Stereoselective Hydrogen Exchange at the Methylene Group of Glycine in the ΛR-(N-Benzylglycinato)bis(ethylenediamine)cobalt(III) Ion[**]

By *Bernard T. Golding, Graeme J. Gainsford, Anthony J. Herlt,* and *Alan M. Sargeson*[*]

Several enzymatic reactions involve the methylene group of glycine. Since glycine is a prochiral molecule, it is expected that these reactions will occur either exclusively with the pro-*R* hydrogen atom of the methylene group or exclusively with the pro-*S* atom. Such specificity is difficult to reproduce in "conventional" (non-enzymatic) chemistry[1]. We have engaged this problem with the objective of achieving a non-enzymatic synthesis of optically pure chiral glycines by directed exchange of one of the methylene hydrogen atoms of glycine. By "chiral glycines" we mean (2*R*)-^{2}H(or ^{3}H)-glycine and (2*S*)-^{2}H(or ^{3}H)-glycine. In this paper, we demonstrate how this objective could be reached using *N*-substituted glycinate complexes of cobalt(III).



(1), $R^1 = R^2 = H$
(2), $R^1 = H$, $R^2 = CH_2C_6H_5$
(3), $R^1 = CH_2C_6H_5$, $R^2 = H$



The α-proton of amino-acids coordinated to bis(ethylenediamine)cobalt(III) undergoes fast exchange in weak aqueous alkali[2]. In the chiral cation bis(ethylenediamine)glycinatocobalt(III) *(1)*, the glycinate methylene protons are diastereotopic and should exchange at different rates even under achiral catalysis. However, stereoselective exchange could not be detected by ^{1}H-NMR spectroscopy[3]. We have therefore synthesized the ΛR-(*N*-benzylglycinato)bis(ethylenediamine)-cobalt(III) ion *(2)* and have examined its exchange characteristics in D_2O containing PO_4^{3-} ion at pH 10.5. It was reasoned that the presence of a "bulky" substituent on the nitrogen atom of the glycinato ring might cause deprotonation of the nearby methylene group and reprotonation of the resulting carbanion to occur preferentially on the side of the ring opposite to the *N*-substituent (*i.e.* the pro-*S* hydrogen atom H_S should be exchanged).

Four conditions must be fulfilled for this type of complex to be useful for the synthesis of chiral glycines:

1. It should be easily synthesized (in racemic form) and resolved.
2. The coordination of *N*-substituted glycine to cobalt(III) should be highly regioselective, producing one enantiomeric pair of diastereoisomers out of the possible two pairs.
3. Exchange at the methylene hydrogen atoms should exhibit "enzyme-like stereoselectivity".
4. The labeled glycine should be easily recovered from the cobalt complex and be easily cleaved from the *N*-substituent.

Conditions 1 and 2 are met by the present work. Partial fulfilment of conditions 3 and 4 has been accomplished so far.

The dibromide of the racemic cation *(2)* [*(2)2Br*][4] crystallized directly (60%) after refluxing a solution in methanol (120 ml) containing *N*-benzylglycinium chloride (10 mmol), *trans*-bis(ethylenediamine)dibromocobalt(III) bromide (10 mmol), and lithium hydroxide (20 mmol). It was converted to its water-soluble diacetate *(2)2AcO* (treatment with 2 equiv. silver acetate) and resolved by reaction with monolithium tartrate (2 equiv.) in water and recrystallization to constant rotation of the less soluble diastereoisomer of its bis(hydrogentartrate). Reconversion to the bromide salt with excess sodium bromide in water gave, after further recrystallization to constant rotation $(+)_{589}$-(*N*-benzylglycinato)bis-(ethylenediamine)cobalt(III) dibromide *(2)2Br*: $[\alpha]^{20}_{550} + 550°$, $[\alpha]^{20}_{495} - 926°$. Finally, conversion to the chloride salt, recrystallization from water and then D_2O gave crystals of deuterated *(2)2Cl*. The structure and absolute configuration of the complex *(2)2Cl* (Fig. 1) were established by X-ray crystallography using conventional Patterson functions. Fourier, and anomalous dispersion methods[5]. The observed ΛR complex *(2)* is expected to be appreciably more stable than its epimer the ΛS form *(3)* because of non-bonded interactions between the benzyl group and an ethylenediamine ligand in the latter[6]. This interaction preserves the stereochemistry regardless of the rate of exchange of the glycinate *N*-proton. There was no sign of any complex other than *(2)* (or its enantiomer) in either its preparation or its subsequent manipulation[7].

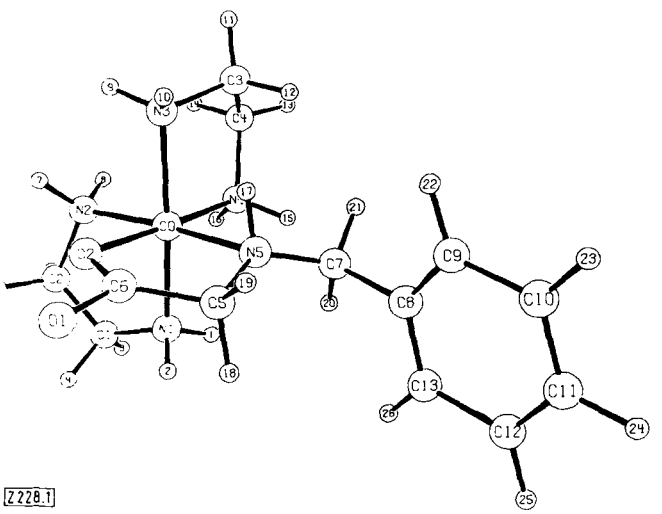


Fig. 1. Crystal structure of ΛR-(*N*-benzylglycinato)bis(ethylenediamine)cobalt(III) dichloride *(2)2Cl*.

The ^{1}H-NMR spectrum of the bis(acetate) of the ion *(2)* in D_2O containing Na_3PO_4 to keep the pH at 10.5 shows initially signals of the glycinato methylene hydrogens at $\delta = 3.3$ (1 H, d, $J = 18$ Hz) and 3.66 (1 H, d, $J = 18$ Hz). Figure 2 shows how this spectrum changes with time: the low field glycinato-

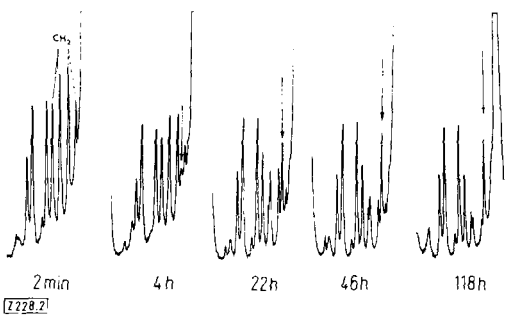


Fig. 2. Change of ^{1}H-NMR spectrum of complex *(2)2AcO* in D_2O (+ Na_3PO_4, pH 10.5) with time. CH_2 signals of glycinatomethylene protons. Concerning arrows, see text.

[*] Dr. B. J. Golding [+]
Department of Molecular Sciences,
University of Warwick,
Coventry, CV4 7AL (England)
Dr. G. J. Gainsford, A. J. Herlt, and Dr. A. M. Sargeson
Research School of Chemistry,
The Australian National University,
Canberra 2600 (Australia)
[+] To whom correspondence should be addressed.

[**] ΛR refers to the absolute configuration at cobalt [cf. Inorg. Chem. 9, 1 (1970)] and glycinate *N*, respectively.

methylene proton exchanges faster than that (arrow) at higher field ($k_{rel} \geq 4$), whilst the benzyl protons are unaffected. Several variations in conditions and buffer did not improve the stereoselectivity of exchange.

If it is true that the pro-*S* hydrogen is preferentially removed (see above) to give a carbanion which is preferentially reprotonated on its face opposite to the benzylgroup face, then the resulting coordinated *N*-benzyl-2-deuterioglycine is mainly the (*S*)-isomer. We will try to improve the stereoselectivity of exchange by modifying the *N*-benzyl group and will then recover 2-^{2}H-glycine from the complex and determine its absolute configuration using D-amino acid oxidase[8].

Received: March 20, 1975 [Z 228 IE]
German version: Angew. Chem. 87, 523 (1975)

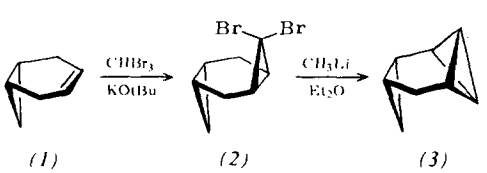
CAS Registry numbers:
trans-bis(ethylenediamine)dibromocobalt(III) bromide, 15005-14-8; $(+)_{589}$-(*N*-benzylglycinato)bis(ethylenediamine)cobalt(III) dibromide, 55590-64-2; Λ*R*-(*N*-benzylglycinato)bis(ethylenediamine)cobalt(III) dichloride, 55590-65-3; Λ*R*-(*N*-benzylglycinato)bis(ethylenediamine)-cobalt(III) bis(methanesulfonate), 55590-67-5

[1] See *E. L. Eliel*, Tetrahedron *30*, 1503 (1974), for a review.
[2] *D. A. Buckingham, L. G. Marzilli*, and *A. M. Sargeson*, J. Amer. Chem. Soc. *89*, 5133 (1967).
[3] *A. M. Sargeson*, unpublished result.
[4] All complexes with cation *(2)* gave satisfactory analytical data.
[5] $R = 0.05$; crystal data: $P2_12_12_1$; $a = 12.508(5)$, $b = 22.97(1)$, $c = 6.544(3)$ Å; $Z = 4$; $d_{calc} = 1.50$ g cm^{-3}.
[6] As in the analogous bis(ethylenediamine)-*N*-methylglycinatocobalt(III) complex; *D. A. Buckingham, S. F. Mason, A. M. Sargeson*, and *K. R. Turnbull*, Inorg. Chem. 5, 1649 (1966).
[7] *E.g.*, chromatography of complex *(2)* on Sephadex SP25 gave a single band. In other work (*J. McB. Harrowfield*, unpublished results) diastereoisomers analogous to those considered here were separated by this method.
[8] *N*-Benzylglycine has been recovered from complex *(2)*2Cl by sublimation (180°C/0.01 torr). In principle, reduction to cobalt(II) complexes should permit the release of *N*-substituted glycine under very mild conditions. Removal of the *N*-substituent *in situ* followed by ion exchange chromatography would yield glycine.

A Facile Conversion of 3-Norcarene into *trans*-Bishomobenzene[**]

By *Richard T. Taylor* and *Leo A. Paquette*[*]

For reasons of expediency, synthetic access to a wide range of simple *trans*-trishomobenzene derivatives[1] would be greatly facilitated if a ready source of *trans*-bishomobenzene (*trans*-tricyclo[5.1.0.0^{2,4}]oct-5-ene) *(5)* were available[2]. Two routes to this hydrocarbon have been reported. As these methods involve its formation (8—10%) together with six other products in the complex direct irradiation of 1,3,6-cyclooctatriene[3] or the further elaboration of dimethyl *trans*-1,2-dihydrophthalate (unspecified overall yield)[4], they do not appear to possess preparative utility. We now describe a convenient route to *(5)* commencing with 3-norcarene *(1)* which itself is obtainable directly by Simmons-Smith cyclopropanation of 1,4-cyclohexadiene[5]. This new approach allows access to *(5)* on a multigram scale if desired.



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

When treated with dibromocarbene generated from bromoform and potassium *tert*-butoxide, *(1)* afforded in 50% yield dibromocyclopropane *(2)*, the *trans* stereochemistry of which has been established previously by dipole moment studies[6]. The methyllithium-promoted carbenoid cyclization of *(2)* in ether solution at −20°C proceeded with high selectivity[7] to provide in 91% yield bicyclobutane (tetracyclo-[5.1.0.0^{2,4}.0^{3,5}]octane) *(3)*. Its structural features follow from elemental analysis, mass spectrum (*m/e* 106.0784; calc. 106.0782), and ^{1}H-NMR spectra (C_6D_6 solution, multiplets at δ = 2.50—2.70 (1H), 2.20 (1H), 1.44—1.84 (2H), 1.08—1.32 (2H), 0.64—0.98 (1H), and 0.16—0.60 (3H)). The infrared spectrum (neat) displays absorptions at 3090, 3065, 3010, 2990, 2910, 2850, 1450, 1440, 1420, 1135, 1020, 800, and 715 cm^{-1}. In accord with this assignment, *(3)* experiences quantitative isomerization to 2,3-homotropilidene *(4)* when exposed to catalytic quantities of silver perchlorate in anhydrous benzene (catalytic rate constant $k_{Ag} = 6.53 \pm 0.32 \times 10^{-4}$ l M^{-1} s^{-1} at 40.0°C). For preparative purposes, this route to *(4)* is preferable to that involving cyclopropanation of tropilidene[8], since contamination by the isomeric 4,5-homotropilidene is completely by-passed.

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

Reaction of *(3)* with catalytic quantities of $BF_3 \cdot (C_2H_5)_2O$ (2 h in ether at room temperature) results in acid-catalyzed ring opening to provide the desired *(5)* in 30—40% yield. Although additional minor products (unidentified) are formed simultaneously, these are readily removed by preparative VPC.

In contrast to these smooth bond reorganizations, vapor phase pyrolysis of *(3)* at temperatures of 500°C (contact time ≈ 1 s) gave rise to a ten-component mixture, the major constituents of which (1-vinyl-1,3-cyclohexadiene, 2,3-homotropilidene, 1,3,5- and 1,3,6-cyclooctatrienes, benzene, *etc.*) compare well with those realized from analogous thermal activation of the isomeric C_8H_{10} hydrocarbon, bicyclo-[4.2.0]octa-2,7-diene[3].

Received: April 1, 1975 [Z 230 IE]
German version: Angew. Chem. 87, 488 (1975)

CAS Registry numbers:
(1), 16554-83-9; *(2)*, 55701-53-6; *(3)*, 55701-54-7; *(4)*, 55701-55-8; *(5)*, 3786-99-0

[*] R. T. Taylor and Prof. Dr. L. A. Paquette [+]
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210 (USA)
[+] To whom correspondence should be addressed.

[**] Support from the National Science Foundation is acknowledged.

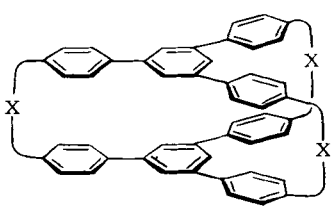
[1] *D. L. Dalrymple* and *S. P. B. Taylor*, J. Amer. Chem. Soc. *93*, 7098 (1971); *E. Vogel, H.-J. Altenbach*, and *C.-D. Sommerfeld*, Angew. Chem. *84*, 986 (1972); Angew. Chem. internat. Edit. *11*, 939 (1972); *H. Prinzbach* and *R. Schwesinger*, Angew. Chem. *84*, 988 (1972); Angew. Chem. internat. Edit. *11*, 940 (1972); *E. Vogel, H.-J. Altenbach*, and *E. Schmidbauer*, Angew. Chem. *85*, 862 (1973); Angew. Chem. internat. Edit. *12*, 838 (1973); *P. Binger, G. Schroth*, and *J. McMeeking*, Angew. Chem. *86*, 518 (1974); Angew. Chem. internat. Edit. *13*, 465 (1974).
[2] Other derivatives of this fundamental ring system have been reported in ref. [1]; see also: *M. Regitz, H. Scherer*, and *W. Anschütz*, Tetrahedron Lett. *1970*, 753; *H.-J. Altenbach* and *E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. internat. Edit. *11*, 937 (1972).
[3] *W. Roth* and *B. Peltzer*, Angew. Chem. *76*, 378 (1964); Angew. Chem. internat. Edit. *3*, 440 (1964); Liebigs Ann. Chem. *685*, 56 (1965); *J. Zirner* and *S. Winstein*, Proc. Chem. Soc. 1964, 235.
[4] *M. Engelhard* and *W. Lüttke*, Angew. Chem. *84*, 346 (1972); Angew. Chem. internat. Edit. *11*, 310 (1972).
[5] *E. C. Friedrich*, J. Org. Chem. *34*, 528 (1968).
[6] *W. D. Kumler, R. Boikess, P. Bruck*, and *S. Winstein*, J. Amer. Chem. Soc. *86*, 3126 (1964).
[7] *L. A. Paquette, G. Zon*, and *R. T. Taylor*, J. Org. Chem. *39*, 2677 (1974), and references contained therein.
[8] *W. von E. Doering* and *W. R. Roth*, Tetrahedron *19*, 715 (1963).

Triply Clamped Helical Triphenylmethane Systems[**]

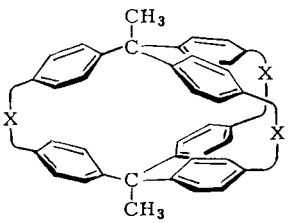
By *Fritz Vögtle* and *Gerd Hohner*[*]

Benzene rings compressed on one another in parallel planes can be realized particularly well among the helicenes[1] and cyclophanes[2]. We now report attempts to fix π-systems such as triphenylbenzene and triphenylmethane in face-to-face arrangements[3, 4]. In this connection the question had to be answered whether the propeller conformation of the triphenylmethane system can be fixed by bridging in such a way that a chiral (helical[5]) skeleton results.

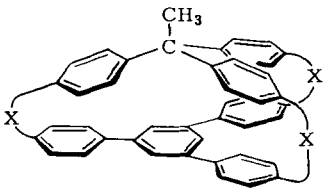
The starting points for our syntheses are the triply bridged systems *(1a)*—*(3a)*. In analogy to the synthetic method that we described previously for *(1a)*[6] and that we now applied for elaboration of the reaction sequence *(a)*→*(f)*, we synthesized *(2a)* and *(3a)* by treating 1,1,1-tris[4-(bromomethyl)-phenyl]ethane, m. p. 199—200 °C[7], with the corresponding tris(mercaptomethyl) compounds by the dilution method[8].



(1a)-(1f)



(2a)-(2f)



(3a)

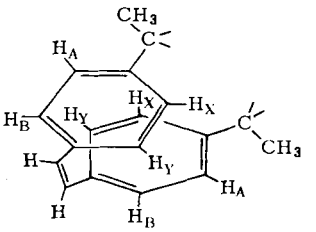
(a), X = $-CH_2-S-CH_2-$
(b), X = $-CH_2-\overset{\oplus}{S}(CH_3)-CH_2-$
(c), X = $-CH_2-CH(SCH_3)-$
(d), X = $-CH_2-CH[\overset{\oplus}{S}(CH_3)_2]-$
(e), X = $-CH=CH-$
(f), X = $-CH_2-CH_2-$

Extrusion of sulfur *via* *S*-methylation, Stevens rearrangement, renewed methylation and elimination[4] lead to the desired trienes *(1e)* and *(2e)*; *(3e)* could not yet be obtained by this route. Hydrogenation with H_2/Pt afforded the hydrocarbons *(1f)* and *(2f)*[9]. *(2f)* is also formed from *(2c)* by desulfuration with Raney nickel.

The changes in structure resulting during passage from the trisulfides *(a)* to the trienes *(e)* are shown up particularly clearly in the ^{1}H-NMR spectra (Fig. 1). In the aromatic region, the trithia compound *(2a)* expectedly shows an AA'BB' system shifted slightly upfield; however, two AA'BB' systems were found for the corresponding protons of the triene *(2e)*, one system at unusually high field strength (centered around δ = 5.84 ppm), the other in the region customary for aromatic protons. A symmetrical structure for the molecule, composed of triphenylethane units arranged mirror-image-wise, must therefore be excluded; instead, one must assume two triphenylethane systems, fixed in propeller form but mutually displaced, such that in each case only two—neighboring—protons on each benzene ring (H_X and H_Y in Fig. 1) lie in the anisotropy region of the opposing nucleus and thus absorb at the typically high field strength. Since the pairs of complementary aromatic rings do not lie in exactly parallel planes but approach each other more closely towards the periphery of the molecule, the anisotropic shielding of the "inner" protons H_X and thus the upfield shift of the corresponding peaks should be less marked than for the "outer" protons H_Y. The relatively high value of 0.76 ppm is accordingly found for the difference $\delta H_X - \delta H_Y$ in chemical shifts.

The corresponding AA'BB' systems of *(2f)* appear yet slightly farther upfield. In addition, an AA'BB' system is found for the bridging-CH_2 protons, which supports the fixed twisting of the phenyl rings.

The proton resonance of the two propeller molecules *(2e)* and *(2f)* is temperature-independent up to more than 130 °C (in $CDBr_3$). Consequently, we have a new type of helically chiral molecular skeleton[10] that may be suitable as chirospecific molecule receptor[11].



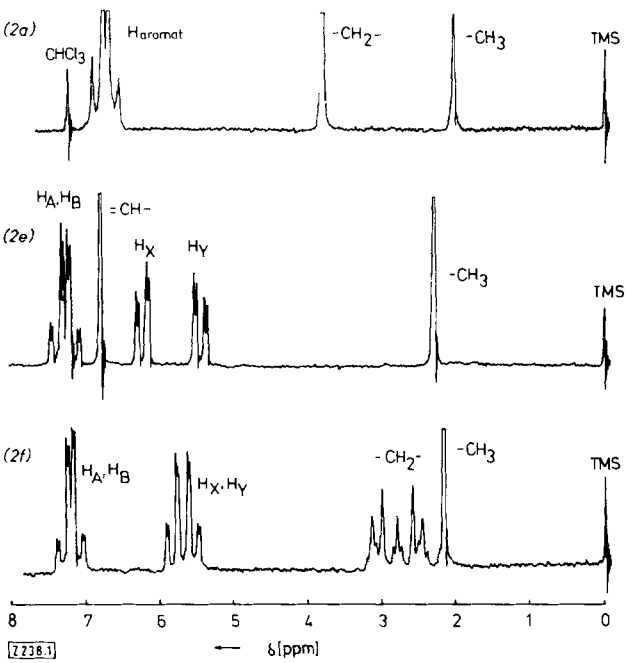


Fig. 1. ^{1}H-NMR spectra of *(2a)*, *(2e)*, and *(2f)* (in $CDCl_3$, 60 MHz).

Less striking differences in the ^{1}H-NMR spectra are observed on going from *(1a)* to the hydrocarbons *(1e)* and *(1f)*. The protons of the *para*-phenylene rings absorb as a singlet [*(1a)*] or as AA'BB' systems shifted diamagnetically by 0.14 ppm [*(1e)*] and 0.24 ppm [*(1f)*] relative to the singlet.

Received: April 8, 1975;
in shortened form April 24, 1975 [Z 238 IE]
German version: Angew. Chem. 87, 522 (1975)

CAS Registry numbers:
(2a), 55701-68-3; *(2e)*, 55701-69-4; *(2f)*, 55701-70-7

[*] Prof. Dr. F. Vögtle [+] and Dipl.-Chem. G. Hohner
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

[+] To whom correspondence should be addressed.

[**] Reported in part at Basel on February 7, 1975.—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

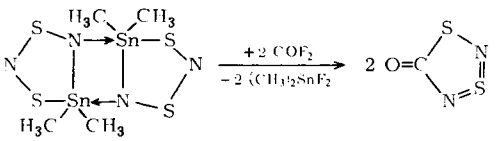
[1] Review: *R. H. Martin*, Angew. Chem. *86*, 727 (1974); Angew. Chem. internat. Edit. *13*, 649 (1974).
[2] Reviews: a) *F. Vögtle* and *P. Neumann*, Angew. Chem. *84*, 75 (1972); Angew. Chem. internat. Edit. *11*, 73 (1972); b) Top. Curr. Chem. *48*,

67 (1974); c) *D. J. Cram* and *J. M. Cram*, Accounts Chem. Research *4*, 204 (1971).
[3] *D. J. Cram* and *H. Steinberg*, J. Amer. Chem. Soc. *73*, 5691 (1951).
[4] a) *V. Boekelheide* and *R. A. Hollins*, J. Amer. Chem. Soc. *92*, 3512 (1970); b) *M. Haenel* and *H. A. Staab*, Chem. Ber. *106*, 2203 (1973).
[5] See *K. Mislow, D. Gust, P. Finocchiaro*, and *R. J. Boettcher*, Top. Curr. Chem. *47*, 1 (1974).
[6] *F. Vögtle, G. Hohner*, and *E. Weber*, J. C. S. Chem. Comm. *1973*, 366.
[7] Correct elemental analyses or highly resolved mass spectra were obtained for all the compounds.
[8] For methods see *F. Vögtle*, Liebigs Ann. Chem. *735*, 193 (1970); Chem.-Ztg. *96*, 396 (1972); *R. G. Lichtenthaler* and *F. Vögtle*, Chem. Ber. *106*, 1319 (1973).
[9] *(1a)*, *(2a)*, *(3a)*, *(1e)*, and *(1f)* melt above 410°C; *(2e)* and *(2f)* decompose at 330 and 390°C, respectively.
[10] The cycles *(2e)* and *(2f)* belong to the rare point group D_3. Only two configurationally stable organic propeller molecules with this symmetry property were previously known: *M. Farina*, Tetrahedron Lett. *1963*, 2097; *R. K. Hill* and *D. W. Ladner*, *ibid. 1975*, 989.
[11] *B. Dietrich, J. M. Lehn*, and *J. Simon*, Angew. Chem. *86*, 443 (1974); Angew. Chem. internat. Edit. *13*, 406 (1974).

5-Oxo-1,3λ⁴,2,4-dithiadiazole—A Five-Membered Heterocyclic Ketone[**]

By *Herbert W. Roesky* and *Erwin Wehner*[*]

Dimeric 5,5-dimethyl-1,3λ⁴,2,4,5-dithiadiazastannole *(1)*, obtained by reaction of tetrasulfur tetranitride with tris(trimethylstannyl)amine[1], reacts with an excess of carbonyl difluoride at room temperature to form 5-oxo-1,3λ⁴,2,4-dithiadiazole *(2)* and dimethyltin fluoride.



(1) *(2)*

The cyclic ketone is the first representative of a new class of compounds that have become readily accessible by this method. Other carbon components can be used in place of COF_2 for condensation with the sulfur-nitrogen fragment to form five-membered rings. Phosgene reacts similarly with *(1)*, but separation of *(2)* from dimethyltin dichloride proves difficult.

The yellow crystalline compound *(2)*, m.p. 40.5°C, can be sublimed in a vacuum at room temperature. It was characterized by elemental analysis and its mass spectrum: $m/e = 120$ molecular ion (rel. int. 12%), 92 M−CO (1), 78 M−NCO (25), 74 M−NS (1), 64 M−N_2CO (7), 46 M−NSCO (38), 32 M−N_2SCO (20), 28 M−S_2CO, or M−N_2S_2 (100). *(2)* exists as the monomer in $CHCl_3$ (osmometric molecular weight determination: 128). The IR spectrum contains the CO stretching vibration at 1727 cm^{-1} as characteristic strong band; the other absorption bands appear in the region expected for SN vibrations.

Procedure:

COF_2 is passed into a stirred suspension of $(CH_3)_4Sn_2N_4S_4$ (7.4 g, 0.018 mol) in CCl_4 (300 ml) for 1 h. The solvent is removed at water-pump vacuum. Yellow crystals of composition N_2S_2CO sublime over from the residue (oil-pump vacuum/room temperature; yield 1.75 g, 48.7%).

Received: April 28, 1975 [Z 239 IE]
German version: Angew. Chem. *87*, 521 (1975)

CAS Registry numbers:
(1), 50661-48-8; *(2)*, 55590-17-5; carbonyl difluoride, 353-50-4; phosgene, 75-44-5

[*] Prof. Dr. H. W. Roesky and E. Wehner
Anorganisch-chemisches Institut I der Universität
6 Frankfurt am Main 50, Niederurseler Hang (Germany)

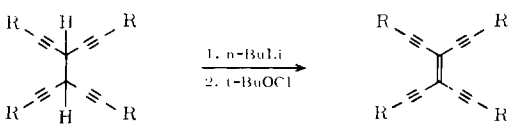
[**] This work was supported by the Fonds der Chemischen Industrie.

[1] *H. W. Roesky* and *H. Wiezer*, Angew. Chem. *85*, 722 (1973); Angew. Chem. internat. Edit. *12*, 674 (1973).

Tetraethynylethylenes

By *Hagen Hauptmann*[*]

As the first derivative of tetraethynylethylene *(2)*, 1,6-diphenyl-3,4-bis(phenylethynyl)-3-hexene-1,5-diyne *(2a)* was prepared by dimerization of 1,4-pentadiyne units[1]. Using a similar synthetic principle—dimerization of diethynylcarbenes—the *tert*-butyl and the trimethylsilyl derivatives *(2b)* and *(2c)* have in the meantime also been obtained[2]. A disadvantage of this method, however, is the formation of isomeric mixtures, in which the tetraethylnylethylene *(2)* is present in only small yields. In addition, simpler alkyl-substituted derivatives, *e.g. (2d)*, cannot be synthesized in this way.



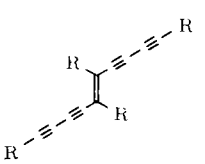
(1) *(2)*

(1a), *(2a)*: R = C_6H_5; *(1b)*, *(2b)*: R = $(CH_3)_3C$;
(1c), *(2c)*: R = $(CH_3)_3Si$; *(1d)*, *(2d)*: R = CH_3

Both the phenyl- and the alkyl-substituted tetraethynylethylenes *(2)* are readily accessible[4] by dehydrogenation of the tetraethynylethanes *(1)*[3], the dihydro derivatives of *(2)* (see experimental procedure). Mercury can also be used as oxidizing agent for the preparation of *(2b)* (yield 36%) (cf. Ref. [5]).

The tetraethynylethylenes *(2)* are good examples of cross-conjugated compounds with planar arrangement of the π-electron skeleton[6]. Thus the absorption maxima of 5,6-bis-(3,3-dimethyl-1-butynyl)-2,2,9,9-tetramethyl-5-decen-3,7-diyne *(2b)* ($\lambda_{max} = 331$ nm) and the silicon compound *(2c)* ($\lambda_{max} = 349$ nm) show only a relatively slight hypsochromic shift of 14 or 18 nm[2], respectively, as against those of comparable linear systems such as *(3)* ($\lambda_{max} = 345$ nm) and *(4)* ($\lambda_{max} = 367$ nm).

Analogous results were already obtained on comparison of the UV spectra of *(2a)* and *(5)*[1].



(3), R = $(CH_3)_3C$
(4), R = $(CH_3)_3Si$
(5), R = C_6H_5

Experimental

n-Butyllithium (2 equivalents in hexane) is rapidly added dropwise at −40°C to a stirred solution of the tetraethynyleth-

[*] Dr. H. Hauptmann
Fachbereich Chemie und Pharmazie der Universität
84 Regensburg, Universitätsstrasse 31 (Germany)

Table 1. Tetraethynylethylenes *(2)*.

Cpd.	Yield [%]	M.p. [°C]	^{1}H-NMR [δ]	UV λ_{max} (log ε) (in ethanol)	MS [*m/e*] (rel. int.) 70 eV
(2a) [a]	45	146—147	7.1—7.7 (m)	404 (4.40), 363 sh (4.21), 302 (4.53), 292 (4.49), 253 (4.61), 242 (4.64)	
(2b)	42	226—228	1.27 (s)	331 (4.53), 318 (4.17), 309 (4.37), 299 sh (4.18), 265 (3.93), 252 (4.04), 238 sh (3.93)	348, M^+ (100 %)
(2c)	43	203—205	0.23 (s)	349 (4.55), 334 (4.43), 325 (4.34), 312 sh (4.11), 283 (3.91), 268 (3.95), 259 sh (3.81), 223 (4.23), 213 (4.11)	412, M^+ (100 %)
(2d)	36	[b]	2.50 (s)	324 (4.39), 311 (4.35), 303 sh (4.27), 263 (3.82), 249 (3.88), 243 sh (3.84)	180, M^+ (100 %)

[a] Cf. ref. [1].
[b] Polymerizes at 150 °C.

ane *(1)* in ether [5 ml/mmol *(1)*]. After 30 minutes the reaction mixture is treated with 2 equivalents of *tert*-butyl hypochlorite and allowed to react for 5 minutes. After addition of 10 % aqueous ferrous sulfate [10 ml/mol *(1)*] for decomposition of peroxides the mixture is stirred at 0 °C for 15 minutes and any precipitated iron oxide is taken into solution by addition of a little glacial acetic acid. The organic phase is washed with water, dried, and evaporated under vacuum. On heating the oily residue under oil-pump vacuum *(2d)* sublimes at 120 °C, and *(2b)* and *(2c)* at 130—140 °C, as colorless crystals (recrystallization from ethanol). On rubbing the crude product with ether/ethanol (1 : 1), *(2a)* crystallized as yellow needles (recrystallization from chloroform/ethanol).

Received: March 26, 1975;
supplemented: April 4, 1975 [Z 226 IE]
German version: Angew. Chem. 87, 490 (1975)

CAS Registry numbers:
(1a), 54623-70-0; *(1b)*, 54623-69-7; *(1c)*, 54623-72-2; *(1d)*, 54623-71-1; *(2a)*, 17531-26-9; *(2b)*, 55660-75-8; *(2c)*, 55660-76-9; *(2d)*, 55660-77-0

[1] *Y. Hori, K. Noda, S. Kobayashi*, and *H. Taniguchi*, Tetrahedron Lett. *1969*, 3563.
[2] *H. Hauptmann*, unpublished.
[3] *H. Hauptmann*, Tetrahedron Lett. *1974*, 3587.
[4] *(2b)* is also accessible by elimination of lithium hydroxide from monolithiated *(1b)*: *H. Hauptmann*, Tetrahedron Lett., in press.
[5] *W. Schlenk* and *E. Bergmann*, Liebigs Ann. Chem. *463*, 6 (1928).
[6] *F. Bohlmann*, Chem. Ber. *89*, 2191 (1956).

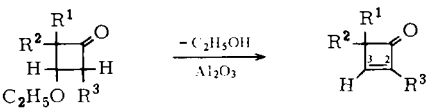
A New Synthesis of Cyclobutenones

By *Herbert Mayr* and *Rolf Huisgen*[*]

3-Alkoxycyclobutanones are readily accessible by [2+2]-cycloaddition of ketenes to enol ethers[1]. During column chromatography on neutral or basic alumina (activity grade I) the adducts *(1)* eliminate ethanol and afford the pure cyclobutenones *(2)*—*(9)* (Table 1). The active catalyst sites—polyfunctional catalysis is supposed—are blocked by the alcohol. Complete conversion requires about 10—30 g of alumina per mmol of *(1)*.

[*] Dr. H. Mayr and Prof. R. Huisgen [+]
Institut für Organische Chemie der Universität
8 München 2, Karlstrasse 23 (Germany)
[+] To whom correspondence should be addressed.

Disregarding the direction of addition, *(2)*—*(9)* appear to be the formal products of ketene addition to alkynes; this reaction is feasible only with ketenes bearing electron-withdrawing substituents[2]. Adopting the circuitous route *via (1)* one is able to exploit the pronounced ketenophilic activity of the enol ethers which far surpasses that of the alkynes[3]. Since the elimination of alcohols was successful in all ketene-enol ether adducts tried so far, we assume that the limits of this cyclobutenone synthesis are set by the ketene cycloaddition.



(1) *(2)*-*(9)*

Table 1. Cyclobutenones *(2)*—*(9)* from 3-ethoxycyclobutanones of type *(1)* with alumina.

Cpd.	R^1	R^2	R^3	Yield [%]
(2)	C_6H_5	C_6H_5	H	15—35
(3)	C_6H_5	C_6H_5	CH_3	65—80
(4)	C_6H_5	C_6H_5	C_2H_5	86
(5)	C_6H_5	C_6H_5	$CH(CH_3)_2$	58
(6)	C_6H_5	CH_3	CH_3	56
(7)	C_6H_5	C_2H_5	CH_3	55
(8)	C_6H_5	$CH(CH_3)_2$	CH_3	70
(9)	CH_3	CH_3	CH_3	75

The cyclobutenones can be recognized by the C=O vibration at 1741—1758 cm^{-1}, by their UV absorption ($n\rightarrow\pi^* \approx$ 320 nm, $\pi\rightarrow\pi^* \leq 227$ nm), and by their ^{1}H-NMR spectra ($\tau_{3\text{-H}} = 1.42$—2.07). *(2)* was catalytically hydrogenated to the known 2,2-diphenylcyclobutanone[4]. While *(6)*—*(9)* can be vacuum distilled, the crystalline cyclobutenones *(2)*—*(5)* decompose already at room temperature.

2-Ethyl-4,4-diphenyl-2-cyclobutenone (4)

3-Ethoxy-4-ethyl-2,2-diphenylcyclobutanone (1.10 g, 3.74 mmol) in anhydrous ether (10 ml) was applied to a column (2 cm diam.) of Al_2O_3 (70 g; Woelm, activity grade I) and eluted with ether (280 ml); the solvent was removed on a rotary evaporator; yield 0.80 g (85 %) of crystalline *(4)*.

2,4,4-Trimethyl-2-cyclobutenone (9)

3-Ethoxy-2,4,4-trimethylcyclobutanone (19.0 g, 0.12 mol) in ether (290 ml) was mixed to a paste with neutral Al_2O_3 (230 g); after 24 h the mixture was poured onto a column of dry Al_2O_3 (100 g) and eluted with ether (800 ml). The solvent was removed by fractional distillation; *(9)* distilled at 49 to 51 °C/28 torr as a colorless liquid with a pungent odor; yield 10.0 g (75%).

Received: April 16, 1975 [Z 233a IE]
German version: Angew. Chem. *87*, 491 (1975)

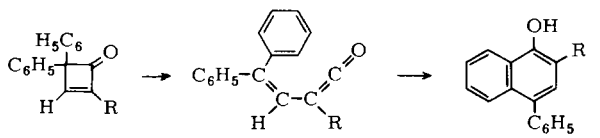
CAS Registry numbers:
(1) ($R^1=R^2=C_6H_5$, $R^3=H$), 4173-53-9;
(1) ($R^1=R^2=C_6H_5$, $R^3=CH_3$), 55701-86-5;
(1) ($R^1=R^2=C_6H_5$, $R^3=C_2H_5$), 55701-87-6;
(1) ($R^1=R^2=C_6H_5$, $R^3=CH(CH_3)_2$), 55701-88-7;
(1) ($R^1=C_6H_5$, $R^2=R^3=CH_3$), 55701-89-8;
(1) ($R^1=C_6H_5$, $R^2=C_2H_5$, $R^3=CH_3$), 55701-90-1;
(1) ($R^1=C_6H_5$, $R^2=CH(CH_3)_2$, $R^3=CH_3$), 55701-9-2;
(1) ($R^1=R^2=R^3=CH_3$), 55701-92-3; *(2)*, 55701-93-4;
(3), 55701-94-5; *(4)*, 55701-95-6; *(5)*, 55701-96-7;
(6), 55701-57-0; *(7)*, 55701-97-8; *(8)*, 55701-98-9;
(9), 55701-64-9

[1] *R. Huisgen, L. A. Feiler*, and *P. Otto*, Chem. Ber. *102*, 3405 (1969), and references cited therein; *H. Mayr* and *R. Huisgen*, Tetrahedron Lett. *1975*, 1349.
[2] Bis(trifluormethyl)ketene: *Y. A. Cheburkov, N. Mukhamadaliev*, and *I. L. Knunyants*, Tetrahedron *24*, 1341 (1968); *D. C. England* and *C. G. Krespan*, J. Org. Chem. *35*, 3308 (1970); dichloroketene: *H. Knoche*, Liebigs Ann. Chem. *722*, 232 (1969); *tert*-butylcyanoketene: *M. D. Gheorghiu, C. Draghici, L. Stanescu*, and *M. Avram*, Tetrahedron Lett. *1973*, 9.
[3] *R. Huisgen, L. A. Feiler*, and *P. Otto*, Chem. Ber. *102*, 3444 (1969).
[4] *R. Huisgen* and *L. A. Feiler*, Chem. Ber. *102*, 3391 (1969).

Vinylketenes from Cyclobutenones by Electrocyclic Ring Opening

By *Herbert Mayr*[*]

Optically active 2,4-dichloro-3-phenylcyclobutenone racemizes *via* the open-chain vinylketene present in low equilibrium concentration[1]. The intermediate role of cyclobutenones and vinylketenes in the thermal formation of α-naphthols from diphenylketene and alkynes was suspected as long ago as 1941[1,2]; the participation of cyclobutenones was confirmed at a later date[3]. We now report the electrocyclic ring opening of the readily accessible cyclobutenones[4].



(1), R = H
(2), R = CH_3
(3), R = C_2H_5

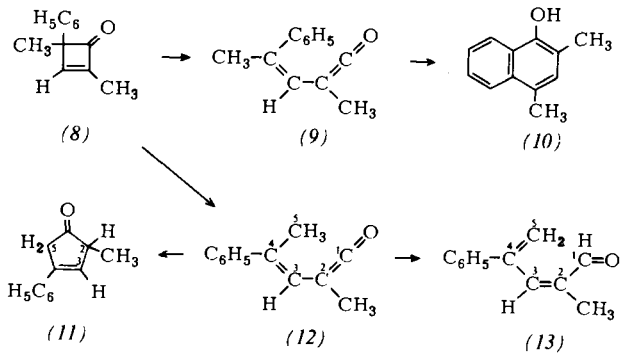
(4)

(5), R = H
(6), R = CH_3
(7), R = C_2H_5

The 4,4-diphenylcyclobutenones *(1)*—*(3)* undergo quantitative conversion into the α-naphthols *(5)*[5]—*(7)* on boiling for 1 h in cyclohexane. The appearance of β,γ-unsaturated carboxylic esters alongside the naphthols in the presence of alcohols, without any associated increase in the overall rate constant[6], suggests the vinylketenes *(4)* as logical intermediates. α-Naphthol formation occurs *via* an intramolecular electrophilic aromatic substitution which is so fast that the yellow color of *(4)* is not observed.

After 24 h in boiling cyclohexane the cyclobutenone *(8)* gave 64% of a mixture consisting of 49% of *(10)*, 21% of *(13)*, and 30% of *(11)*. Of the *cis,trans* isomeric vinylketenes

[*] Dr. H. Mayr
Institut für Organische Chemie der Universität
8 München 2, Karlstrasse 23 (Germany)



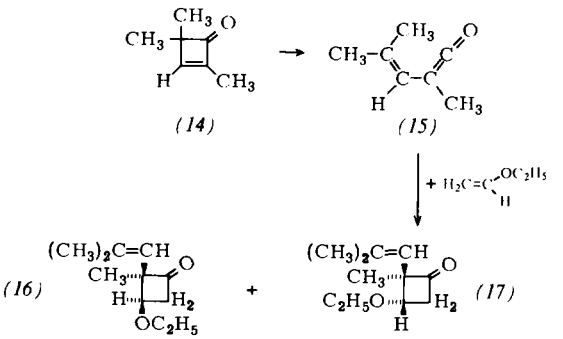
(8) *(9)* *(10)* *(11)* *(12)* *(13)*

(9) and *(12)*, only *(9)* satisfies the structural prerequisites for naphthol ring closure to give *(10)*. The isomer *(12)* appeared in a higher steady-state concentration than *(9)* and was recognized by its yellow color, which disappeared immediately on addition of alcohol. Fast further reaction *via (9)* would have been expected in the case of a mobile equilibrium *(8)*⇄*(12)*.

The structure of the pentadienal derivative *(13)* followed from the CO band at 1684 cm^{-1} and the ^1H-NMR spectrum ($CDCl_3$), which displays the aldehyde proton at τ = 0.51. The two 5-H give an AB spectrum at τ = 4.26 and 4.58 with $J = 1.5$ Hz; the triplet at 4.58 indicates an additional coupling with 3-H by the same constant J. The allylic coupling constant of 2-CH_3 (d at 8.31) amounts to 1.5 Hz so that 3-H appears as a quintuplet at 3.00. The visible absorption of the dark red 2,4-dinitrophenylhydrazone of *(13)* (λ_{max} = 3.82 nm, log ε = 4.53, ethanol) was as expected.

The IR absorption of *(11)* at 1733 cm^{-1} suggested a nonconjugated ketone, as did the spectra of the semicarbazone prepared in acetate buffer. The 2,4-dinitrophenylhydrazone (violet-red needles, obtained with sulfuric acid/2,4-dinitrophenylhydrazine), however, is derived from an isomeric conjugated ketone. Authentic 5-methyl-3-phenyl-2-cyclopentenone[7] gave the same 2,4-dinitrophenylhydrazone (λ_{max} = 402 nm, log ε = 4.58). The ^1H-NMR spectrum of *(11)* exhibits the isochronous 5-H_2 as a doublet at τ = 6.77, only split by 3-H with $J = 2.0$ Hz.

The 1,5-sigmatropic H shift of *(12)* to *(13)* has a prototype in a cyclic *cis*-fixed system[8]. *(13)* is not transformed into *(11)*.



(14) *(15)* *(16)* *(17)*

Compound *(14)* also suffers ring opening in boiling cyclohexane to form the vinylketene *(15)*, as demonstrated by the yellow coloration which disappears on addition of alcohol. *(15)* could be trapped *in situ* by ethyl vinyl ether to give a 63% yield of the cyclobutanones *(16)* and *(17)* (28:72).

Irradiation of *(14)* in CCl_4 at 10 °C led to a yellow solution of *(15)* displaying the typical ketene absorption at 2097 cm^{-1}[9]. The extinction of *(15)* decreased by one half within three days at room temperature without any corresponding increase in that of the cyclobutenone *(14)*. The reaction

(15) → *(14)* is therefore either too slow or lacking in thermodynamic driving force.

Received: April 16, 1975 [Z 233b IE]
German version: Angew. Chem. *87*, 491 (1975)

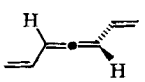
CAS Registry numbers:
(8): 55701-57-0; *(9)*, 55701-58-1; *(10)*, 4709-20-0; *(11)*, 55701-59-2; *(11)* 2,4-DNPH, 55701-60-5; *(12)*, 55701-61-6; *(13)*, 55701-62-7; *(13)* 2,4-DNPH, 55701-63-8; *(14)*, 55701-64-9; *(15)*, 55701-65-0; *(16)*, 55701-66-1; *(17)*, 55701-67-2

[1] *E. F. Jenny* and *J. D. Roberts*, J. Amer. Chem. Soc. *78*, 2005 (1956).
[2] *L. I. Smith* and *H. H. Hoehn*, J. Amer. Chem. Soc. *61*, 2619 (1939); *63*, 1181 (1941).
[3] *J. Druey*, *E. F. Jenny*, *K. Schenker*, and *R. B. Woodward*, Helv. Chim. Acta *45*, 600 (1962); *E. W. Neuse* and *B. R. Green*, Liebigs Ann. Chem. *1974*, 1534.
[4] *H. Mayr* and *R. Huisgen*, Angew. Chem. *87*, 491 (1975); Angew. Chem. internat. Edit. *14*, 499 (1975).
[5] *W. Borsche*, Liebigs Ann. Chem. *526*, 1 (1936).
[6] Reactions of vinylketenes with nucleophilic reagents: *H. Mayr* and *R. Huisgen*, manuscript in preparation.
[7] *H. A. Weidlich* and *G. H. Daniels*, Ber. Deut. Chem. Ges. *72*, 1590 (1939).
[8] *P. Schiess* and *C. Suter*, Helv. Chim. Acta *54*, 2636 (1971).
[9] *O. L. Chapman* and *J. D. Lassila*, J. Amer. Chem. Soc. *90*, 2449 (1968), observed the IR band of a ketene after irradiation of perchlorocyclobutenone at −190 °C.

Synthesis of 1,3,4,6-Heptatetraene (Divinylallene)[1]

By *Ursula Mödlhammer* and *Henning Hopf*[*]

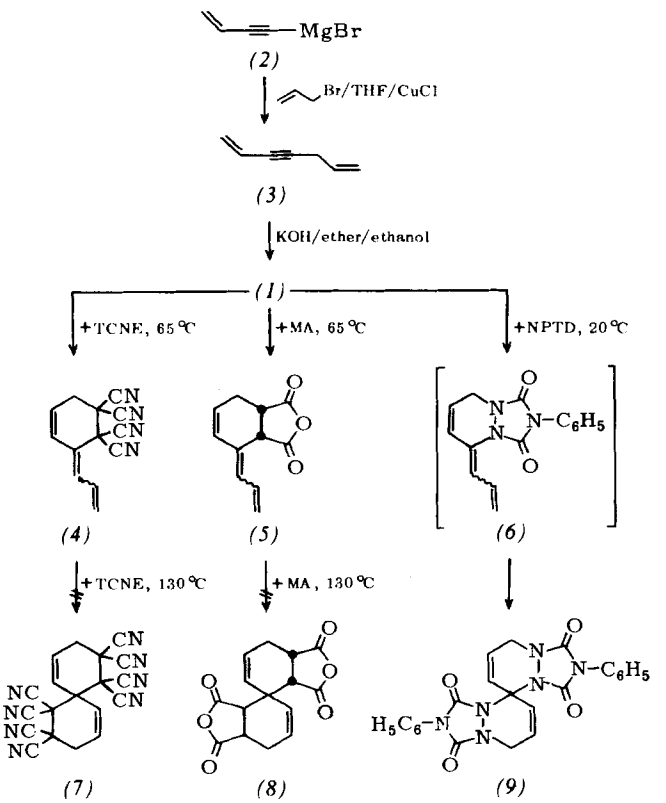
1,3,4,6-Heptatetraene (divinylallene) *(1)* consists of two mutually orthogonal 1,3-butadiene units;



(1)

Synthesis of this chiral C_7H_8 hydrocarbon (C_2 symmetry) appeared desirable for a number of reasons. Viewed preparatively, *(1)* could provide a one-step entry to spiro compounds by double Diels-Alder addition. Mechanistic interest attaches to the thermal behavior of divinylallene[2]; current ideas about the height of the thermal isomerization barrier of allenes could be tested, and possibly extended, with the aid of the optically active molecule[3]. Finally, the spectroscopic properties of this unusual "butadiene dimer" are of interest[4]. In the present communication we report the synthesis and various reactions of *(1)*.

3-Buten-1-ynylmagnesium bromide *(2)*[5] was coupled with allyl bromide in the presence of catalytic quantities of copper(I) chloride in tetrahydrofuran to give 1,6-heptadien-3-yne *(3)* (74%)[6]. Treatment of an ethereal solution of *(3)* with a saturated solution of potassium hydroxide in ethanol afforded divinylallene *(1)* in 61% yield, along with the isomeric C_7H_8 hydrocarbons *cis*- and *trans*-1,5-heptadien-3-yne[7]. Gas chromatography on a Carbowax column (70 °C) yields pure *(1)* as a colorless volatile liquid (b. p. 115 °C/760 torr; $n_D^{20} = 1.5338$)[6]. Mass spectrum: molecular peak at *m/e* 92 (C_7H_8); ^{1}H-NMR spectrum ($CDCl_3$, TMS internal reference); partially overlapping multiplets in the vinyl (6.64—5.12 ppm, 6H) and allene (5.12—4.74 ppm, 2H) regions; vibrational spectrum (CCl_4): 3095 (m), 3018 (m), 1612 (s), 987 (s), 905 (vs, terminal double bonds), and 1930 cm^{-1} (s, disubstituted allene function); electronic spectrum (ethanol): $\lambda_{max} = 224$ ($\varepsilon = 73000$) and 230 nm (70600). Divinylallene can be kept for several hours in a closed vessel at room temperature but rapidly polymerizes on exposure to air. The hydrocarbon reacts with tetracyanoethylene (TCNE) and maleic anhydride (MA) at 65 °C in benzene to give the 1:1 adducts *(4)* and *(5)*[6], respectively. No further reaction to form the spiro dienes *(7)* and *(8)* takes place with excess dienophile, even at 130 °C, presumably because the bulky substituents on the cyclohexene rings of *(4)* and *(5)* thwart attack by the second dienophile molecule. Moreover, the energetics of the second addition are unfavorable, destroying the conjugated triene systems of the monoadducts. The desired spiro system *(9)* was only obtained on use of the modestly substituted and highly reactive dienophile *N*-phenyltriazolinedione (NPTD)[6]; the monoadduct *(6)* was not isolated in this case.



In a further experiment, a saturated solution of sodium (−)-mentholate in (−)-menthol was employed for isomerization of *(3)*. The isolated divinylallene was optically active ($[\alpha]_{365}^{20} = -6 \pm 2°$), but the optical yield of this rearrangement is probably very small: a screw shaped molecule such as *(1)* should display a much higher specific rotation.

Received: April 28, 1975 [Z 240 IE]
German version: Angew. Chem. *87*, 492 (1975)

CAS Registry numbers:
(1), 55712-04-4; *(3)*, 5150-80-1; 3-buten-1-ynyl bromide, 40083-64-5; *cis*-1,5-heptadien-3-yne, 55712-05-5; *trans*-1,5-heptadien-3-yne, 55712-06-6

[*] Priv.-Doz. Dr. H. Hopf and U. Mödlhammer
Institut für Organische Chemie der Universität
75 Karlsruhe 1, Richard-Willstätter-Allee 2 (Germany)

[1] Alkynes and Cumulenes, Part 5. Reported in part at the Chemiedozenten-Tagung, Düsseldorf, April 1975. This work was supported by the Fonds der Chemischen Industrie.—Part 4: *K. J. Drachenberg* and *H. Hopf*, Tetrahedron Lett. *1974*, 3267.
[2] *L. A. Hulshof* and *H. Wynberg*, J. Amer. Chem. Soc. *96*, 2191 (1974), consider the formation of *(1)* during pyrolysis of spiro[3.3]hepta-1,5-diene. Although the ring-opening is symmetry allowed, *(1)* is not found among the pyrolysis products.
[3] *W. R. Roth*, *G. Ruf*, and *P. W. Ford*, Chem. Ber. *107*, 48 (1974), and references cited therein.
[4] Regarding the vibrational spectrum of 1,2,4-pentatriene (vinylallene) present as a subunit of *(1)*, see *P. Klaboe*, *T. Torgrimsen*, *D. H. Christensen*, *H. Hopf*, *A. Eriksson*, *G. Hagen*, and *S. J. Cyvin*, Spectrochim. Acta *30 A*, 1527 (1974).

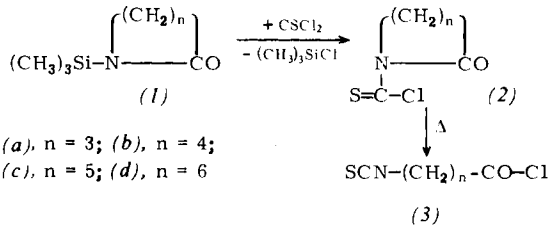
[5] *L. Brandsma:* Preparative Acetylenic Chemistry. Elsevier, Amsterdam 1971, p. 122.
[6] The new compounds were characterized by their spectroscopic properties and elemental analysis.
[7] The isomeric 1,5-heptadien-3-ynes are the sole rearrangement products under more drastic conditions (potassium *tert*-butoxide in *tert*-butyl alcohol at room temperature, sodium methoxide in methanol at 80 °C). The best procedure was found to consist in monitoring the isomerization *(3)* → *(1)* by NMR spectroscopy and interrupting the reaction at a suitable moment (after 10—60 min at room temperature, depending upon the concentration of the ethereal solution of *(1)*).

Synthesis of Isothiocyanato Acyl Chlorides from Lactams

By *Hans R. Kricheldorf*[*]

Acylation of lactams is best performed *via* the *N*-trimethylsilyl derivatives[1, 2]. We have now found that the *N*-trimethylsillactams *(1a)*—*(1d)* undergo rapid exothermic reaction with thiophosgene at −10 °C, liberating trimethylchlorosilane in the process. Disappearance of the CO band of *(1a)*—*(1d)* (1665 cm^{-1}) is accompanied by the appearance of a new CO band at 1730 cm^{-1}, *i.e.* at a frequency expected for the *N*-(chlorothioformyl)derivatives *(2a)*—*(2d)*. These compounds rearrange already at 0 °C to the isomeric ω-isothiocyanato acyl chlorides *(3a)*—*(3d)*, which can be isolated by distillation.

The high-boiling acyl chloride *(3d)* was only obtained impure and in poor yield owing to slight decomposition above −150 °C/10^{-3} torr during distillation.



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

(a), n = 3; *(b)*, n = 4; *(c)*, n = 5; *(d)*, n = 6

[*] Dr. H. R. Kricheldorf
Institut für makromolekulare Chemie der Universität
78 Freiburg, Stefan-Meier-Strasse 31 (Germany)

The isothiocyanato acyl chlorides *(3)* are of interest for the synthesis of low-molecular and polymeric ω-amino acid derivatives[2–5], which were formerly only accessible in several steps from ω-amino acids[6].

Phosgenation of *(1a)*—*(1d)* above 100 °C leads to ω-isocyanato acyl chlorides; however, the latter can only be isolated with difficulty, if at all, because of the numerous side products formed.

5-Isothiocyanatovaleryl chloride (3b)

N-Trimethylsilyl-δ-valerolactam[1] (0.8 mol) is added dropwise to a solution of thiophosgene (1 mol) in anhydrous toluene (300 ml) cooled to *ca.* −10 °C at such a rate that the internal temperature does not rise above +10 °C. The reaction mixture is heated to boiling for 10 min, concentrated at *ca.* 12 torr, and subjected to short-path distillation in as small an apparatus as possible; yield 72% *(3b)*, b.p. 98—100 °C/10^{-3} torr; $n_D^{20} = 1.5343$; ^{1}H-NMR ($CDCl_3$): τ = 8.23 (m), 7.00 (m), 6.40 (m), intensity ratio 2:1:1.—*(3a)*: yield 65%; *(3c)*: yield 75%.

6-Isothiocyanatohexanoyl chloride (3c)

ε-Caprolactam (1 mol), trimethylchlorosilane (1.05 mol), and triethylamine (1.05 mol) are heated to boiling for 1 h in anhydrous toluene (1.2 l). The reaction mixture is cooled with ice and filtered; the filter cake is washed with toluene (2 × 100 ml). The combined filtrate is concentrated to about 300 ml and then added to an ice-cold solution of thiophosgene (1 mol) in anhydrous toluene (200 ml). *(3c)* is isolated in the same way as *(3b)*. [*(3d)*: yield 35%, $n_D^{20} = 1.5186$; analysis: calc: C 43.86, H 5.25, N 7.30; found: C 44.97, H 5.52, N 6.99.]

Received: April 30, 1975 [Z 241 IE]
German version: Angew. Chem. *87*, 517 (1975)

CAS Registry numbers:
(1b), 3553-93-3; *(1c)*, 3553-94-4; *(3a)*, 39243-51-1; *(3b)*, 55712-31-7; *(3c)*, 39243-52-2

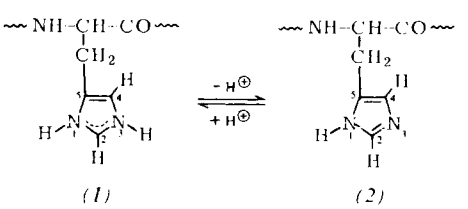
[1] *M. Rothe* and *T. Toth*, Chem. Ber. *99*, 3820 (1966).
[2] *H. R. Kricheldorf*, Makromol. Chem. *170*, 89 (1973).
[3] *H. R. Kricheldorf*, Synthesis *1972*, 551.
[4] *H. R. Kricheldorf*, Angew. Chem. *83*, 539 (1971); Angew. Chem. internat. Edit. *10*, 507 (1971).
[5] *H. R. Kricheldorf, E. Leppert*, and *G. Schilling*, Makromol. Chem. *175*, 1705 (1974).
[6] *H. R. Kricheldorf*, Liebigs Ann. Chem. *748*, 101 (1971).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

The observation of histidine residues in proteins by means of NMR spectroscopy is reported by *J. L. Markley*. Histidine is the only amino acid that can be present as acid *(1)* or as base *(2)* in the physiological pH range. With proteins having molecular weights <30000 it is generally possible to recognize and assign 2-H and 4-H peaks in the ^{1}H-NMR



(1) *(2)*

spectrum. N—H protons of the imidazole ring which slowly exchange with water are also resolvable. ^{13}C-NMR investigations are resorted to if, for example, 2-H does not give a reasonable peak. The ^{1}H-NMR spectra allow, *inter alia*, titration curves to be recorded, the involvement of histidine residues in conformational equilibria to be established, and the effect

of adjacent charged groups to be studied. [Accounts Chem. Res. *8*, 70—80 (1975); 112 references]

[Rd 778 IE—L]

The UV spectra and excited states of formaldehyde are the subject of a review by *D. C. Moule* and *A. D. Walsh*. The main emphasis is on the molecular structure of H_2CO in the lowest electronically excited singlet and triplet states; in this connection special interest is shown in the states in which the molecule is nonplanar. A few data on the readily accessible isotopic molecules HDCO and D_2CO are also given. [Ultraviolet Spectra and Excited States of Formaldehyde. Chem. Rev. *75*, 67—84 (1975); 104 references]

[Rd 780 IE—L]

The use of sodium cyanotrihydridoborate, $NaBH_3CN$, as a highly selective reducing agent for organic functional groups is dealt with in a review by *C. F. Lane*. A summary of the preparation and chemical and physical properties is followed by a discussion of the potential applications of the reagent. The stability of $NaBH_3CN$ in protonic solvents at low pH allows reductions under conditions in which $NaBH_4$ rapidly hydrolyzes. Amides, ethers, lactones, nitriles, nitro compounds, and epoxides do not react with $NaBH_3CN$. Individual sections are devoted to: the reduction of aldehydes and ketones to alcohols, of oximes to *N*-alkylhydroxylamines, and of enamines *via* the iminium salt to saturated amines; the reductive alkylation of amines and hydrazines, the reductive elimination of iodine, bromine and of the tosyloxy group (here tetrabutylammonium cyanotrihydrioborate reacts more selectively), as well as the deoxygenation of aldehydes, ketones, and sulfoxides. [Sodium Cyanoborohydride—A Highly Selective Reducing Agent for Organic Functional Groups. Synthesis *1975*, 135—146; 43 references]

[Rd 781 IE—M]

The chemistry of vision forms the theme of a special issue of "Accounts of Chemical Research". An overview by *D. S. Kliger* and *E. L. Menger* (pp. 81—84, 18 references) is followed by an article by *W. L. Hubbell* on the characterization of the isolated visual pigment rhodopsin in synthetic systems, *e.g.* detergents and synthetic membranes (pp. 85—91, 55 references). *B. Honig, A. Warschel*, and *M. Karplus* deal with theoretical investigations on 11-*cis*-retinal, the chromophore of rhodopsin (pp. 92—100, 76 references). Dynamic processes in visual pigments of the rods in the retina of mammals and in the membranes of these structures are reviewed by *E. W. Abrahamson* (pp. 101—106, 91 references). The concluding contribution by *T. P. Williams* (pp. 107—112, 24 references) is devoted to the dynamics of opsin, the protein component of rhodopsin. [Special Issue on the Chemistry of Vision. Accounts Chem. Res. *8*, 81—112 (1975)]

[Rd 782 IE—L]

Introduction of the nitrosyl group into coordination compounds is the subject of a review by *K. G. Caulton*. In contrast to CO, NO is an oxidizing agent and unstable at high pressure and high temperature, conditions often used in kinetically sluggish reactions. Therefore a large number of methods for introducing NO into metal complexes have been developed which, instead of NO, use the NO^+ ion, nitrosyl halides, *N*-nitroso amides, coordinated NO, NH_2OH, NO_2^- in acidic solution, alkyl nitrites, or HNO_3. Another possibility is the transformation of coordinated NO_2 into NO. [Synthetic Methods in Transition Metal Nitrosyl Chemistry. Coord. Chem. Rev. *14*, 317—355 (1975); 253 references]

[Rd 783 IE—H]

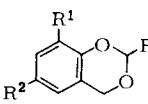
The function of glutamate dehydrogenase in rat liver as source of ammonia for the urea cycle is questioned in an article by *J. D. McGivan* and *J. B. Chappell*. The rates of glutamate deamination and urea production are not only different but are also influenced in different ways by the same effectors. The authors suggest a reaction scheme in which the two nitrogen atoms in urea originate from aspartate, while the role of glutamate dehydrogenase is limited to the formation of glutamate for the storage of nitrogen in glutamine. [On the Metabolic Function of Glutamate Dehydrogenase in Rat Liver. FEBS Lett. *52*, 1—7 (1965); 22 references]

[Rd 785 IE—R]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Defence against phytocidal bacteria, in particular *Pseudomonas* and *Xanthomonas* species, can be effected with 6,8-disubstituted 4*H*-1,3-benzodioxane derivatives *(1)*. In *(1)*, R^1 and R^2 represent chlorine or bromine, and R^3 denotes hydrogen,

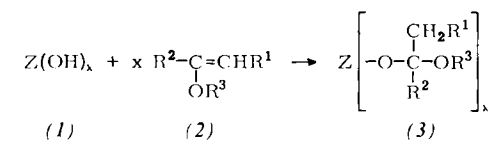


(1)

alkyl (C_1—C_6), alkenyl (C_2—C_6) or styryl. [DOS 2434462; Ciba Geigy AG, Basel (Switzerland)]

[PR 271 IE—S]

Protected polyols of formula *(3)* are prepared from polyols *(1)* by treatment with an unsaturated ether *(2)*, *e.g.* methyl isopropenyl ether. The compounds *(3)* are less viscous than the polyols *(1)* and can be used together with polyisocyanates



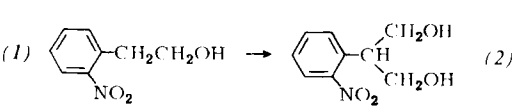
(1) *(2)* *(3)*

Z = multivalent group of a polyol $Z(OH)_x$; R^1, R^2 = H, hydrocarbon radical (C_1—C_6), or R^1—R^2 = —$(CH_2)_4$—; R^3 = hydrocarbon radical (C_1—C_6); $x = 2$—8.

for the preparation of single-vessel coatings hardening at room temperature. Crosslinking occurs by hydrolytic removal of the protecting groups in atmospheric moisture. [DOS 2424522; The Dow Chemical Co., Midland, Mich. (USA)]

[PR 272 IE—D]

2-(*o*-Nitrophenyl)-1,3-propanediol *(2)* is obtained in good yield if *o*-nitrophenethyl alcohol *(1)* is treated with 1.2—1.5 mole

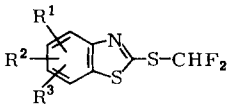


(1) *(2)*

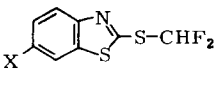
of formaldehyde in the presence of dialkyl sulfoxides or *N,N*-dialkylsubstituted amides and a small amount of a strong base at 20—40 °C. [DOS 2327961; Rütgerswerke AG, Frankfurt]

[PR 273 IE—D]

2-(Difluoromethylthio)benzothiazoles *(1)*, which are obtained from benzothiazole-2-thiols and difluorohalomethanes, are potent acaricides that can be used both against spinning mites and against ticks. Compounds *(2)* and *(3)* are specifically



(1)



(2), X = NO_2
(3), X = OCH_3

mentioned. In *(1)*, R^1, R^2, and R^3 denote hydrogen, alkyl, halogen, trifluoromethyl, phenyl, alkoxy, phenoxy, or nitro. [DOS 2334356; Farbwerke Hoechst AG, Frankfurt/M.]

[PR 274 IE—S]

BOOK REVIEWS

Low-Energy Electrons and Surface Chemistry. Monographs in Modern Chemistry 4. By *G. Ertl* and *J. Küppers*. Verlag Chemie, GmbH, Weinheim 1974. 1st Edit., x, 251 pp., 152 figs., 3 tables, bound, DM 98,—.

The authors' objective for this monograph was to provide the non-expert with a readily understandable introduction to the most important methods used in the chemistry and physics of solid surfaces. This objective has been excellently achieved, within the limitations that the authors imposed on themselves, but the book may also prove useful to experts, particularly because of the detailed literature references added to each chapter. The limitations mentioned result in a preference for practical applications, with omission of a detailed presentation of the theoretical fundamentals and the omission of—also important—methods of investigation in which slow electrons do not take part (*e.g.* SIMS, ion back-scattering, RHEED). The latter is a disadvantage.

The main emphasis of the book is in the 60 pages that make up Chapter 9 (Low-Energy Electron Diffraction = LEED). This is preceded by chapters on the methods that are usually termed "supplementary techniques", among which Chapter 2 concerning the important topic of Auger electron spectroscopy occupies the largest space (33 pages). Secondary-electron, photoelectron, and X-ray excitation spectroscopy (APS) and the problems of the work function are treated more tersely. Field-emission and ion-neutralization spectroscopy, and also phonon effects on surfaces, are treated only very briefly,

Chapter 11 (the last) which deals, unfortunately rather too shortly, with the application of methods previously discussed to problems of adsorption is particularly impressive. This makes it clear that only a suitable combination of many different techniques, if possible in the same UHV apparatus, is at present able to provide tenable statements about adsorption processes on crystal surfaces. One gets the impression that some of the individual problems discussed in Chapter 11 should have been treated in more detail in special chapters. On the other hand, the brief presentation is advantageous for an introductory text, and the interested reader can find more detailed information in the extensive literature references.

K. Molière [NB 259 IE]

Natural Products Chemistry. Vol. 1. Edited by *K. Nakanishi, T. Goto, S. Itô, S. Natori*, and *S. Nozoe*. Kodansha Ltd., Tokyo/Academic Press, Inc. New York—London 1974. 1st Edit., 562 pp., bound $ 32.50.

The chemistry of natural products has undergone a renaissance in recent years, though unfortunately not in Germany. The intention of the well known Japanese publishers was that this, the first of two volumes planned to cover natural products chemistry, should fill a gap between textbooks of organic chemistry and special presentations of more restricted fields of natural products chemistry. The introductory chapters on the classification of natural products and on physicochemical data are followed by four chapters on mono- and sesquiterpenes, diterpenes, sester-, tri-, and higher terpenoids, and steroids. The emphasis of the presentation is on a wealth of clearly arranged formulas that permit rapid orientation in the subject. The brief accompanying text contains information on structure elucidation, syntheses, reactions, and biosynthesis as well as data on origin and physiological action. In respect of biosynthesis, however, little is included about work on the enzymic aspects. Physicochemical data are given for each compound including the position of the most important proton-resonance peaks.

The book contains an enormous amount of information, special consideration being given to the newer literature up to 1973. Classical work on structure determination is reported only in the steroid chapter. This textbook could be a most valuable source of information to the natural products chemist, but it is also suitable for the preparation of lectures to students and symposia, since the structural formulas are so arranged that they can be used directly for the preparation of diapositives. Furthermore, the chemist active in other fields can certainly be stimulated by the many synthetic methods illustrated. The second volume is awaited impatiently, but it is not too early to wish the book a wide readership.

Hans Grisebach [NB 272 IE]

Recent Analytical Developments in the Petroleum Industry. Edited by *D. R. Hodges*. Applied Science Publishers Ltd., Barking 1974. 1st Edit., IX, 337 pp., 109 figs., 56 tables, bound, £ 10.—.

This volume contains the text of lectures given at a symposium organized by the Institute of Petroleum in London, together with the relevant discussions. There are 19 contributions, opened by *A. S. Curry* who reports on the progress in analytical chemistry during the last 10—20 years. Subsequent chapters of the book are devoted to special methods of analysis of hydrocarbons and additives; each of these chapters gives a critical review and a comparison with similar methods and marks out the limits and possibilities; critical remarks at the discussions, often kept very short, round off each theme.

J. P. Coates compares the possibilities of IR spectroscopy and laster Raman spectroscopy. The section by *D. E. Hillman, T. J. Paul*, and *D. G. Cobbold* is devoted to the determination of corrosion inhibitor Hitec E 515 in aircraft fuel by gel

permeation chromatography. *E. R. Allard* and *P. H. D. Matthews* describe selective detectors for the determination of organically bound nitrogen by gas chromatography. *Coulson*'s conductometric detector is shown to be particularly useful; its selectivity for nitrogenous compounds is 10^6:1 against hydrocarbons; and sulfur-, chlorine- and phosphorus-containing compounds do not interfere. *N. G. MacTaggart* and *P. Glaysher* show how boiling curves for curde petroleums can be determined by gas chromatography; the need for internal standards to provide accurate results is particularly emphasized.

The next chapter is devoted to the determination of additives in the usual machine oils by thin-layer chromatography and densitometry. *A. J. W. Brook*, *J. E. Davies*, and *B. M. J. King* give experimental directions for various types of additives (sulfonate, phosphate, and esters of organic acids). *C. B. Grump* and *A. Lynes* outline the application of ion-exchange resins to the analysis of petroleum products; particular attention is directed at combination of anionic and cationic exchangers and the possibilities of determination by means of liquid chromatography. *K. Marron* then described the determination of the proportion of saturated hydrocarbons in Ellesmere-Port oil after separation on silica gel from the refractive indices of the fractions; the contents of aromatics are determined by UV spectroscopy and taken into account as corrections. *W. R. McLean* describes a microwave plasma detector that allows the elemental composition of gaschromatographically obtained fractions to be assessed by spectroscopy. The chapter by *F. A. Killer* contains a method for microcoulometric determination of sulfur in "sub"-ppm amounts. *J. F. P. Lush* reports the possible applications of atomic absorption to the determination of trace elements in the petroleum industry. Possible applications of X-ray fluorescence spectroscopy are described by *E. W. Williams*.

A BP-ARL-Solfa monitor for the determination of the total sulfur content of petroleum fractions and residual oils by means of a non-dispersive X-ray fluorescence method is described by *C. F. Gamage* and *W. H. Topham*; the reproducibility between two measurements with this apparatus is 0.02%, and the long-term accuracy is 0.03 to 0.05% for sulfur contents between 1.0 and 5.0%. Classification of mass spectra by statistical methods is the concern of *A. G. Baker*, *M. Camp*, *E. Huntington*, *W. T. Pike*, and *M. A. Shaw*. *G. B. Levy* and *D. M. Seltzer* describe a method for coulometric determination of moisture, and *R. W. Hooks* describes the determination of the total basicity number (mg of KOH, which are equivalent to the amount of mineral acid neutralized by 1 g of the oil); the latter author proposes addition of filtration through cellulose acetate filters of defined porosity for titration by perchloric acid in acetic acid (IP 276) when dealing with oils containing oil-insoluble residues. *A. G. Butlin* and *A. Lynes* describe the characterization of dialkyl dithiophosphates; after fission of the zinc dialkyl dithiophosphate by hydrogen iodide the dialkyl sulfides and the alkyl iodides are determined by gas chromatography. Trace analysis of vanadium down to the ppB region is discussed by *J. N. Wilson* and *C. Z. Marczewski*; the vanadium is obtained for spectrophotometry as a ternary complex with PAR-sephiramine (pyridyl-*azo*-resorcinol, zephiramin = -benzyldimethyltetradecylammonium chloride). A rapid method for spectrophotometric determination of phosphorus in lubricating oils is described by *S. T. Holding* and *J. Rowson*.

The contributions can be recommended as useful for specialist in the analysis of petroleum products. It would have been useful to have a section of individual and group analyses and a critical consideration of the data obtained by these analyses and their industrial applications.

Hermann Kienitz [NB 269 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Handbook of Naturally Occurring Compounds, Vol. 1: Acetogenins, Shikimates, and Carbohydrates. By *T. K. Devon* and *A. I. Scott*. Academic Press, New York 1975. XI, 644 pp., bound, $ 32.00.

The World of Quantum Chemistry. Proceedings of the First International Congress of Quantum Chemistry, Menton/France 1973. Edited by *R. Daudel* and *B. Pullman*. D. Reidel Publishing Co., Dordrecht 1974. XIV, 316 pp., bound, Dfl. 100.—

Molecular and Quantum Pharmacology. Edited by *E. D. Bergmann* and *B. Pullman*. Vol. 7 of the series "The Jerusalem Symposia on Quantum Chemistry and Biochemistry". D. Reidel Publishing Co., Dordrecht 1974. VII, 591 pp., bound, Dfl. 135.—

Proteinase Inhibitors. Proceedings of the 2nd International Research Conference on Proteinase Inhibitors held at Grosse Ledder bei Köln, 16.—20. October 1973. Edited by *H. Fritz*, *H. Tschesche*, *L. J. Green*, and *E. Truscheit*. Bayer-Symposium V. Springer-Verlag, Berlin 1974. XVI, 751 pp., bound, DM 128.—.

Ionic Diffusion in Oxide Glasses. By *G. H. Frischat*. From the series "Diffusion and Defect Monograph Series". Edited by *Y. Adda*, *A. D. LeClaire*, *L. M. Slifkin*, and *F. H. Wöhlbier*. Trans Tech Publications, Clausthal 1975. 200 pp., bound, $ 17.50.

Technische Chemie. Eine Einführung in die Chemische Reaktionstechnik. By *E. Fitzer* and *W. Fritz*. Springer-Verlag, Berlin 1975. XIII, 552 pp., stitched, DM 44.—

Silicate Science. Vol. VI: Silicate Structure and Dispersoid Systems. By *W. Eitel*. Academic Press, New York 1975. XVIII, 819 pp., bound, $ 59.50.

Gas-Phase Electron Diffraction. By *A. Haaland*, *L. Vilkow*, *L. S. Khaikin*, *A. Yokozeki*, and *S. H. Bauer*. Vol. 53 of the series "Topics in Current Chemistry—Fortschritte der chemischen Forschung". Edited by *F. Boschke*. Springer-Verlag, Berlin 1975. IV, 119 pp., bound, DM 42.—

Triplet States I. By *A. Devaquet*, *W. G. Dauben*, *G. Lodder*, *J. Ipaktschi*, *A. H. Maki*, and *J. A. Zuclich*. Vol. 54 of the series "Topics in Current Chemistry—Fortschritte der chemischen Forschung". Edited by *F. Boschke*. Springer-Verlag, Berlin 1975. IV, 163 pp., bound, DM 68.

Vergleichende Anatomie der Wirbeltiere. By *M. von Dehn*. Vol. 30 of the series "taschentext". Verlag Chemie/Physik Verlag, Weinheim 1975. VIII, 197 pp., stitched, DM 28.80

Handbook of Metal Ligand Heats and Related Thermodynamic Quantities. By *J. J. Christensen*, *D. J. Eatough*, and *R. M. Izatt*. Marcel Dekker Inc., New York 1975. 2. improved and enlarged edit., VII, 495 pp., bound, $ 25.00.

Low-Dimensional Cooperative Phenomena. The Possibility of High-Temperature Superconductivity. Edited by *H. J. Keller*. From Series B (Physics) of the series "Nato Advanced Study Series" of the NATO Scientific Affairs Division. Plenum Press, New York 1975. VIII, 350 pp., bound, $ 30.10.

Chemical and Biochemical Reactivity. Proceedings of an International Symposium held in Jerusalem, 9.—13. April 1973. Edited by *E. D. Bergmann*. Vol. VI of the series "The Jerusalem Symposia on Quantum Chemistry and Biochemistry". The Israel Academy of Sciences and Humanities, Jerusalem 1974. VIII, 578 pp., bound, $ 39.00.

Gmelins Handbuch der Anorganischen Chemie. System Nr. 46: Zinn. Part C 3: Verbindungen mit Alkali- und Erdalkalimetallen. Springer-Verlag, Heidelberg 1975. VIII, XX, 206 pp., bound, DM 361.—.

Membranes in Separations. By *S.-T. Hwang* and *K. Kammermeyer*. Vol. 7 of the series "Techniques of Chemistry". Edited by *A. Weissberger*. John Wiley & Sons, London 1975. XXII, 558 pp., bound, £ 17.50.

Handbook of Reactive Chemical Hazards. By *L. Bretherick*. Butterworths, London 1975. XX, 976 pp., bound, £ 20.00.

Colloque International sur l'Analyse par Activation de Tres Faibles Quantites d'Elements—International Colloquium on Activation Analysis of Very Low Amounts of Elements (2.—6. October 1972 at C.E.N. Saclay/France). Akadémiai Kiadó, Budapest 1975. VIII, 390 pp., bound, DM 216.80.

Quantum Mechanics for Organic Chemists. By *H. E. Zimmermann*. Academic Press, New York 1975. X, 215 pp., bound, $ 16.50.

Dynamic Nuclear Magnetic Resonance Spectroscopy. Edited by *L. M. Jackman* and *F. A. Cotton*. Academic Press, New York 1975. XIV, 660 pp., bound, $ 48.00.

Foundations of Ultra-Centrifugal Analysis. By *H. Fujita*. Vol. 42 of the series "Chemical Analysis". Edited by *P. J. Elving* and *J. D. Winefordner*. John Wiley & Sons, New York 1975. XVIII, 459 pp., bound, £ 11.40.

Carbenes, Vol. II. Edited by *R. A. Moss* and *M. Jones, Jr.* From the series "Reactive Intermediates in Organic Chemistry". Edited by *G. A. Olah*. John Wiley & Sons, New York 1975. XIII, 373 pp., bound, £ 12.00.

The Infrared Spectra of Complex Molecules, Vol. 1. By *L. J. Bellamy*. Chapman and Hall, London 1973. 3rd Edit. XIX, 433 pp., bound, £ 8.00.

Einführung in die Physikalische Chemie. By *H. Labhart*. From the series "Hochschultext". Springer-Verlag, Berlin 1975. Teil 1: Chemische Thermodynamik. XII, 167 pp., stitched, DM 16.—; Teil 3: Molekülstatistik. XI, 126 pp., stitched, DM 14.—; Teil 4: Molekülbau. X, 171 pp., stitched, DM 16.—; Teil 5: Molekülspektroskopie. X, 138 pp., stitched, DM 14.—.

Handbook of Organosilicon Compounds. Advances since 1961. Vol. 1. Edited by *V. Bazant, M. Horak, V. Chvalovsky*, and *J. Schraml*. Marcel Dekker, Inc., New York 1975. 761 pp., bound, $ 75.00.

Explosivstoffe. By *R. Meyer*. Verlag Chemie, Weinheim 1975. 4th improved Edit., 327 pp., stitched, DM 66.—

Comparative Biochemistry, Molecular Evolution (Continued). Vol. 29. Part B of the series "Comprehensive Biochemistry". Edited by *M. Florkin* and *E. H. Stotz*. Elsevier Publishing Company, Amsterdam 1975. XII, 284 pp., bound, Dfl. 75.00.

Vom Wasser, Band 44. Published by "Die Fachgruppe Wasserchemie in der Gesellschaft Deutscher Chemiker". Responsible for text: *W. Husmann*. Verlag Chemie, Weinheim 1975. 323, A 94 pp., bound, DM 88.—.

Mathematik für Naturwissenschaftler und Ingenieure. Band 2: Lineare Algebra, Vektoranalysis, Differentialgleichungen. By *A. Jeffrey*. Verlag Chemie Weinheim 1975. VIII, 378 pp., stitched, DM 39.—

Supplements to the 2nd Edition of Rodd's Chemistry of Carbon Compounds. Edited by *M. F. Ansell*. Supplement to Vol. 1: Aliphatic Compounds. Part A: Hydrocarbons, Halogen Derivatives; Part B: Monohydric Alcohols, their Ethers and Esters, Sulphur Analogues, Nitrogen Derivatives, Organometallic Compounds. Elsevier Scientific Publishing Company, Amsterdam 1975. XVI, 268 pp., bound, Dfl. 110.00.

Handbook of Enzyme Biotechnology. Edited by *A. Wiseman*. Ellis Horwood Ltd., Chichester/Halsted Press, a Division of John Wiley & Sons, New York 1975. XII, 275 pp., bound, £ 15.00.

Advances in Chromatography, Vol. 12. Edited by *J. C. Giddings, E. Grushka, R. A. Keller*, and *J. Cazes*. Marcel Dekker, Inc., New York 1975 XIV, 278 pp., bound, $ 22.75.

International Review of Science. Inorganic Chemistry Series Two. Vol. 10: Solid State Chemistry. Consultant Editor: *H. J. Emeléus*. Volume Editor: *L. E. J. Roberts*. Butterworths, London/University Park Press, Baltimore 1975. 264 pp., bound, £ 13.45.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. - Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form - by photoprint, microfilm, or any other means - nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 14036. Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and 24 28 Oval Road, London NW1, England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim, Pappelallee 3, P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 8
August 1975
Pages 507 – 580

Organic Compounds in Nature: Limits of Our Knowledge[**]

By Max Blumer[*]

Current geochemical and environmental research reveals the presence in soils and sediments of extremely complex assemblages of organic compounds. Their recognition has long been delayed by both conceptual and analytical limitations. Even today the best techniques cannot fully resolve these mixtures into their individual components. Yet, the knowledge of their structures and abundances is needed in geochemistry, and especially for the assessment of their potential biological effect and ecological impact. The classical "natural products approach" is unlikely to provide this information; therefore, I foresee the need for a more realistic assessment of nature, that acknowledges the limitations of our present analytical powers and of our knowledge.

What we have learnt, is like
a handful of Earth,
While what we have yet to learn
is like the whole World.[1]

1. Organic Geochemistry and Environmental Chemistry, Two Parallel Research Areas

The existence of organic compounds within the lithosphere has long been recognized because of their unusual properties, for instance the inflammability of coal and the semiliquid or liquid nature of earthwax, petroleum, and asphalt. However, the scientific study of the origin, effect, and fate of carbon compounds in nature is relatively recent. It is being pursued principally in two related interdisciplinary sciences, organic geochemistry and environmental chemistry. Both are in the midst of rapid growth, but in spite of their close relationship they have remained relatively isolated. I believe that both areas could gain from a better exchange of information, and that an appreciation of the staggering complexity of geochemistry might help environmental chemists and biologists to assess the limits of our present capability to analyze and understand nature.

Organic geochemistry attempts to understand in terms of chemical, physical, and biological processes the formation, composition, and destruction of organic compounds in nature and their interaction with the environment during geologic time spans. It is older than environmental chemistry and traces its origin to the discovery by *Treibs*[2] of anthraquinone pigments and of chlorophyll and hemin derivatives in ancient sediments. These discoveries have provided the stimulus for the search for other fossil biochemicals. Many have now been found, some apparently unaltered but most modified by chemical and physical processes in the subsurface.

The main goal of *environmental organic chemistry* is similar: to understand the origin, composition, and fate in today's environment, especially of those organic compounds that affect living organisms, and particularly man in his best use of natural resources. Most of the activity in this field has followed the discovery of the environmental effects and of the transmission in the food web of synthetic organics, and also the growing awareness of fossil fuels as environmental pollutants. Many

[*] Dr. M. Blumer
Woods Hole Oceanographic Institution
Woods Hole, Massachusetts 02543 (USA)

[**] Woods Hole Oceanographic Institution Contribution Number 3443.

of the discoveries have been accidental, in response to unanticipated environmental problems, such as those caused by DDT, the chlorinated biphenyls, alkylmetal compounds, chlorinated olefins, *etc.*

Table 1. Geochemistry and environmental chemistry of organic compounds.

Areas of inquiry	Scope and time scale	
	Geochemistry	Environmental chemistry
Sources	biochemical and geochemical	synthetic and fossil
Composition	wide molecular weight and compositional range	molecular weight *ca.* 100—300, mainly C, H, halogen, metal
Interaction	all parts of environment	biosphere, foodweb, man
Transformation	long term; slow reactions	short term; fast reactions
Fate	10^8 years and longer	decades

The scope of organic geochemistry and that of environmental chemistry overlap (Table 1). The former field is more comprehensive in its study of the sources, compositional range, and environmental interaction of organic compounds, and it deals principally with the slow transformation over geologic time spans of natural carbon compounds. Conversely, within its more limited scope, environmental chemistry concentrates on the early environmental history of organic compounds, especially of synthetics, and on their interaction with the biota.

These differences in emphasis also describe areas of potential interaction. For instance, hydrocarbon geochemistry with its background of composition, persistence, and degradation of petroleum hydrocarbons in nature, should be meaningful to the environmental chemist; on the other hand, the relatively rapid reactions of some organics in the recent environment may provide the geochemist with knowledge on the early events of chemical transformations in nature.

Yet, the two areas have more in common: both deal with similar samples and methods of analysis, and both with similar contamination problems and analytical interferences. Recent environmental samples commonly contain fossil chemicals, while samples for geochemical analysis appear increasingly contaminated with synthetic organics, *e.g.* polychlorinated biphenyls and plasticizers.

The present article reviews some fundamental aspects of organic geochemistry, emphasizing its complexity and the interaction between the growth of analytical methodology and our insight into nature; this should then point to gaps in our present knowledge and in our ability to anticipate the environmental effect of organic chemicals.

Why not inventory the gaps
in our factual knowledge
and general understanding
in every field?[3]

2. Principles and Status of Organic Geochemistry

Organic geochemistry deals with the slow conversion of biochemical products at relatively low temperatures during geologic time spans into fossil compounds and eventually to graphite ("diagenesis", Table 2). Most of the starting materials have been formed through biosynthesis with the input of solar energy. They have a high energy content and a low thermodynamic stability, and they are protected from rapid structural degradation by the characteristic metastability of carbon compounds. Out of the very large number of possible structures, selective enzymatic processes in living organisms have chosen only a limited number. The typical repetitive building pattern (*e.g.* of the isoprenoids) permits the recognition of biochemical origin even in fossil compounds after considerable geochemical scrambling.

Table 2. Organic geochemistry: biochemicals on their way to graphite.

	Biosynthesis	Diagenesis	Graphite
Energy balance	solar input	release, cycling	end of release
Energy content	high	intermediate	low
Thermodynamic stability	low	intermediate	high
Metastability	high	low	—
Reactivity	intermediate	high	low
Structural order	high	low	high
Complexity	moderate	extreme	low
Information content	high	extreme	low
State of knowledge	excellent	poor	excellent

During thermodynamic stabilization by diagenesis, the biochemicals lose some of their excess energy. These processes start with the deposition of the organic material and terminate eventually with the formation of the highly ordered and stable structure of graphite. However, diagenesis is not a monotonous process. Inter- and intra-molecular disproportionation reactions may form temporarily less stable compounds while the overall stabilization of the entire system takes place.

The most characteristic feature of organic diagenesis, and the most important one in the context of this discussion, is the appearance of extreme structural complexity and disorder at an intermediate stage, interposed between the high degree of biochemical order in the starting material and the even greater crystallographic order in graphite, the end product of diagenesis.

Yet, in spite of the formation of a wide array of products from the relatively small number of precursors, diagenetic products are not completely randomized. Petroleum, for instance, is not a random mixture of hydrocarbons. This is important both in geochemistry and in environmental sciences. The study of a random mixture would be far less challenging, and since the relative abundance of the components would be predictable and constant, the environmental effect could be more readily anticipated.

Our understanding of the principles of organic geochemistry is adequate for many applications, for instance in the exploration for fossil fuels. We know the sources of carbon compounds and recognize the driving forces and the trends in their diagenetic transformation, and their ultimate fate. On a more detailed molecular and mechanistic level we are far less knowledgeable, uncertain even of the degree of chemical transformation in the subsurface, limited in our compositional assessment of the chemicals in nature, and virtually ignorant of the specific mechanisms and rates of the diagenetic transformation reactions[4].

The reason why we have not yet penetrated more deeply into the detailed understanding of organic geochemistry lies in its very complexity and in the difficulty of resolving complex organic mixtures analytically. In view of the importance of geochemical products in today's environment I wish to discuss further the question of their compositional complexity.

"Information explosion" is a
well recognized phrase ...
but all viable theories have
led to an ignorance explosion.[3]

3. How Complex is the Organic Chemistry of Nature?

Natural products chemistry has achieved great triumphs with the isolation and structural elucidation of the principal organic building blocks of living organisms. Similarly, the discovery in geologic specimens of fossil biochemicals has contributed much to the growth of organic geochemistry. The importance of these findings may have suggested that we are now close to an understanding of the origin and composition of most organic compounds in nature. Yet there is much evidence that this is not so, especially with regard to the ubiquitous organic background in water, soils, and sediments. These contain numerous organic compounds that exhibit no readily apparent structural relationship to biochemicals, and range from low molecular weight gases to complex polymers, and from non-polar hydrocarbons to multifunctional and polar compounds. The study of these materials has in the past seemed less important than the search for specific compounds of demonstrable biochemical origin. However, with the increased resolution of newer analytical techniques, we now recognize more and more often in environmental samples such complex mixtures.

3.1. Petroleum

Of course, it is well established and accepted that petroleum is complex and contains a staggering array of parallel and overlapping homologous series of hydrocarbons and of sulfur-, nitrogen-, oxygen-, and metal compounds, few of them bearing obvious resemblances to their biochemical ancestors. Though gas chromatography resolves the lowest boiling hydrocarbons of petroleum, no complete resolution has yet been accomplished for the higher boiling components of any crude oil. Even with the best analytical tools, *Coleman et al.*[5] demonstrated in high boiling petroleum distillates a complexity that far exceeds the resolving power of their analytical techniques. Consequently, the characterization is still limited to a description of the molecular weight distribution within the overlapping homologous series, without resolution of the many isomers, and without measurement of the abundance of individual components.

The hydrocarbon mixtures in ancient sediments and oil shales appear even more complex, though they have been less thoroughly studied. In addition, sediments contain a wider range of polymers, with structures that overlap the lower molecular weight hydrocarbons and non-hydrocarbons; these are still unresolved and structurally nearly unexplored.

Is this well established compositional complexity of fossil hydrocarbons unique, or is it approached or even surpassed in other classes of environmental carbon compounds? Increasing evidence suggests that the fossil hydrocarbons are not unique in their complexity. The introduction of functional groups into the hydrocarbon molecule makes possible additional structural permutations, and many of these may be realized in nature. That these have not generally been recognized may be ascribed principally to the insufficient resolving power of our analytical methods.

3.2. Porphyrins

An interesting example is found in the fossil porphyrins. *Treibs* and other investigators used in their initial analyses classical organic techniques: crystallization, column chromatography, and visible spectrophotometry. The analyses appeared to demonstrate the presence of a few easily anticipated and explainable components that were thought to have been recovered in pure form (Fig. 1). The same techniques continued to be used during three decades after the discovery, and the number of recognized fossil pigments increased only slowly until the mid-1960's. This slow growth was not due

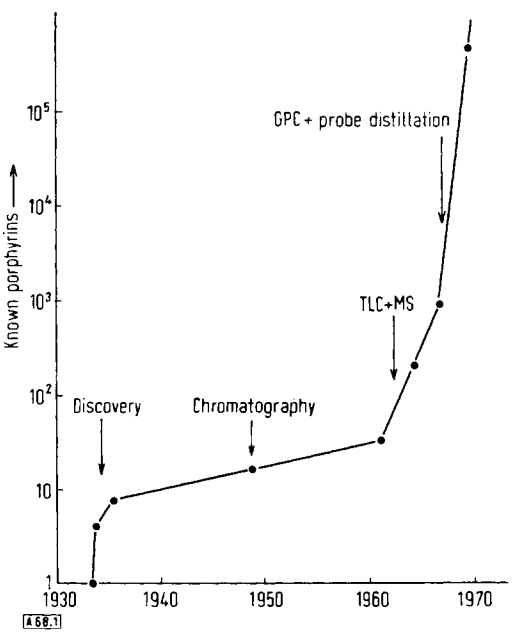


Fig. 1. *Treibs'* discovery of fossil chlorophyll derivatives marks the beginning of organic geochemistry [2]. After the discovery, limitations in analytical resolution prevented during three decades the recognition of the compositional complexity of these pigments—and of the intensity of the geochemical processes which shape them.

to a lack of activity in this field, but primarily to a limitation in the resolving power of the methods which were used. In fact, during that period intense research was pursued by acade-

mic and industrial laboratories, since the fossil porphyrins were thought to offer promise for crude oil and sediment correlation and for other geochemical studies. Ironically, some laboratories abandoned as unproductive the effort in this area just before new separating methods finally demonstrated the great complexity and, therefore, the great geochemical information content of these fossil pigments.

For someone who worked in this field at that time, it is humbling to think of the tens of thousands of pigments which he handled daily, but to whose existence he was totally oblivious! This is an example of "pure ignorance"[3], "the ignorance of which we are not yet even aware".

The combination of new separating methods, thin layer chromatography and gel filtration, and of new methods of final analysis—especially mass spectrometry and probe distillation—in joint application, eventually demonstrated the existence of numerous extended and overlapping homologous and isomeric series, with individual compounds probably numbering in the 10^5 range, even in a single sediment[6]. As in petroleum chemistry, little hope remains now in this area that we will isolate many pure compounds, except possibly at their lowest molecular weights; even if this becomes possible we will no longer attribute as much significance to the exact structural knowledge of a few selected compounds as we would have in the past.

3.3. Carboxylic Acids

Fossil carboxylic acids are another class of environmental organic compounds that may rival the hydrocarbons in their compositional complexity[7]. Some years ago I was involved in a cooperative study with Professor *Eglinton* and his coworkers of the fatty acids in some oil shales[8]. We searched specifically for possible iso- and anteiso acids and isoprenoid acids, in addition to the known straight chain acids. Characteristically, those acids whose presence we anticipated were discovered. How difficult it is to penetrate into the "pure ignorance" is demonstrated by our statement, relating to evidence for several series of unanticipated acids, that "extended speculation cannot be justified at this time"! Also, it appears now much more significant to us, that our analyses on packed gas chromatograph columns revealed exactly as many compounds as these columns were theoretically capable of resolving (five acids per C-number)! This demonstrated presence of unanticipated compounds, and the further suggestion from gas chromatography of additional unresolved components should have led us to a more thorough search, with additional techniques, for the structures of the unanticipated acids; such an extension of this study might well have yielded a more comprehensive and geochemically more realistic interpretation.

The understanding of environmental organic chemistry and of the processes of formation, transformation, and destruction of the organic compounds hinges on the recognition of the full compositional complexity, which may be a common feature of fossil compounds. So far this may have been primarily the concern of geochemists. However, since fossil compounds enter today's world through weathering and spillage, they also become increasingly the concern of environmental chemists and biologists. But, long term geochemical processes may not be the only source of complex organic series in the present environment.

3.4. Polycyclic Aromatic Hydrocarbons

Our work on polycyclic aromatic hydrocarbons (PAH)[9] in soils and young sediments suggests that complex hydrocarbon mixtures may be formed presently; these are as difficult to resolve with present analytical techniques as their fossil analogs. The realization of the complexity of the PAH mixture has developed over a long time period—in surprising agreement with the historical development in the porphyrin field (Fig. 2).

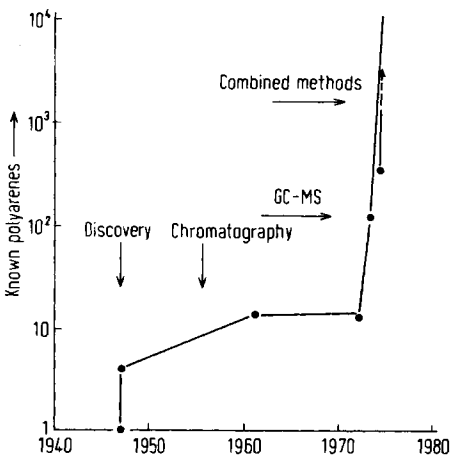


Fig. 2. Our insight into the composition of environmental polycyclic aromatic hydrocarbons has been held back by inadequate methodology. During more than two decades after *Kern*'s discovery [10] we remained oblivious to the existence of extended and overlapping homologous series of these hydrocarbons and their cycloalkyl- and sulfur analogs.

After *Kern*[10] discovered chrysene in soil, he was immediately led to the recognition of several other aromatic compounds. The marked biological activity of some polycyclic hydrocarbons consequently justified numerous additional research efforts in this area. Again, the classical methods of analysis yielded only limited insight into the number of compounds that are actually present in the environment; and, again we handled daily sediment extracts that contained hundreds or thousands of substituted polycyclic aromatic hydrocarbons, to whose existence we were totally oblivious! More than two decades elapsed after the discovery, until new techniques (thin layer-, gel permeation- and gas chromatography, mass spectrometry, and probe distillation) provided greater resolution and revealed those unanticipated hydrocarbons.

In each of the above four areas of natural organic chemistry, recent analytical progress, especially the combination of independent techniques, has improved our analytical resolution by several orders of magnitude. In each case the boundary of the unknown receeded rapidly, while we thought we were approaching it. In each of these areas a full compositional analysis is still lacking and appears to lie beyond the present state of the analytical art. These are not likely to be isolated examples. The relationship between existing analytical limitations and our insight into the complexity of nature (Fig. 1 and 2) may be typical of the situation in other rapidly growing areas of observational sciences.

3.5. Synthetic Organic Compounds in the Environment

All of the compounds discussed so far are the products of natural organic processes. However, within the last decades

increasing amounts of synthetic organic compounds have appeared in the environment. How simple or how complex is their composition?

Many organic syntheses yield, in addition to the desired product, considerable quantities of waste materials. The proverbial "black tar" of the synthetic laboratory exemplifies these structurally unexplored by-products, which may span a wide range of functionalities, reactivities, and molecular sizes. Other synthetic processes, especially in petrochemistry, are relatively clean; but even there the products may be accompanied by lesser concentrations of complex and undesired by-products. Such wastes and by-products enter the environment through disposal or through dispersal by the normal use of the principal products. They may be recognized only when they present unanticipated environmental problems. With their often inherent complexity, and especially after their dilution and mixing with other environmental chemicals, these synthetics may pose problems for environmental analysis that are just as severe as those with geochemical products.

The analysis of environmental samples serves different purposes, such as industrial applications, geochemical research, environmental studies or ecological investigations. The time required for an analysis and, therefore, its costs, depends on the magnitude of the effort. If we accept that nature is so complex that a complete analysis is presently impossible, we need to ask how thorough an analysis must be, and how extensive our understanding of nature, so we can avoid pitfalls in the interpretation of the analyses.

It seems likely
that our ignorance
is as great as it ever was.[3]

4. Do We Need to Understand the Chemical Complexity of Nature?

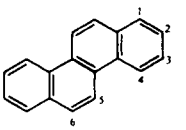
Just as the applications of environmental analyses vary, so does the need for analytical resolution. Industrial chemistry, insofar as it deals with the destruction or gross rearrangement of chemical fine structures, *e.g.* in petroleum refining, requires only a relatively coarse knowledge of compositional detail. The situation in geochemistry is different; without an adequate understanding of the complexity of fossil organic compounds we may attain only a limited insight into the complexity of natural processes. This is clearly illustrated by the history of porphyrin geochemistry: inadequate analytical resolution has held back during several decades the recognition of the intensity of the geochemical processes which modify the structures of these pigments.

Yet, in spite of the need for more detailed structural analyses, geochemists may only occasionally require a comprehensive study of all components of a geochemical sample; and much more important than the determination of a few selected compounds is the thorough understanding of geochemicals in terms of their principal structural features, their molecular weight range, and the general distribution patterns within homologous series. These are among the principal features which have been shaped by and which reflect geochemical processes. Even with such partial analyses and with techniques that are inadequate for the complete resolution of complex mixtures into individual compounds, geochemists have made important contributions to pure and applied (*e.g.* exploration) science. In fact, as has been pointed out[11], some fundamental geochemical questions may still be amenable to relatively simple analytical work.

An even higher level of structural insight into the composition of complex organic mixtures is required in environmental chemistry and biology. The biological effects of chemicals are immediately related to their chemical fine structures, in a fashion that is still not generally understood, in spite of intensive pharmacological research. Therefore, all components of a natural organic mixture should be known before its biological impact can be fully anticipated. Even if such a detailed analysis were possible, the interpretation hinges on the recognition of any synergistic and antagonistic effects and on the availability of all components in the pure state for bioassays, with all their shortcomings.

This critical dependence of biological activity on chemical fine structure is illustrated by *Hoffman et al.*[12]. These authors assayed the carcinogenicity of pure chrysene and of its six isomeric methyl derivatives (Table 3). While unsubstituted chrysene is at most a weak carcinogen and the other five methyl isomers are inactive by themselves, 5-methylchrysene is a powerful carcinogen. The same compound, as well as the isomeric 3-methylchrysene is a strong tumor initiator, if it is applied simultaneously with a tumor promotor, which is inactive by itself.

Table 3. Carcinogenicity of chrysene and its methyl derivatives [12].



	Chrysene	Methylchrysenes 1-Me	2-Me	3-Me	4-Me	5-Me	6-Me
Carcinogen	?	–	–	–	–	++	–
Initiator [a]	+	+	+	++	+	++	+

[a] Effective only when applied simultaneously with a tumor promotor.

Question: A staggering array of other alkylated chrysenes (and other aromatics) occur in recent and ancient sediments and in petroleum [9, 13]. How can we assess their biological effects, alone and in complex mixtures?

At a higher degree of alkyl-substitution, many additional isomeric compounds become formally possible, and many of these may occur in fossil fuels[5] and in soils and recent sediments[9, 13] together with chrysene and methylchrysenes. Their fine molecular detail is unexplored and so is their biological activity; and few if any pure standard compounds are available for bioassays. Clearly, the environmental chemist and biologist cannot predict their physiological effect and ecological impact from the mere knowledge that such potentially active compounds exist in environmental samples, without having detailed insight into their abundance and structure.

Thus, this discussion suggests that environmental chemists and biologists require the most complete analysis and the most thorough understanding of the complexity of natural carbon compounds. In their need and attitude they are most remote from those chemists who are satisfied with a rather cursory understanding of nature. In considering, for instance, the effects of an oil spill, the latter would be most likely to think in terms of gross compositional parameters: volatility, solubility, content of sulfur, nitrogen, and trace metals, relative

hydrocarbon distribution between alkanes, naphthenes, and aromatics, *etc.* To the environmental chemist these terms are foreign and he requires—and is frustrated by the difficulty in obtaining—detailed structural information which he can interpret into an assessment of the biological impact. I now ask how well suited the present analytical art is to resolving the complexity of natural organic mixtures and to provide the insight that is needed to anticipate the biological effects of environmental chemicals.

We have heard the paeans
for our great capabilities
and the criticisms for these
at the same time.[3]

5. Is Present Analysis Adequate to Study the Complexity of Nature?

The art of analytical organic chemistry has advanced rapidly during the last decades. Compositional and structural analyses that would have been an adequate basis for entire doctoral theses are now carried out routinely within days, if not within hours. The phenomenal growth of gas chromatography has enabled us to recognize and often identify even minor components of complex mixtures. Mass spectrometry is still growing rapidly and appears to have great potential, especially in combination with gas- and liquid-chromatography, with automatic data processing and with newer ion sources that give a much finer control over the excitation process.

Most scientists and instrument manufacturers are enthusiastic about these tools and their research and sales potential. But now that we have obtained a glimpse of the staggering complexity of nature and understand the need for detailed structural information, we should again look at the adequacy of our methods and tools in terms of their resolving power (Table 4).

Table 4. Analytical resolution.

Method	Number of compounds resolved
Spectroscopy of crude mixtures	
ultraviolet	2—5
infrared	2—5
fluorescence	2—5
mass spectrometry	10—100
Separations	
countercurrent distribution	5—10
thin layer chromatography	5—10
distillation	10 and more
column chromatography, graded elution, including ion exchange	20 and more
high performance liquid chromatography	20 and more
gas chromatography (packed column)	100 (5/C number)
gas chromatography (capillary column)	1000 (50/C number)

Combined methods: In the ideal case, when each method responds to a different chemical or physical property of the molecules, the overall resolution approaches the product of all individual resolutions

It appears that, in general, the analysis of crude unresolved mixtures—even by the most selective spectral techniques—permits only the recognition of a limited number of components. Among these methods, mass spectrometry is the best, but it serves more readily the identification of compound classes than of their individual members. It performs well on samples or with excitation techniques that favor the molecular ion over the fragments, but at the same time this suppression of fragmentation deprives us of the structural information that is needed to recognize individual compounds. Mathematical analysis of the complex spectra obtained without the suppression of fragmentation is possible, but reaches its limits rapidly because of the lack of reproducibility in excitation and because of statistical scatter. Thus, even mass spectrometry can resolve at best a few tens of components in a complex mixture without previous sample fractionation, and this is rarely adequate in the analysis of environmental samples.

Considerably higher analytical resolution is attainable in multistep separations, especially in chromatography. As *Kovats*[14] has demonstrated so ably for the case of gas chromatography, such separating techniques also provide excellent insight into the structural features of the compounds undergoing separation. The highest resolution has been reached in capillary gas chromatography, which may resolve 10^3 compounds in a single run. Many chemists hold out hope that liquid chromatography will eventually equal gas chromatography or even surpass it in resolution, and that it will resolve samples that are not readily handled by gas chromatography.

In spite of the good resolution of chromatographic techniques, they are incapable of fully resolving the complex natural mixtures described here. Gas chromatography, which is ideally suited for the analysis of hydrocarbons because of their high volatility, low polarity, and modest reactivity, is inadequate even in the petroleum field. The number of components in an oil sample may exceed the admittedly high resolving power of gas chromatography by another factor of 10^3 or higher! In other words: a gas chromatogram of an oil may reveal to us fewer than one tenth of one percent of all components present in the sample! Other environmental samples which contain polar materials of higher molecular weights, cannot even be handled by gas chromatography, and no other single technique of similar efficiency is available for their resolution.

The recent rapid increase in our ability to recognize the true complexity of natural organic mixtures has resulted not from any single analytical technique, whose resolution is still limited, but from the introduction into geochemical and environmental research of analytical procedures that combine several principles of analysis. The highest resolution is obtained when the contributing methods respond to independent physical and chemical properties of the substances under investigation. Ideally, the resolving power of the combined effort then approaches the product of the individual resolutions.

The power of this approach is well illustrated by the analysis of high boiling crude oil distillates by *Coleman et al.*[15]. These authors have applied distillation, gel permeation, and adsorption chromatography, elemental analysis, and mass and NMR spectroscopy. Each of these techniques explores and responds to different structural features of the hydrocarbons and heterocompounds in petroleum; and in the final combination a far more thorough insight into the composition of crude oil is provided than would be possible even with capillary gas chromatography. Such a combination of techniques not only provides higher resolution but approaches it rapidly, and often with relatively simple individual steps. It is far less expensive than the extreme pursuit of high resolution with one single method.

It is significant that even the best combinations of analytical techniques, providing the highest degree of resolution, have

not yet separated into individual components any crude oil, or the porphyrins and acids of ancient sediments, or the aromatic hydrocarbons of the recent ones. Most environmental organics occur together with a complex background of biochemicals, geochemicals, and synthetics, and I have little hope that complete analysis in these cases is simpler than in the cases discussed. So far each new analytical advance appears to have revealed a greater complexity of nature and the "explosion of knowledge" has been paralleled by an equal "explosion of ignorance"[3]. This, of course, implies that we are presently often unable to provide environmental chemists and biologists with the detailed analyses which they require to understand the interaction of complex environmental chemicals with living organisms.

It might be helpful
to remind ourselves
of the sizeable incompleteness
of our understanding of nature
and the world around us.[3]

6. The Consequences

The recognition that organic geochemistry—and probably also the organic chemistry of the recent environment—is so extremely complex is relatively recent, even if petroleum has long been acknowledged as a very difficult analytical problem. Thus, in our study of the environment the natural products approach which has been so successful in biochemistry and, initially, also in geochemistry suddenly appears frustrated, probably not so much by principal limitations in our ability to separate and analyze, but by the sheer complexity of environmental chemicals, by the forbidding cost of a complete analysis, and by the limited resources of funding and trained manpower.

It appears now that important questions may go unanswered (*e.g.* "What are the structures of all alkylated chrysenes in recent sediments, and what is their biological impact?"), not because these questions are principally unanswerable, but because of the sheer number of equally important other questions and their complex interrelationships ("What are the structures of all alkylated benzanthracenes, benzothiophenes, benzopyrenes, *etc.* in the environment, what is their biological impact and what are the synergisms and antagonisms in the action, within this group, and with other environmental chemicals, *etc.*?").

At this point the research of the natural products chemist and that of the environmental- and geochemist diverges. Natural organic compounds in non-living systems are far too complex to yield to the demanding but slow approach of the former, and it is difficult to comply with his criteria for the acceptability of an investigation: purity of the isolated compounds and completeness of the physical and chemical description of every component. Even if this goal could be accomplished for one or a few components of a mixture, the significance would be less than it is in biochemistry, because we would neglect the existence and significance of a far larger number of compounds with equal information content.

A considerable fraction of the research effort in geochemistry is still tied to the natural products approach; similarly, much of the present environmental analysis, such as the search for specific pollutants, follows that same approach. I do not wish to imply that it is suddenly invalid to pursue such an effort; many of the resulting answers continue to be important. But we must not overlook that these answers may be far less comprehensive than we had thought before we came to appreciate the extreme complexity of the background of natural organic compounds in nature. In the strictest sense, because of the limited view of nature which it provides, the natural products approach may solve few of the fundamental problems of natural organic chemistry. We now need to look for a transition to a more realistic study of nature that acknowledges the limitations of our present analytical powers and the gaps in our understanding.

I will not speculate how rapidly this adjustment will come, what path it will take and what new concepts and tools we must develop to deal with the complexity of carbon compounds in nature and their interaction with organisms. However, in my research area, which straddles environmental and organic geochemistry, it appears important to strive for analyses that provide the greatest possible resolution and the most complete insight into all components of natural mixtures. In our work we must guard against bias, both in analysis and in the planning of experiments. We need to realize that our present knowledge of organic compounds in nature is very incomplete. The examples given—our limited understanding of petroleum, of porphyrins, of carboxylic acids, and of environmental carcinogens and mutagens—are only limited illustrations of our present ignorance. This ignorance has the most severe consequences where we attempt to assess or predict the biological impact of chemicals in nature. We must remain cautious in adopting tolerance levels, as long as our analyses are so incomplete, and we should suggest and demand safety factors that are adequate to protect against the unanticipated effects of yet unsuspected biologically active compounds in the environment.

Chemists are now often asked to make baseline measurements, for instance of organic compounds in the sea. Presumably, later analyses with the same standardized (but frozen) methods would then reveal changes in the environmental chemistry. Yet, when that time arrives, we may realize that our ignorance had prevented both a meaningful definition of the problem and the selection of the best methods. Therefore, the overemphasis of such programs over flexible exploratory research bears the danger of hindering, rather than aiding our eventual understanding of nature and of its changing processes.

Most major discoveries in organic geochemistry have been accidental, and most of the severe problems of environmental toxicology have been unanticipated. In view of this, it is distressing to know that scientists still advise policy-makers that "environmental (chemical) research is pure development and can be planned" and that it "should be aimed at the practical and immediately useful"[15]. I hope that the insight into natural organic processes and into the complexity of natural organic compounds, which has grown out of geochemical research, will protect us from the potentially disastrous overestimation of our present analytical and conceptual powers—and that it will remind us of the continuing existence of "pure" ignorance.

The Office of Naval Research and the National Science Foundation have enabled me over many years to look into aspects of oceanography, geochemistry, and environmental science that

may have seemed unconnected. I hope that jointly these efforts may help us to appreciate the complexity of nature, and express my gratitude for the freedom in the support of my work. Present funding: ONR Contract NOOO14-74-C-0262 and NSF Grant DES74-22781.

Received: October 7, 1974 [A 68 IE]
German version: Angew. Chem. *87*, 527 (1975)

[1] *Saint Avvaiyar*, Indian poetess, first century B. C., quoted by *S. S. Iyer*, Science *185*, 400 (1974).
[2] *A. Treibs*, Liebigs Ann. Chem. *509*, 103 (1934); *510*, 42 (1934); *517*, 172 (1935); *520*, 144 (1935), Angew. Chem. *49*, 682 (1936).
[3] *N. Hackerman*, Science *185*, 401 (1974).
[4] *M. Blumer*, Pure Appl. Chem. *34*, 591 (1973).
[5] *H. J. Coleman, D. E. Hirsch*, and *J. E. Dooley*, Anal. Chem. *41*, 800 (1969); *H. J. Coleman, J. E. Dooley, D. E. Hirsch*, and *C. J. Thompson*, *ibid. 45*, 1724 (1973).
[6] *M. Blumer* and *M. Rudrum*, J. Inst. Petrol. *56*, 99 (1970).
[7] *W. K. Seifert*, Progr. Chem. Org. Natur. Prod. (Fortschr. Chem. Org. Naturst.) *32*, 1 (1975).
[8] *A. G. Douglas, M. Blumer, G. Eglinton*, and *K. Douraghi-Zadeh*, Tetrahedron *27*, 1071 (1971).
[9] *W. Giger* and *M. Blumer*, Anal. Chem. *46*, 1663 (1974).
[10] *W. Kern*, Helv. Chim. Acta *30*, 595 (1947).
[11] *M. Blumer*, Ann. Acad. Brasil. Cienc., in press.
[12] *D. Hoffmann, W. E. Bondinell*, and *E. L. Wynder*, Science *183*, 215 (1974).
[13] *M. Blumer* and *W. W. Youngblood*, Science *188*, 53 (1975).
[14] *E. Kovats*, Helv. Chim. Acta *41*, 1915 (1958), *A. Wehrli* and *E. Kovats*, *ibid. 42*, 2709 (1959).
[15] Schweizerischer Wissenschaftsrat, Forschungsbericht, Band 2, p. 43, Bern 1973.

Nonenzymatic Simulation of Nitrogenase Reactions and the Mechanism of Biological Nitrogen Fixation

By G. N. Schrauzer[*]

The development of biologically relevant model systems of nitrogenase permitted the simulation of virtually all known reactions of the nitrogen reducing enzymes under nonenzymatic conditions. On the basis of these experiments, a mechanism of biological nitrogen fixation is formulated which is in accord with the available enzymological evidence. The key reactions of the substrates of nitrogenase occur at a molybdenum active site. The non-heme iron, which is bound to sulfur and protein-$S^{\ominus}$ groups, mediates the transport of electrons to the molybdenum active site but does not participate directly in the reduction of the substrates. ATP is required for the acceleration of the reduction and activation of the molybdenum site and is hydrolyzed to ADP and inorganic phosphate. Diimine and hydrazine were detected as intermediates in the reduction of molecular nitrogen under nonenzymatic conditions.

1. Introduction

The importance of biological nitrogen fixation in the maintenance of the nitrogen cycle is so well appreciated that it needs no further emphasis: Only recently, the historical developments and biochemical aspects of this essential natural process have been outlined in this Journal[1]. The nitrogen reducing enzyme, commonly known as nitrogenase, has been isolated[2] from various microorganisms, *e. g.* those belonging to the genus *Azotobacter*, as well as from other soil bacteria and blue-green algae. During the past decade much information has been accumulated on the properties and reactions of the enzyme, but in spite of considerable efforts, most of the observed reactions remained obscure and no acceptable mechanism of the reduction of nitrogen could be formulated. In view of the complexity of the enzyme, formulation of a mechanism of action would remain a difficult task even if it were possible to elucidate the structure of the enzyme by x-ray crystallographic methods.

A number of investigators have for this reason studied the reduction of nitrogen to ammonia under mild conditions in simple inorganic systems. After the discovery of the first complexes of molecular nitrogen with transition metals in 1965, several workers tried to reduce coordinatively bound nitrogen in complexes of this kind. Although this has apparently been successful in a few instances, the reaction conditions which had to be employed were quite different from those in the enzymatic assays. The nitrogen complexes chosen as a rule contained additional ligands such as phosphanes or diphosphanes, which by no stretch of the imagination could be regarded as biologically relevant, and the majority of studies were carried out with complexes or compounds of metals which are not present in the enzyme. Since this work is primarily of interest to coordination chemists and it does not establish a direct connection with the biological process, it is not necessary to describe it here; interested readers are referred to a recent review[3].

2. General Comments Concerning Enzyme Models

Many attempts have been made in the past to mimic enzymatic reactions in simple model systems. For comparatively simple processes, insight into the mechanism may be gained by such studies, but in order to minimize the danger of misinterpretations, model studies must be conducted within the framework of certain criteria which will be outlined for the specific case of nitrogenase:

1. The model systems must contain the metals present in the enzyme, *i. e.* molybdenum and iron, for the simulation of nitrogenase reactions.

[*] G. N. Schrauzer, Professor of Chemistry
Department of Chemistry, The University of California at San Diego
Revelle College, La Jolla, Calif. 92037 (USA)

2. The attachment of the metal ions to the apoprotein must be simulated with ligands containing the proven or postulated coordination sites in the enzyme.

3. The model systems should be functional in homogeneous solution and under approximately enzymatic reaction conditions.

4. The model systems must be devised initially by the principle of maximum simplicity. They should contain only a minimum of truly essential components.

5. The experimental results obtained with the model systems must correlate, at least qualitatively, with those of the enzyme.

The study of enzymatic reactions with model systems is only possible if sufficient information is available on the primary system in question. For nitrogenase, this is fortunately the case. It is also necessary, however, to test all experimental results for biological relevancy, since some of the observed similarities or discrepancies may be trivial. If a given model system exhibits a number of gross inconsistencies, appropriate modifications must be introduced; in the worst case, the model must be rejected. However, even if a far-reaching qualitative and quantitative similarity with the primary system is observed, the important question remains whether model studies can be used to support hypotheses, or to formulate a theory concerning the primary system. Controversies regarding the validity of models and analogies in science have occurred so frequently that his problem has been subjected to detailed philosophical analysis. Without entering into this topic in any detail, interested readers are referred to a recent book by *Hesse*[4], which examines the role of models and analogies in science. For the present purpose it is not necessary to defend the model approach, since the results to be described in the following speak for themselves.

3. Properties and Reactions of Nitrogen Reducing Enzymes

3.1. Composition of Enzymes

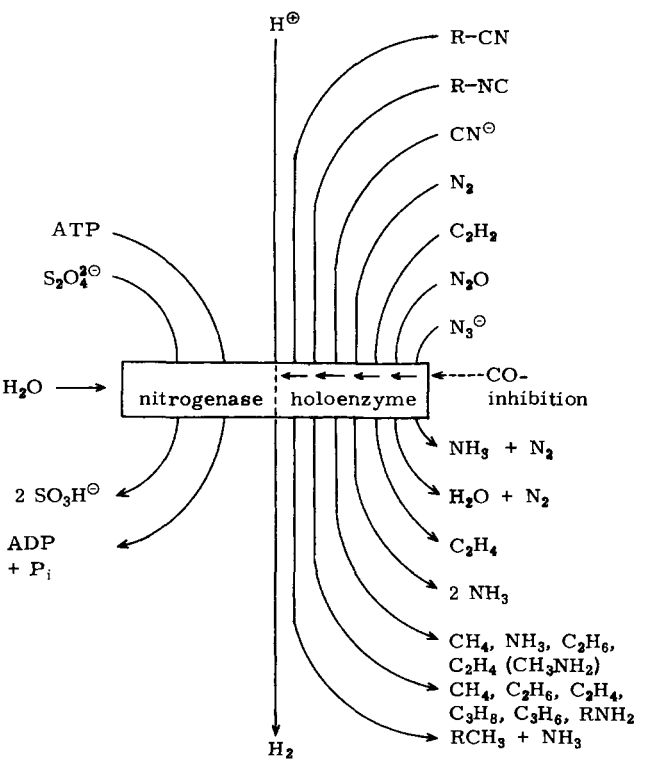
Nitrogenases have been isolated from various microorganisms. It is known[5] by now that the enzymes are invariably composed of two components. The so-called "Protein I", also known as "Mo—Fe-Protein" or "Azofermo" has a molecular weight of about 200000—300000 daltons and contains molybdenum, iron, labile sulfide and cysteine sulfur. Typically, 1—2 atoms of molybdenum are found together with 20—40 Fe, 20—40 $S^{2\ominus}$ ions and more than 40 cysteinyl residues. The variations of the Mo : Fe : $S^{2\ominus}$: cys-$S^{\ominus}$ ratios suggest the possibility that the Mo—Fe-Protein exists in a dimeric as well as in a monomeric form. The molybdenum is presumably attached to a cysteinyl residue and may be expected to be present as an oxomolybdate. The iron is bound in a form typical of the ferredoxins. Although full structural details are not yet available, it is reasonable to assume that the protein contains quasicubic aggregates of composition Fe_4S_4(S-protein)$_4$.

The "Protein II", also designated "Fe-Protein" of "Azofer", has a molecular weight of about 40000—50000 daltons and is a typical ferredoxin, containing, as a rule, 4 Fe, 4 $S^{2\ominus}$ and 4 cysteinyl residues, most likely in a quasicubic arrangement as outlined above. The amino acid composition of Protein II varies somewhat with the microbial source. Active nitrogenase preparations are obtained if the two proteins are combined from different sources; the species-dependent differences in the composition thus are not of fundamental importance. The activity of nitrogenase preparations *in vitro* reaches a maximum if both components are present in the molar ratio of 1 : 1.

For typical assays, sodium dithionite, $Na_2S_2O_4$, but occasionally also KBH_4, are employed as reducing agents. The reduction of all substrates is ATP-dependent. To transfer two electrons to the substrates up to 5 molecules of ATP are consumed, *i.e.* hydrolyzed to ADP and inorganic phosphate. Since ADP exerts an inhibitory effect, an enzymatic ATP generating system utilizing creatin phosphate as the source of active phosphate, is employed for most experiments. A bivalent metal cation is also required for activity, as a rule $Mg^{2\oplus}$, optimally at the ratio of 1 : 2 relative to ATP. Active nitrogenase preparations are also obtained, however, if $Mg^{2\oplus}$ is replaced by $Mn^{2\oplus}$, $Co^{2\oplus}$, $Fe^{2\oplus}$ or $Ni^{2\oplus}$; the bivalent metal thus is relatively nonspecific and probably not of primary mechanistic significance.

3.2. Substrate Reactions[5]

Nitrogenase discharges protons of the medium to yield hydrogen if no other reducible substrates are present. This hydrogen evolution is ATP dependent and, in contrast to the reduction of the substrates, is not inhibited by CO. The evolution of hydrogen is inhibited by acetylene, the latter is reduced exclusively to ethylene. In D_2O, *cis*-1,2-dideuterioethylene is formed. Ethylene itself is not reduced and has no inhibitory effect. The most important substrate reactions of nitrogenase are summarized in Scheme 1.



Scheme 1. Reactions of nitrogenase.

It is remarkable that the enzyme reduces C_2H_2, N_2O and $N_3^{\ominus}$ only through the transfer of two electrons, while up to 14 electrons are transferred in the reduction of other substrates, *e.g.* of isocyanides. In the reduction of the latter as well

as in the reactions with $CN^{\ominus}$, nitrogenase also catalyzes the formation of new carbon-carbon bonds, to yield saturated and unsaturated C_2- and C_3-hydrocarbons (see Scheme 1). Aliphatic or olefinic nitriles are converted to hydrocarbons, but no new C—C bonds are generated in this case. In all reactions electrons as well as protons of the medium are transferred to the substrate, indicating that the active site of the enzyme is in a hydrophilic environment. So far attempts to detect complexes of nitrogenase with substrates have proven unsuccessful. It has also not been possible to detect reaction intermediates; in the simplest case, this could mean that the substrate remains attached to the enzyme until it is fully reduced. Steric hindrance of the active site is indicated by the fact that propyne and (slowly) also 1-butyne are enzymatically reduced to the corresponding olefins, whereas 2-butyne is apparently not a substrate.

3.3. Reduction of Nitrogen

Nitrogenase reduces nitrogen at about 1/4 of the rate of the reduction of acetylene. Intermediates of this reduction have not been detected, but two interesting phenomena have been observed which suggest that diimine, N_2H_2 is produced during the reaction (see Section 8). The first phenomenon concerns the evolution of molecular hydrogen, which occurs even if the reaction is performed at saturating N_2 pressures[6, 7], and which cannot be suppressed. Since the hydrogen evolution is completely inhibited by acetylene it was concluded that only about 75 % of the available electrons are actually utilized for nitrogen reduction, and that the remaining 25 % are for some reason diverted to yield hydrogen. We shall discuss this peculiar property of nitrogenase in Section 8. At this point it should only be mentioned that it may be *incorrect* to represent the stoichiometry of the reaction in terms of the simple equation (a):

$$N_2 + 6e^- + 6H^+ = 2NH_3 \qquad (a)$$

If the hydrogen evolution during N_2 reduction is taken into account, the reaction stoichiometry would have to be formulated in terms of eq. (b) instead:

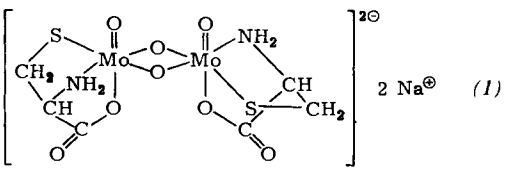
$$N_2 + 8e^- + 8H^+ = 2NH_3 + H_2 \qquad (b)$$

The second mechanistically relevant phenomenon concerns a $D_2/H^{\oplus}$ exchange reaction which leads to the production of HD when nitrogen is present as the substrate[8, 9]. This reaction is not observed with other reducible substrates, and we shall also discuss it in Section 8.

4. Functional Models of Nitrogenase

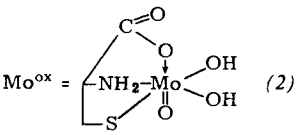
4.1. Composition

The addition of small amounts of simple alkali molybdates to aqueous alkaline solutions of $NaBH_4$ or $Na_2S_2O_4$ does not induce significant catalytic activity for the reduction of most nitrogenase substrates. If, however, thiol ligands are added as well, active catalytic systems are obtained at the optimal Mo-thiol ratio of 1:1. The first experiments were performed with systems containing molybdate and 1-thioglycerol at the 1:1 ratio[10, 11]. In later studies thioglycerol was replaced by L(+)-cysteine; the latter forms a well-defined, oxo-bridged binuclear complex with Mo^{V}[12] whose structure *(1)* was elucidated by X-ray analysis[13]:

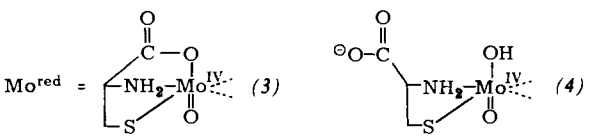


(1)

This complex, which has been designated "Complex I" reduces the substrates of nitrogenase in the presence of reducing agents but is not the actual catalyst. Under the reaction conditions it undergoes partial dissociation into mononuclear molybdenum-cysteine species whose probable structures are *(2)* in the oxidized, and *(3)* or *(4)* in the active reduced form:



(2)



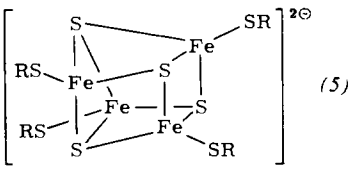
(3) *(4)*

The active reduced form (Mo^{red}) is in all probability a derivative of $Mo^{4\oplus}$[14] and possesses the properties of a metallonucleophile. It is a highly reactive species, reacts with water to yield hydrogen, and utilizes two coordination sites in *cis*-position during its interaction with the substrates. In the catalytic process, "Mo^{red}" is oxidized to Mo^{ox}; the conversion of the latter back to Mo^{red} must occur under the reaction conditions, but is a relatively slow process. We have found, however, that the reduction of Mo is significantly stimulated by ATP as well as by other nucleoside phosphates. Even simple protic acids accelerate the conversion of Mo^{ox} to Mo^{red}, but ATP is the most efficient of all. We shall discuss the ATP effect in greater detail in Section 6; it is sufficient at this point to state that the study of the ATP effect in the model systems has provided important clues regarding its function in the enzymatic reaction.

It was at first not clear whether iron is directly involved in the reduction of the substrates. Experiments with catalytic systems containing iron as the only metal indicated that iron possesses only a very limited propensity to reduce typical nitrogenase substrates. The addition of simple iron salts in trace-amounts to the molybdothiol catalysts enhances the catalytic activity, but does not alter the course of the reactions in any significant way. It was therefore concluded that the iron functions as a nonspecific electron transfer catalyst, facilitating the transport of electrons from the reductant ($BH_4^{\ominus}$) to the oxidized form of the catalyst, Mo^{ox}. However, simple iron salts show little or no stimulatory effect, if $S_2O_4^{2\ominus}$ is employed as the reducing agent, and they can be regarded at best only as crude approximations for the hon-heme iron components of the enzyme.

The reactions of the molybdothiol catalysts were for this reason also investigated in the presence of ferredoxin model compounds, *i.e.* anions of the type $[Fe_4S_4(SR)_4]^{2\ominus}$, whose synthesis was described by *Holm et al.*[15, 16]. These ions possess

a quasicubic structure *(5)* similar to the naturally occurring ferredoxins:



(5)

On reaction with reducing agents, the ions *(5)* are converted into reduced species of composition $[Fe_4S_4(SR)_4]^{3\ominus}$ and $[Fe_4S_4(SR)_4]^{4\ominus}$, respectively. These ferredoxin model compounds thus seemed to be ideally suited for the study of the possible role of iron in nitrogenase. They were found to be efficient electron transfer catalysts in the molybdothiol model systems, even when $S_2O_4^{2\ominus}$ was employed as the reducing agent[17, 18]. It thus became possible to investigate the reduction of typical substrates of nitrogenase in systems containing Mo, Fe, $S^{2\ominus}$ and Cys-$S^{\ominus}$ in the same molar ratios as found in the enzyme. Moreover, the iron cluster complexes could also be synthesized or generated in the reduced forms, and these were successfully employed as *stoichiometric* reducing agents. Finally, we also investigated the effect of $Mg^{2\oplus}$ in some of the reactions[19], but the results of this work will not be discussed here.

5. Results of the Model Studies

The systematic investigation of the reduction of all known substrates of nitrogenase demonstrated unequivocally that all are catalyzed by molybdenum[20]. The iron functions as an electron transfer catalyst but does not participate in the substrate-dependent reactions. The currently available nitrogenase model systems are still significantly less active than nitrogenase itself. It is possible to achieve turnover numbers corresponding to 1% of those observed with the enzyme with C_2H_2 as the substrate, *e.g.* by lowering the molybdenum concentration; most experiments were performed at higher molybdenum concentrations, however, at which the turnover numbers reach only 0.001—0.01% of those of nitrogenase.

The lower activity of the model systems has a number of reasons. Due to the tendency of Mo^{V} to form oxobridged dimeric species, only about 1% of the total molybdenum present is converted into the mononuclear active species Mo^{red}. Moreover, the electron transfer efficiency, *i.e.* the number of electrons transferred from the reductant to the active catalyst, is considerably lower than in the enzyme, obviously because of the comparative crudeness of the electron transfer system employed. Nevertheless, the turnover numbers and Michaelis-Menten constants as determined with typical nitrogenase substrates follow the same trend as those observed with the enzyme (Table 1). The statistical correlation between the enzymatic and nonenzymatic data pairs is highly significant, with $P<0.001$. The model systems thus may be regarded as biologically relevant, and it appears permissible to apply mechanistic conclusions from the model studies to the enzymatic processes. Some of the most important reactions will be discussed in the following.

5.1. Acetylene and Alkynes[21]

The available experimental evidence suggests that Mo^{red} interacts with C_2H_2 to yield a labile side-on bonded intermediate which on subsequent hydrolysis produces ethylene and Mo^{ox} [eq. (c)]:

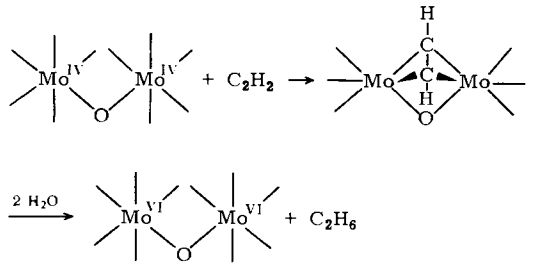
$$Mo^{red} + C_2H_2 \longrightarrow Mo\begin{matrix}CH\\ \|\\ CH\end{matrix} \xrightarrow[(H_2O)]{+2\,H^{\oplus}} Mo^{ox} + C_2H_4 \qquad (c)$$

In D_2O, *cis*-1,2-dideuterioethylene is formed; with 2-butyne, *cis*-2-butene is formed exclusively. In the model systems, acetylene is in part also reduced to ethane. The formation of the latter can be suppressed, however, *e.g.* by lowering the catalyst concentration. Since C_2H_4 is not a substrate, the formation of C_2H_6 was assumed to involve oxobridged binuclear derivatives of Mo^{red} which react with acetylene in the manner indicated in eq. (d):

Table 1. Comparison of properties and reactions of nitrogenase and of nitrogenase model systems.

Characteristic	Nitrogenase:		Model systems:	
Metals present	Mo, Fe, $Mg^{2\oplus}$		Mo, (Fe, $Mg^{2\oplus}$ not obligatory)	
ATP-Effect	activating, obligatory		rate enhancing, not obligatory	
Binding site for Mo	Protein-Cys—$S^{\ominus}$ (?)		Cys—$S^{\ominus}$, $RS^{\ominus}$	
Electron transfer system	Non-heme iron, ferredoxin-like		Ferredoxin model compounds (not obligatory)	
Reducing agent(s)	$S_2O_4^{2\ominus}$, ($BH_4^{\ominus}$)		($S_2O_4^{2\ominus}$), $BH_4^{\ominus}$	
Optimal pH	7—8		7—10	
Maximum turnover number for C_2H_2 reduction (mol·min^{-1}, per mol Mo):	200		1.7	
Activation energy for C_2H_2 reduction (kcal/mol, above 20 °C):	14.6		13—15	
Relative rates of reduction (V_{rel}) and K_M values (mmol·l^{-1}) for reduction of	V_{rel}	K_M	V_{rel}	K_M
C_2H_2	1	0.1—0.4	1	0.33
$N_3^{\ominus}$	0.75	0.2—1.0	0.50	0.5
N_2O	0.75	1.0	0.50	2.4
N_2	0.25	0.03—0.1	0.25 [a]	2—10 [a]
CH_3NC	0.20	0.2—1.0	0.01	8—100
$CN^{\ominus}$	0.15	0.4	0.01	12
CH_2=CH—CN	0.06	10—25	0.005	250
CH_3CN	0.005	500	0.001	1000

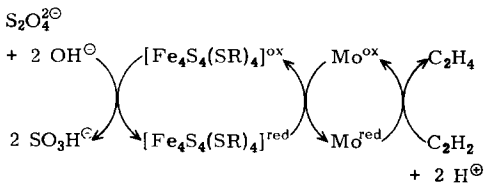
[a] For the reduction of N_2 to N_2H_2 in the presence of ATP.



(d)

The fact that 2-butyne is reduced in the model system but not by the enzyme is indicative of steric hindrance at the enzymic substrate binding site.

In the presence of ferredoxin model compounds, the Mo^{red} catalyzed reduction of C_2H_2 is formulated as shown in Scheme 2; $[Fe_4S_4(SR)_4]^{red}$ and $[Fe_4S_4(SR)_4]^{ox}$ denote the reduced or oxidized derivatives of the Fe_4-cluster anions:

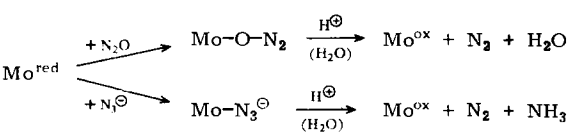


Scheme 2. Reduction of acetylene by Mo^{red} in the presence of ferredoxin model compounds.

In the absence of reducible substrates, H_2-evolution has been observed[18]. The system in Scheme 2 could not yet be stimulated by ATP but reacts with N_2 as the substrate to yield hydrazine *via* diimine[17].

5.2. Dinitrogen Oxide and Azide[19]

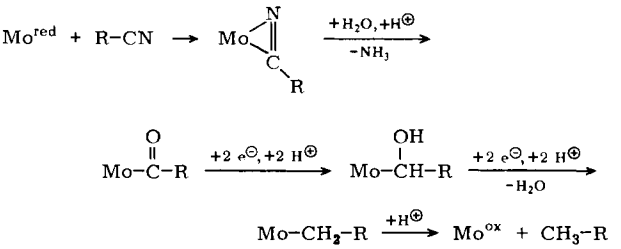
The reduction of these substrates can be plausibly represented in terms of eq. (e) and needs no further discussion.



(e)

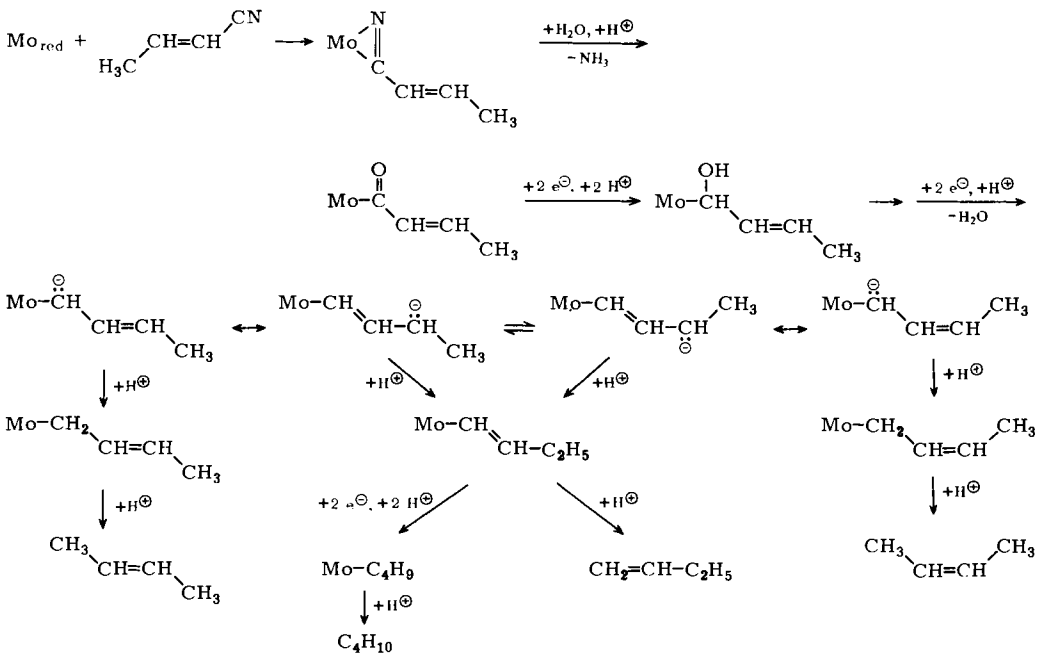
5.3. Nitriles[22]

Nitrogenase reduces acetonitrile to ethane and ammonia[5]. Higher *n*-alkanenitriles react analogously, but secondary or tertiary nitriles are reduced only slowly, if at all. A detailed study of the reduction of nitriles in the model systems indicates that the nitrile group interacts with the catalyst Mo^{red} in the side-on fashion. The overall reaction is shown in Scheme 3.



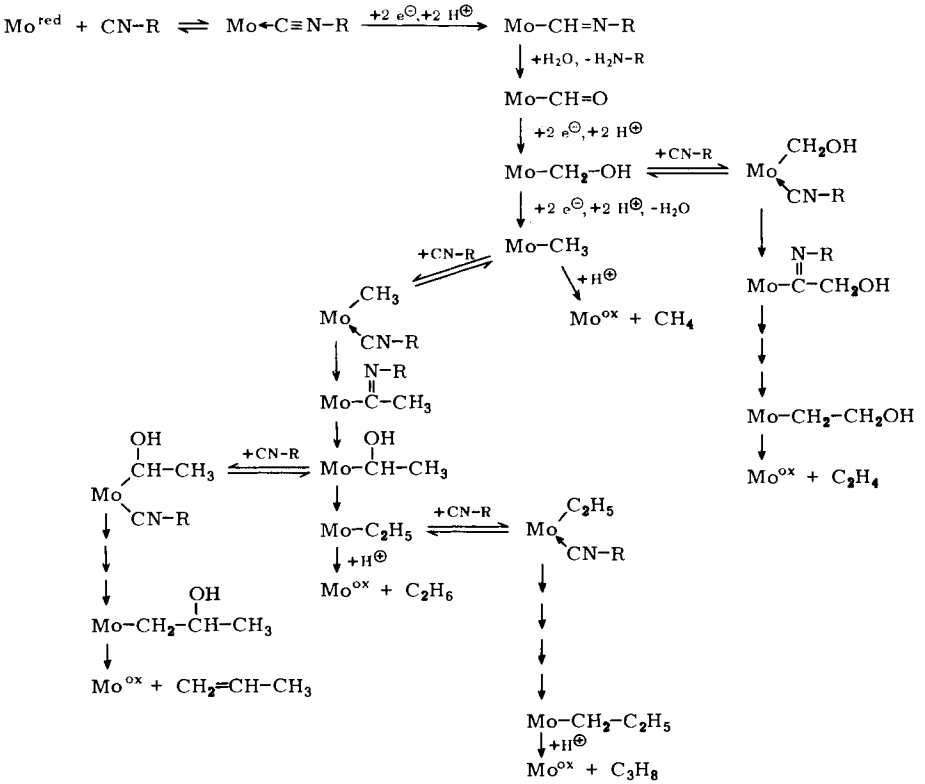
Scheme 3. Nitrile reduction.

Unsaturated nitriles are reduced by nitrogenase as well as by molybdothiol catalysts with a higher rate than saturated nitriles[22, 23]. Saturated as well as unsaturated hydrocarbons and ammonia are formed. From the product distribution it is concluded that the reaction takes place *via* allylic organomolybdenum intermediates. The molybdenum-bound organic residue undergoes double-bond as well as *cis-trans*-isomerization reactions, this is exemplified for the *trans*-isomer of crotononitrile (Scheme 4)[22].



Scheme 4. Reduction of *trans*-crotononitrile.

The comparison of the enzymatic and the nonenzymatic reduction of *cis*- and *trans*-crotononitrile is particularly instructive. In the model system, *cis*- and *trans*-crotononitrile are both reduced to a mixture of *cis*- and *trans*-2-butene, in addition to butene and *n*-butane. With nitrogenase, *cis*-crotononitrile is reduced to 1-butene, *n*-butane and *cis*-2-butene; *trans*-2-butene is not detected. Conversely, *trans*-crotononitrile is reduced mainly to *trans*-2-butene; the *cis*-isomer of 2-butene is again not formed. This was attributed to a steric hindrance of the active site in nitrogenase, preventing the rotation of the molybdenum-bound crotonyl-residue under the enzymatic

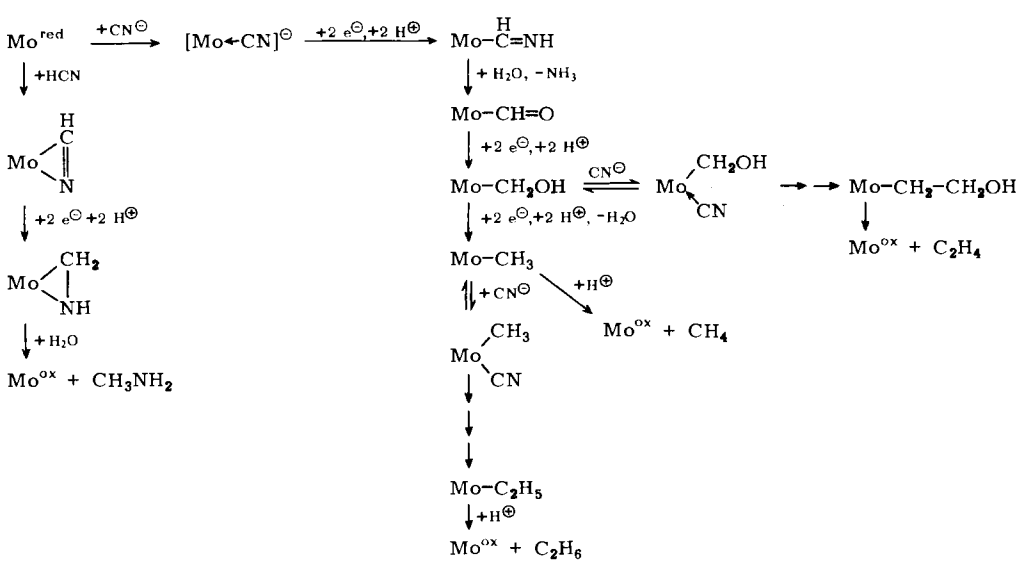


Scheme 5. Reduction of isocyanides.

conditions of reduction. In the model systems with cysteine as the thiol component, this rotation is not seriously impaired, but if cysteine is replaced by the bulkier glutathione residue, it is possible to prevent the *cis-trans*-isomerization to a significant extent; evidently some steric hindrance was introduced. It turns out that *cis*- and *trans*-crotononitrile are interesting probes for comparative studies with nitrogenase model systems, since the hydrocarbon reaction products can be easily determined by gas-chromatographic methods. Using these substrates it should be possible to examine other nitrogenase model systems in which the thiol components are oligopeptides; in this manner finer details of the stereochemistry of the active site in the enzyme could well be duplicated or simulated under nonenzymatic conditions.

5.4. Isocyanides

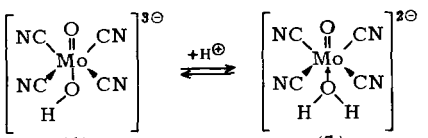
The reduction of isocyanides by nitrogenase[5, 24, 25] is of interest in that it occurs with the formation of new carbon-carbon bonds. With methyl isocyanide, for example, CH_4 and CH_3NH_2 are the main products, but small amounts of saturated and olefinic C_2- and C_3-hydrocarbons are formed as well. The same reactions were tested in the molybdothiol model systems; Scheme 5 summarizes the essential features of the mechanism. The formation of C_2- and C_3 hydrocarbons evidently occurs through isocyanide insertion processes in the organomolybdenum intermediates. Similar reactions are known to occur with isocyanide complexes of palladium and platinum.



Scheme 6. Reduction of cyanide.

5.5. Cyanide[19]

The reduction of cyanide by nitrogenase yields CH_4 and NH_3 as the main products in addition to smaller amounts or traces of CH_3NH_2, C_2H_6 and C_2H_4[5]. Except for the formation of CH_3NH_2, the mechanism of reduction of this substrate can be formulated in analogy to the reduction of isocyanides (Scheme 6). Formation of CH_3NH_2 occurs possibly through side-on interaction of HCN with the active reduced molybdenum site and its subsequent reduction without hydrolysis of the C=N bond. The reduction of $CN^{\ominus}$ was fully simulated with the molybdothiol catalysts. However, in most recent experiments, some of the key mechanistic assumptions in Scheme 6 have been confirmed through studies of the reduction of coordinated cyanide in the complex anion $[Mo(O)(OH)(CN)_4]^{3\ominus}$, *(6)*, which provides a rare example for an isolable mononuclear Mo^{IV} compound. The structure of *(6)* has recently been determined[27] and it was shown that this species is protonated to an aquoderivative *(7)*, whose structure is also known[27]. The anion *(7)* reacts with reducing agents to yield CH_4, C_2H_6, C_2H_4, NH_3 and traces of CH_3NH_2, the reduction is significantly ATP-stimulated [eq. (f)]:



(6) *(7)* (f)

$$\xrightarrow[+H^{\oplus}]{\text{reduction}} CH_4 + C_2H_6 + C_2H_4 + NH_3$$

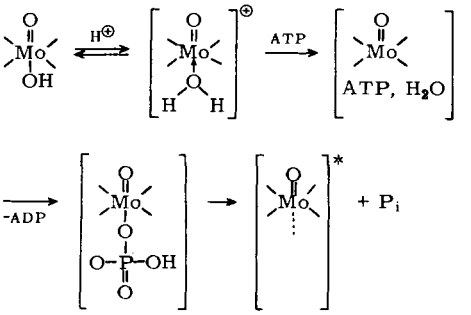
(H_2O)

These experiments[26] show that monomeric Mo^{IV} complexes behave indeed as postulated in Scheme 6. They furthermore provide the first stereochemical information on postulated reaction intermediates, since *(6)* and *(7)* may be considered as models of catalyst-substrate intermediates.

6. The ATP Effect

The stimulatory action of ATP in the model systems was attributed to the acceleration of the transfer of electrons from the reducing agent to the oxidized molybdenum catalyst[19, 20]. There are also indications for the intermediate formation of a complex of Mo^{ox} with ATP, which is more rapidly reduced than Mo^{ox} itself[28]. Moreover, ATP is hydrolyzed to ADP and inorganic phosphate during the reduction. The fact that ATP is catalytically hydrolyzed by molybdate(VI) has been known already for quite some time, especially through the work of *Weil-Malherbe* and *Green*[29]. The ATP requirement of nitrogenase could thus be associated with the interaction of ATP with the molybdenum active site. We have recently shown[28] that the activation of Mo^{ox} by ATP is accompanied by the addition of one proton. Russian workers hypothesized, that this protonation is solely responsible for the ATP effect in the model systems[30]. A comparison of the effect of various protic acids in molybdothiol catalyzed reactions clearly revealed that the acid anions participate in this process; the activation of Mo^{ox} by acids thus involves both the proton as well as the acid anion[28]. ATP was furthermore found to be significantly more active than all simple protic acids studied, suggesting a specific interaction of ATP with the molybdothiol catalyst. We have previously assumed[19, 20] that two molecules or ions of ATP interact with Mo^{ox}. The recent experiments show, however, that most likely only one ion of ATP forms a complex with Mo^{ox}, the second ATP furnishes a proton[28], but presumably does not enter the inner coordination sphere of molybdenum. ATP appears to facilitate the removal of inert molybdenum-bound OH-group(s) as shown in eq. (g).

We assume furthermore that the $Mg^{2\oplus}$-requirement of nitrogenase is in some way connected with this process of site activation ($Mg^{2\oplus}$ may facilitate the removal of ADP or of phosphate from the active molybdenum center).



(g)

This interpretation of the ATP effect resembles a previous postulate of *Hardy* and *Knight Jr.*[31] and *Parshall*[32]. Experiments[33, 34] with the nitrogenase proteins revealed that the magnesium salt of ATP forms a complex with the Fe-protein without the hydrolysis of phosphate bonds. If this complex is combined with the Fe—Mo-protein ("Protein I"), one observes ATP hydrolysis as well as electron transfer reactions from the Fe-protein to the Mo—Fe-component. This suggests that the reduced Fe-protein functions as the electron source, while ATP is required for the activation of the molybdenum center. The latter interaction is accompanied by the hydrolysis of ATP to ADP and inorganic phosphate; it is possible that some of the energy which is released during the hydrolysis of the phosphate bond is transferred to the molybdenum active site, leading to a reactive dehydroxylated or deaquated species which is more rapidly reduced; the overall process could well be similar to that shown in eq. (g).

In spite of the complexity of the ATP effect, it can now be stated with a reasonable degree of certainty that the ATP requirement is not linked directly with the reduction of the substrates, not only because all reactions catalyzed by nitrogenase are exothermic anyway, but also because even the evolution of hydrogen in the absence of substrates is ATP dependent.

7. The Role of Iron

All model experiments have shown that neither simple iron salts nor anions of the type $[Fe_4S_4(SR)_4]^{z\ominus}$ are directly involved in the reduction of the substrates. However, the ferredoxin model compounds are efficient electron transfer catalysts, possessing a considerable affinity for the molybdenum complexes. The non-heme iron components in nitrogenase may thus be safely assumed to function as electron transport catalysts[17, 18]. Moreover, the ferredoxin cluster units in the enzyme may be regarded as storage compartments of electrons, which assure a constant supply of electrons

to the molybdenum active site. The high concentration of iron as compared to molybdenum in the enzyme supports this interpretation.

8. The Reduction of Nitrogen

Since the reduction of acetylene by nitrogenase yields only ethylene it is plausible to assume that the reduction of the isoelectronic nitrogen should produce diimine as the first intermediate, as was postulated as early as in 1922 by *H. Wieland*. But what are the subsequent reactions of diimine? The highly endothermic diimine is known to decompose in aqueous media rapidly, yielding hydrazine and nitrogen through a disproportionation, as well as nitrogen and hydrogen through direct decomposition[33]; traces of ammonium azide are also formed[34]. Diimine itself is a powerful reducing agent and even reduces isolated C=C bonds[35, 36]. To test its behavior under conditions simulating the enzymatic reduction, experiments with chemically generated diimine were performed in the presence of the components of the molybdothiol model system. It was found that diimine cannot be reduced and that neither its decomposition nor its disproportionation are significantly influenced by the molybdothiol catalysts, the ferredoxin model compounds and/or the reducing agents employed[17]. In weakly alkaline media at room temperature, diimine undergoes disproportionation and spontaneous decomposition fairly accurately according to eq. (h):

$$3\,N_2H_2 = 2\,N_2 + H_2 + N_2H_4 \qquad (h)$$

The hydrazine produced is reduced, however; this reaction is clearly catalyzed by Mo^{red} and stimulated by ATP [eq. (i)]:

$$Mo^{red} + N_2H_4 \xrightarrow[(ATP)]{H^{\oplus}} Mo{-}NH_2{-}\overset{\oplus}{N}H_3 \xrightarrow[(H_2O)]{} Mo^{ox} + 2\,NH_3 \qquad (i)$$

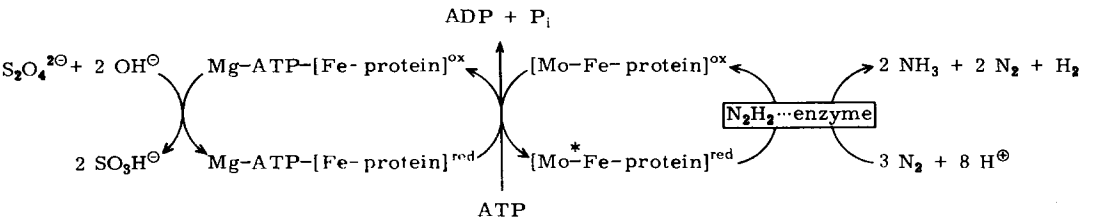
The fact that diimine is not a substrate in the model system is actually not surprising, considering its endothermicity and other chemical properties. Diimine is isoelectronic with ethylene, the latter is also not reduced by molybdothiol catalysts. We thus conclude that diimine should also not be reducible by nitrogenase itself. It probably accumulates in the vicinity of the active site and subsequently undergoes decomposition and disproportionation as shown in eq. (h). The hydrazine formed is reduced to ammonia and the overall process of nitrogen reduction is thus plausibly formulated by eq. (j). This interpretation of the mechanism of enzymatic nitrogen reduction explains why only 75% of the available electrons are formally utilized for the formation of ammonia, and that 25% of the electrons are used for the production of hydrogen.

$$3\,N_2 \xrightarrow[-n\,ADP,\,-n\,P_i]{+6\,e^{\ominus},+6\,H^{\oplus},+n\,ATP} [3\,N_2H_2] \rightarrow [N_2H_4] + 2\,N_2 + H_2$$
$$[N_2H_4] \xrightarrow[-n\,ADP,\,-n\,P_i]{+2\,e^{\ominus},+2\,H^{\oplus},+n\,ATP} 2\,NH_3 \qquad (j)$$

The overall stoichiometry of the biological fixation of nitrogen should therefore be represented in terms of eq. (b) rather than eq. (a), and the observed hydrogen evolution at saturating N_2 pressures is strongly indicative of the intermediate formation of diimine under enzymatic conditions. With the nitrogenase model systems, a slow reduction of N_2 to NH_3 was observed in the absence of ATP. In the presence of ATP, the intermediate formation of diimine was demonstrated unambiguously, using $^{15}N_2$ as the substrate[17, 20]. The reduction of nitrogen to diimine may thus be formulated in analogy to the reduction of acetylene to ethylene [eq. (k)].

$$Mo^{red} + N_2 \longrightarrow Mo\begin{matrix}N\\ \|\\ N\end{matrix} \xrightarrow[(H_2O)]{+2\,H^{\oplus}} Mo^{ox} + N_2H_2 \qquad (k)$$

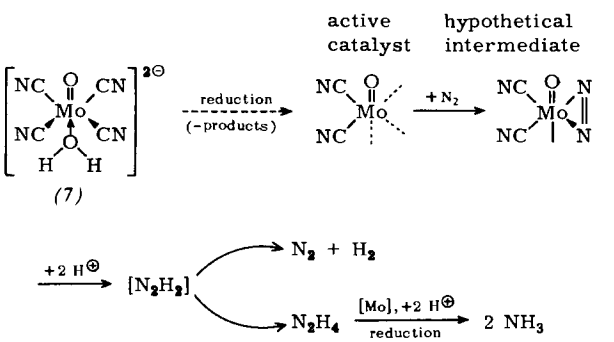
Summarizing the available experimental evidence we may thus describe the mechanism of biological nitrogen fixation as shown in Scheme 7.



Scheme 7. Enzymatic reduction of nitrogen.

Even the observed N_2-dependent $D_2/H^{\oplus}$-exchange[8, 9] may be considered as an indirect proof of the intermediate formation of diimine and its partial decomposition into the elements. Although not all features of this intriguing process are fully understood, it is reassuring that it was fully duplicated under nonenzymatic conditions[17].

In most recent work[26] we have utilized cyano complexes of Mo^{IV} as catalysts for the reduction of nitrogenase substrates including molecular nitrogen. Complexes such as *(7)* are converted to species related to Mo^{red} under reducing conditions. If *(7)* is reduced in the presence of ATP and molecular nitrogen, ammonia is produced in higher yields than obtained in the molybdothiol systems. The mechanism of nitrogen



Scheme 8. Reduction of molecular nitrogen in the cyanomolybdo model systems.

reduction in these "cyanomolybdo" model systems is formulated in Scheme 8. Since ammonia is formed in the reduction of coordinated cyanide, these experiments were performed with $^{15}N_2$ as the substrate; the reduction of molecular N_2 was demonstrated unequivocally.

9. Concluding Remarks

The present account should not be concluded without some remarks concerning the limitations of the model approach. Although simple models may duplicate the primary system rather well, at least qualitatively, it is clear that such simple systems cannot be expected to exhibit the same activity or selectivity of the enzyme. The model systems obviously lack the high degree of structural organization which is present in enzymes; they clearly possess a higher entropy and for this reason alone must be considered as imperfect relative to the primary systems. Any attempt to develop systems which duplicate enzymes more closely or quantitatively would require a substantial increase of their complexity, eventually the partial synthesis of the enzyme itself.

Our work has shown, however, that some of the most important mechanistic clues can be obtained with deliberately simple models, which is perhaps more than one can expect with sophisticated systems. Finally, our work has increased our knowledge on the properties and reactions of molybdenum compounds and could ultimately produce more efficient systems for the reduction of molecular nitrogen. Most recent developments with cyanomolybdo-complexes as catalysts, for example, show some promise in this direction.

The work described in the present account was supported by grants from the National Science Foundation (USA), as well as by Climax Molybdenum Company and Mitsubishi Chemical Industries Ltd. I also wish to express my appreciation to all students and postdoctoral fellows who participated in this project, namely to P. A. Doemeny, G. W. Kiefer, Dr. H. Kisch, E. Moorehead, P. R. Robinson, G. Schlesinger, K. Tano and T. M. Vickrey.

Received: April 21, 1975 [A 79 IE]
German version: Angew. Chem. 87, 579 (1975)

[1] *D. Kleiner*, Angew. Chem. 87, 97 (1975); Angew. Chem. internat. Edit. 14, 80 (1975).
[2] *W. A. Bulen* and *J. R. LeComte*, Proc. Nat. Acad. Sci. USA 56, 979 (1966).
[3] *D. Sellmann*, Angew. Chem. 86, 642 (1974); Angew. Chem. internat. Edit. 13, 639 (1974).
[4] *M. B. Hesse:* Models and Analogies in Science. University of Notre Dame Press. Notre Dame, Ind., 1966.
[5] See recent and more extensive reviews, especially: *R. W. F. Hardy, R. C. Burns*, and *G. W. Parshall* in *G. Eichhorn:* Inorganic Biochemistry. Elsevier, Amsterdam 1973, Vol. 2, Chapt. 23, p. 745ff., as well as *J. R. Postgate:* The Chemistry and Biochemistry of Nitrogen Fixation. Plenum Press, London 1971, and references cited therein.
[6] *R. Silverstein* and *W. A. Bulen*, Biochemistry 9, 3809 (1970).
[7] *R. C. Burns* and *R. W. F. Hardy*, Methods Enzymol. 24, 482 (1972).
[8] *G. L. Turner* and *F. J. Bergersen*, Biochem. J. 115, 529 (1969).
[9] *E. K. Jackson, G. W. Parshall*, and *R. W. F. Hardy*, J. Biol. Chem. 243, 4952 (1968).
[10] *G. N. Schrauzer* and *G. Schlesinger*, J. Am. Chem. Soc. 92, 1808 (1970).
[11] *G. N. Schrauzer*, Advan. Chem. Ser. 100, 1 (1971).
[12] *A. Kay* and *P. C. H. Mitchell*, Nature 219, 267 (1967).
[13] *J. R. Knox* and *C. K. Prout*, Chem. Commun. 1968, 1227.
[14] *M. Ichikawa* and *S. Meshitsuka*, J. Am. Chem. Soc. 95, 3411 (1973).
[15] *B. A. Averill, T. Herskovitz, R. H. Holm*, and *J. A. Ibers*, J. Am. Chem. Soc. 95, 3523 (1973).
[16] *T. Herskovitz, B. A. Averill, R. H. Holm, J. A. Ibers, W. D. Phillips*, and *J. F. Weiher*, Proc. Nat. Acad. Sci. USA 69, 2437 (1972).
[17] *G. N. Schrauzer, G. W. Kiefer, K. Tano*, and *P. A. Doemeny*, J. Am. Chem. Soc. 96, 641 (1974).
[18] *K. Tano* and *G. N. Schrauzer*, J. Am. Chem. Soc., in press.
[19] *G. N. Schrauzer, G. W. Kiefer, P. A. Doemeny*, and *H. Kisch*, J. Am. Chem. Soc. 95, 5582 (1973).
[20] *G. N. Schrauzer*, J. Less Common Metals 36, 475 (1974).
[21] *G. N. Schrauzer* and *P. A. Doemeny*, J. Am. Chem. Soc. 93, 1608 (1971).
[22] *G. N. Schrauzer, P. A. Doemeny, R. H. Frazier*, and *G. W. Kiefer*, J. Am. Chem. Soc. 94, 7378 (1972).
[23] *W. H. Fuchsman* and *R. W. F. Hardy*, Bioinorg. Chem. 1, 197 (1971).
[24] *M. Kelly, J. R. Postgate*, and *R. L. Richards*, Biochem. J. 102, 1c (1967).
[25] *G. N. Schrauzer, P. A. Doemeny, G. W. Kiefer*, and *R. H. Frazier*, J. Am. Chem. Soc. 94, 3604 (1972).
[26] *G. N. Schrauzer, P. R. Robinson, E. L. Moorehead*, and *T. M. Vickrey*, J. Am. Chem. Soc., in press.
[27] *P. R. Robinson, E. O. Schlemper*, and *R. Kent Murmann*, J. Am. Chem. Soc., in press.
[28] *G. N. Schrauzer, G. W. Kiefer, K. Tano*, and *P. R. Robinson*, J. Am. Chem. Soc., in press.
[29] *H. Weil-Malherbe* and *R. H. Green*, J. Biol. Chem. 49, 286 (1951).
[30] *A. P. Krushch, A. E. Shilov*, and *T. A. Vorontsova*, J. Am. Chem. Soc. 96, 4987 (1974).
[31] *R. W. F. Hardy* and *E. Knight, Jr.*, Bacteriol. Proc. 112 (1967).
[32] *G. W. Parshall*, J. Am. Chem. Soc. 89, 1822 (1967).
[33] *M. Y. W. Tso* and *R. H. Burris*, Biochim. Biophys. Acta 309, 263 (1973).
[34] *G. A. Walker* and *L. E. Mortenson*, Biochem. Biophys. Res. Commun. 53, 904 (1973).
[35] *S. Hünig, H. R. Müller*, and *W. Thier*, Angew. Chem. 77, 368 (1965); Angew. Chem. internat. Edit. 4, 271 (1965).
[36] *N. Wiberg, H. Bachhuber*, and *G. Fischer*, Angew. Chem. 84, 889 (1972); Angew. Chem. internat. Edit. 11, 829 (1972).

Formation, Detection, and Reactions of Phosphinidenes (Phosphanediyls)[**]

By Ulrich Schmidt[*]

Formation and detection of phosphinidenes (R—P:) in the decomposition of cyclophosphanes and in the reaction of dichlorophosphanes with metals are considered critically. Only in the thermolysis of pentaphenylcyclopentaphosphane can phenylphosphinidene be detected with certainty by pyrolysis-mass spectroscopy. "Trapping reactions" such as "insertion" into S—S or As—As bonds, and addition reactions with 1,2-diketones, 1,3-dienes, or alkynes can also be interpreted without the assumption of free phosphinidenes. The pyrolysis products of cyclophosphanes add to 1,3-dienes and alkynes, yielding five- and six-membered heterocycles that contain one to three phosphorus atoms.

1. Introduction

Transformations of highly reactive, neutral, electron-deficient compounds with an even number of electrons have been the center of interest for the last twenty years, and in this time they have enriched preparative chemistry and expanded our views about the course of chemical reactions. The strongest stimulus to this development of the chemistry of "carbenes" and "nitrenes" was certainly that provided by *Doering*'s discovery of the formation of cyclopropane from chloroform, a base, and olefins—a transformation that is now considered among the carbenoid reactions. The much earlier observations by *Staudinger* and *Meerwein* on diazo compounds, which the former author interpreted more than 50 years ago by the assumption of "methylenes", did not stimulate their contemporaries to a study of sextet carbon compounds.—Attempts to detect among the transformations of silicon, phosphorus, and sulfur compounds reactions corresponding to those of "carbenes", "nitrenes", and atomic oxygen have been reviewed several times[1-3].

The present progress report concerns in particular the detection and reactions of "phosphinidenes" (RP). Since the decomposition of their cyclic oligomers $(RP)_{4-6}$ may also possibly lead to reactive dimers and trimers, reactions that might be interpreted by means of such compounds are also considered here.

2. "Sources" and Reactions of Silylenes (Silanediyls) and of Atomic Sulfur

To make it easier for the reader to compare the formation reactions and the reactivities of sextet phosphorus compounds (phosphinidenes) with those of "silylenes"[***] (R_2Si) and of atomic sulfur, the formation and the reactions of these species will first be briefly considered (cf. Refs. [1—3] and literature cited therein).

Silicon dihalides occur in high-temperature reactions of silicon tetrahalides with silicon; they undergo insertion reactions into H—Cl, B—Hal, C—Hal and Si—Hal bonds, add to olefins, dienes, and benzene, but do not dimerize.

Organic derivatives of divalent silicon have been assumed as intermediates in the reaction of dialkyl- or diaryldichlorosilanes with metals (Li, Na, or Mg). In the absence of acceptors such reactions lead to polymers and cyclic oligomers $(R_2Si)_{4-6}$. In the presence of olefins, heterocycles are obtained by an addition reaction. However, for the mechanism of these reactions and of analogous reactions of dihalophosphanes with metals (cf. Section 4), the same criteria are applicable as for cyclopropanation by "carbenoids": these reactions can generally be explained more simply and more plausibly by reference to intermediates consisting of halogen-containing metal compounds of the type R_2SiMCl.

More convincing are the methods of formation of silylenes by cracking of polymers, by thermal elimination from 7-silanorbornadienes, and in particular by mild thermolysis of alkoxysilanes. The dialkyl- and diarylsilylenes thus formed can be trapped by alkenes or alkynes; polymers are formed in the absence of an acceptor.

Only at high temperatures[*] is a noteworthy concentration of atomic sulfur detectable in equilibrium with dimeric and oligomeric sulfur, but it is formed at room temperature in the gaseous state and in solution on irradiation of carbon oxide sulfide[3] or methyl isothiocyanate[4]. In particular, photochemical reaction of the isothiocyanate as the starting material can be exploited for the production of atomic sulfur on the preparative scale. Insertions into C—H bonds and additions to olefins and dienes are characteristic reactions. The stereochemistry and the kinetics of reactions of atomic sulfur and its spin states can be studied by using the clear and simple photochemical formation from carbon oxide sulfide; in studies in the gas state the reactions of singlet and triplet sulfur can be clearly differentiated.

3. Reactive Fragments from Cyclopolyphosphanes[5]

In 1877, on treating phenylphosphane with phenyldichlorophosphane, *Köhler* and *Michaelis* isolated a crystalline product of composition PhP which, in analogy with the structure of azobenzene, they formulated as "phosphobenzene" (PhP=PPh). It was not until almost 90 years later that proof

[*] Prof. Dr. U. Schmidt
Organisch-chemisches Institut der Universität
A-1090 Wien 9, Währinger Strasse 38 (Austria)

[**] According to Chemical Abstracts the species H—P: is termed "phosphinidene" [CAS Registry Number 13967-14-1], and their derivatives are termed "phosphinidenes". According to IUPAC Rule D-5.14 the correct term is "phosphanediyl".

[***] According to IUPAC Rule D-6.12, $(CH_3)_2Si$, for example, should now be termed "dimethylsilanediyl". The older name "dimethylsilylene" is still also in use.

[*] Only at 3000 °C is half of the S_2 dissociated to atomic sulfur.

was provided by X-ray structural analysis that this compound had a five-membered ring structure $(PhP)_5$. In addition to the pentamer there exists a hexamer that is known in at least four crystalline modifications. In the mass spectrum of these two cyclophenylphosphanes the high intensity of the $(PhP)_3^+$ ion is striking[6-8]. Recording of the spectrum in dependence on the sample temperature, time, and ionization energy has shown that the trimer $(PhP)_3$ is present in the melt at 150 °C and vaporizes faster than the pentamer on account of its smaller relative molecular mass[7, 8]. *Baudler* and *Bock*[9] have recently prepared triphenylcyclotriphosphane, which can be preserved for some weeks at −20 °C, by iodine oxidation of $K_2(Ph_3P_3)$[10]; this compound soon rearranges to pentaphenylcyclopentaphosphane at room temperature. In the experiments discribed below it was always the pentamer that was used.—Numerous cyclophosphanes with different substituents are accessible, particularly by the practical method of treating dihalophosphanes with metals. Here we shall mention only the compounds used for pyrolysis to phosphinidenes: trifluoromethylcyclophosphane $(CF_3P)_n$ is known as a tetramer ($n=4$) and as a pentamer ($n=5$) and certified by X-ray analysis. Methylcyclophosphane is pentameric, $(CH_3P)_5$. Ethylcyclophosphane is said to occur as a mixture of tetramer and pentamer; our own mass-spectroscopic studies indicate the pentameric structure $(C_2H_5P)_5$[11, 12].

In connection with the pyrolysis experiments the thermal stability should be briefly touched upon. Pentaphenylcyclopentaphosphane, which melts at 150 °C, decomposes slowly above its melting point; triphenylphosphane, tetraphenyldiphosphane, and a polymeric phenylphosphorus $(PhP_{1.7})_n$ have been detected in the pyrolysis products[13, 14]. The trifluoromethylcyclophosphanes are appreciably more stable, the pentamer rearranging at 255 °C to the tetramer which is stable up to 300 °C. Nothing is known about the behavior of methyl- or ethylcyclophosphane toward heat, but they can be distilled in the range 150—200 °C.

If pentaphenylcyclopentaphosphane is irradiated[8] at −40 to −50 °C by a mercury high-pressure lamp, an intense red color develops within a few minutes; this slowly disappears on warming to room temperature. Similar colors are observed on irradiation of frozen alkyl-substituted cyclophosphanes. A sample of pentaphenylcyclopentaphosphane irradiated at 77 °K gave a strongly anisotropic ESR peak; it is not clear whether the asymmetry of the peak is due to anisotropy of the g factor or to a second radical peak lying underneath. The "red pentaphenylcyclopentaphosphane" is presumably a diradical [PhP—$(PhP)_n$—$\dot{P}Ph$] formed by photolysis of the cyclophosphane. The color and the radical peak can be "conserved" at 77 °K.

3.1. Spectroscopic Findings

The formation of PhP ions on electron-impact fragmentation of compounds containing a phenylphosphanediyl group, in particular that of pentaphenylcyclopentaphosphane, has been observed frequently[15, 16], but is of no importance as evidence for free uncharged phosphinidenes. Measurements of the mass spectrum of pentaphenylcyclopentaphosphane in relation to sample temperature and ionization energy[7, 8] have shown that only $(PhP)_5$ and $(PhP)_3$ are present in the gas space of the ion source at 150 °C and 7 eV.

Thermal formation of phenylphosphinidene from the pentamer could be demonstrated by pyrolysis-mass spectrometry[17].

In this technique[18] the sample is vaporized at a pressure of about 10^{-5} torr through a quartz capillary into the ion source of a mass spectrometer and is pyrolyzed by heating of the quartz capillary a short distance in front of the ion source. The pyrolysis products are trapped after about 10^{-3} s by electron-impact ionization and are detected as ions of corresponding mass. The energy of the ionizing electrons is lowered in this process so far that no fragmentation induced by the electron impact occurs, but only ionization of the molecules and radicals present in the gas space. Such a mass spectrum of the pyrolysis products is called a pyrolysis spectrum.

If the spectrum of pentaphenylcyclopentaphosphane is recorded in a mass spectrometer fitted out for pyrolysis and the capillary is heated to 400 °C, one observes an intensity decrease of 40% of the initial value for the mass line of the trimer; at the same time, a series of new peaks appear, among which only those of the dimer $(PhP)_2$ and phenylphosphinidene PhP are of interest for the purposes of this review. Assignment of the peak at $m/e=108$ to the reactive, unstable phenylphosphinidene is supported by the following observation: when the pyrolyzer is switched off, this disappears almost immediately, while the others, derived from stable molecules, decrease over several minutes in accord with the extent to which these compounds diffuse from the ion-source space.

Thermal decomposition of alkyl-substituted cyclophosphanes has been studied by a crossing experiment with pentamethyl- and pentaethylcyclopentaphosphane[11]. Mass-spectroscopic study of a mixture of the two cyclophosphanes has shown that even at 130 °C complete dismutation to all the possible unsymmetrical pentaphosphanes occurred:

$$(RP)_5 + (R'P)_n \xrightarrow{130\,^\circ C} R_4R'P_5 + R_3R'_2P_5 + R_2R'_3P_5 + RR'_4P_5$$
$$R = CH_3;\quad R' = C_2H_5;\quad n = 4,5$$

This dismutation does not occur in the mass spectrometer: If the two cyclophosphanes are introduced separately but simultaneously through two capillaries opening side by side into the HTE system, then under otherwise identical conditions almost the only peaks observed are those due to the original cyclophosphanes. This makes it probable that the cyclophosphanes decompose by way of phosphinidenes. However, it is also conceivable that the reaction proceeds *via* chain-form diradicals. The value of the experiment is that a negative result would have excluded thermolysis to phosphinidenes.

Experiments with pentamethylcyclopentaphosphane[17] in the pyrolysis-mass spectrometer yielded thermal decomposition products only above 800 °C, and rapid fouling of the ion source made the spectra only poorly reproducible. The peak for methylphosphinidene had only slight intensity (Me_3P_3 : MeP = 100 : 4.6).

In a ^{31}P-NMR spectroscopic investigation of a pentaphenylcyclopentaphosphane melt *Fluck* and *Issleib*[19] found two peaks at higher field along with that of the starting material and ascribed one of them to phenylphosphinidene. According to more recent results, one of these signals should certainly be ascribed to hexaphenylcyclohexaphosphane and the other probably to triphenylcyclotriphosphane[20].

3.2. Trapping Reactions of Fragments Produced Thermally or Photochemically from Cyclophosphanes

Considerable amounts of the unstable phenylphosphinidene can be detected mass-spectroscopically in the thermolysis of pentaphenylcyclopentaphosphane at 400 °C[17]. However, transformations of reactive fragments from the pentaphenylcyclopentaphosphane are generally observed already slightly above the melting point (150 °C), at which temperature slow decomposition sets in. The question whether at these low temperatures it is phenylphosphinidene itself that together with trapping reagents undergoes the transformations described in Sections 3.2.1 to 3.2.3, or whether reactive dimers and trimers are reacting, has not yet been solved. In any event, a cyclotrimer is present in the melt at a temperature as low as 150 °C[6-8]. Thermal formation of a dimeric phenylphosphorus from cyclophosphane at 400 °C has been demonstrated by pyrolysis-mass spectroscopy[17]. Finally, all thermal reactions of cyclophosphanes can also be explained by the formation of diradicals that may be formed by cleavage of one bond and correspond to the polysulfur diradicals formed from S_8.

3.2.1. Insertion into Disulfanes, Diarsanes, Diallyl Sulfides and Biphenylene

Unsuccessful attempts to add phenylphosphinidene (obtained by pyrolysis of pentaphenylcyclopentaphosphane) to cyclohexene, tolan, dienes, or electron-rich olefins have been briefly mentioned[21]. However, insertion of PhP into the S—S bond of disulfanes has been effected at 160 °C, giving almost quantitative yields of products of type *(1)*[8, 22]; the course of the reaction can be interpreted as involving phenylphosphinidene as an intermediate:

$$(PhP)_5 \xrightarrow{160\,^\circ C} \{5\ PhP\} \xrightarrow{C_2H_5S\text{-}SC_2H_5} 5\ PhP(SC_2H_5)_2$$

(1)

Analogous insertion reactions of trifluoromethylphosphinidene (from its cyclophosphane) with *e.g.* dimethyldisulfane have also been reported[23]. *Gallagher et al.*[24] succeeded in detecting an interaction between pentaphenylcyclopentaphosphane and diethyldisulfane, giving *(1)*, in the presence of light, even at room temperature. A corresponding insertion of trifluoromethylphosphinidene (from its cyclophosphane) into the As—As bond of tetramethyldiarsane has also been observed[23]. However, the reactions of cyclophosphanes with disulfanes can be alternatively interpreted as occurring by primary attack of alkylsulfur radicals generated from the disulfanes.

Opening of a C—S bond in allyl ethyl sulfide on reaction with pentaphenylcyclopentaphosphane, with the formation of *(2)*, occurs already at 100 °C[14]. Insertion reactions into the

$$[(PhP)_5 \rightleftharpoons 5\ PhP]$$

$$\downarrow C_2H_5\text{-}S\text{-}CH_2\text{-}CH{=}CH_2$$

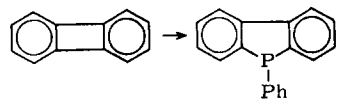
$$PhP(SC_2H_5)_2 + PhP(SC_2H_5)(CH_2\text{-}CH{=}CH_2)$$

(1) *(2)*

C—S bond of allyl sulfides are also known for carbenes[25] and for sulfur itself[26].

However, insertion of phenylphosphinidene into one C—C bond of biphenylene with formation of the phosphole *(3)* occurred only above 400 °C[27], *i.e.* in a temperature region where phenylphosphinidene could be detected by physicochemical methods as formed by thermal dissociation of the cyclophosphane[17]:

$$(PhP)_5 \xrightarrow{400\,^\circ C} PhP +$$

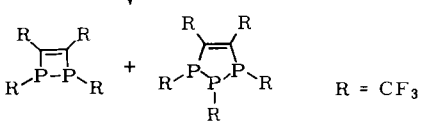


(3)

3.2.2. Addition to Alkynes

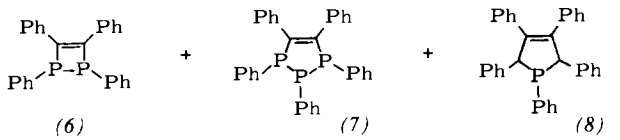
By the action of pentakis(trifluoromethyl)cyclopentaphosphane, which is fairly stable thermally, on hexafluorobutyne *Mahler*[28] obtained the heterocyclic phosphorus compounds *(4)* and *(5)*. The mechanism of the reaction was not investigated. It is not known whether the four-membered ring is formed from the five-membered ring by elimination of a ring member or whether the five-membered ring is formed from the four-membered one by insertion of the phosphinidene into the P—P bond.

$$(RP)_5 + R\text{-}C{\equiv}C\text{-}R \xrightarrow{170\,^\circ C}$$



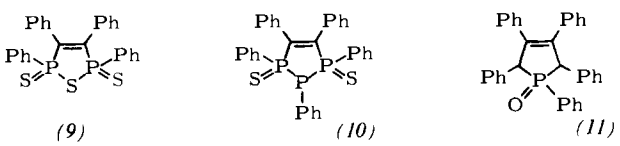
(4) *(5)* R = CF_3

$$(PhP)_5 + Ph\text{-}C{\equiv}C\text{-}Ph \xrightarrow{160\,^\circ C}$$



(6) *(7)* *(8)*

$\downarrow S_8$ $\downarrow S_8$ $\downarrow O_2$



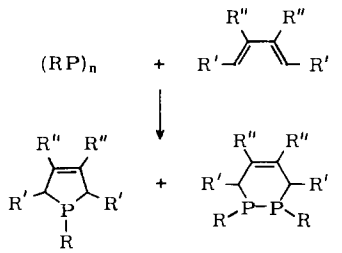
(9) *(10)* *(11)*

Pentaphenylcyclopentaphosphane reacts similarly with tolan at 160 °C[14]. The products *(6)*, *(7)*, and *(8)* were characterized as the stable sulfides *(9)* and *(10)* or the oxide *(11)*. After this reaction it proved impossible to isolate the phosphirene that might be formed by the addition of phenylphosphinidene to tolan, or its dimer, a 1,4-dihydro-1,4-diphosphorin; however, the reaction products are complicated mixtures that may have contained the compounds sought. The possibility cannot be excluded that the phospholene *(8)* is formed by the addition of phenylphosphinidene to tolan, yielding the phosphirene which then adds to tolan with partial uptake of hydrogen.

3.2.3. Addition to 1,3-Dienes

The thermal reaction of aryl- or alkyl-substituted cyclophosphanes with 1,3-dienes is remarkable[8, 29]. A mixture of phospholes *(12)* and 1,2,3,6-tetrahydro-1,2-diphosphorins *(13)* is formed in an overall yield of 30—65%. The five-membered ring compound is not formed as secondary product from the diphosphorin, since the latter is stable at the reaction temperature; the reaction presumably begins with addition of a trimeric organophosphorus species to the diene, this being followed by ring closure to the tetrahydrodiphosphorin with cleavage of aryl- or alkylphosphinidene. The phosphinidene then adds to further amounts of diene.

The scope of this cycloaddition and the corresponding photochemical reaction can be seen from the examples cited below the formulas.



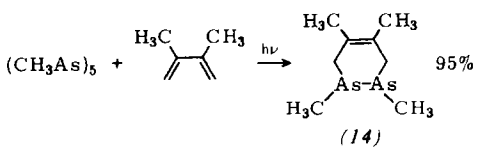
(12) *(13)*

R = CH_3, C_2H_5, C_6H_5
R′ = H, CH_3; R′-R′ = $-CH_2-$, $-CH_2-CH_2-$
R″ = H, CH_3

3.2.4. Photochemical Reactions of the Cyclophosphanes

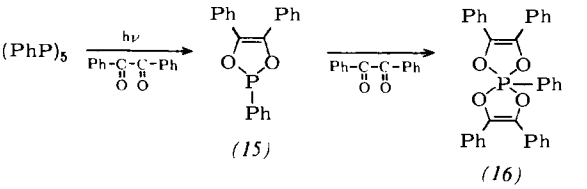
The reaction of cyclophosphanes with disulfanes, yielding dithiophosphonous esters, occurs under the influence of light even at room temperature[24]. Photolytic fragments of cyclophosphanes also add to 1,3-dienes[8, 29]. This photochemical reaction must, however, have a mechanism quite different from that described in Section 3.2.3: it leads exclusively to the formation of tetrahydrodiphosphorins *(13)* in yields of up to 50% *without* the simultaneous formation of a phospholene. The reaction has not failed in any case examined so far. In this photoreaction it is not the diene but the cyclophosphane that is excited: thus, the reaction can be carried out in a Duran vessel with irradiation by a mercury high-pressure lamp, under which conditions no diene excitation is possible. A fragment such as PhP=PPh may be the active intermediate; a peak for an ion of this composition was found in the pyrolysis-mass spectrum from 400 °C upward[17].

Cycloarsanes undergo an analogous cycloaddition[8]. The cycloadduct *(14)* is obtained in 95% yield from pentamethylcyclopentaarsane and dimethylbutadiene. If the tetrahydrodiphosphorins or tetrahydrodiarsenines are assumed to arise by 1,4-cycloaddition of a diphosphorus or diarsenic species to the diene, then these reactions can be considered as analogous to the photochemical formation of endoperoxides.



(14)

Pentaphenylcyclopentaphosphane can also be brought into photochemical reaction with benzil[8]; the reaction presumably leads first to the cyclic phosphonous ester *(15)*, which adds benzil in a "Ramirez reaction" to afford *(16)*. We have not observed thermal formation of this spirocyclic orthophosphonic ester.

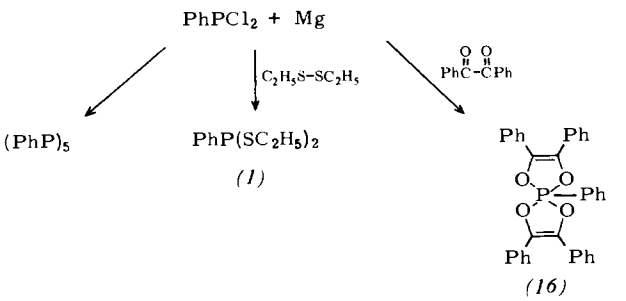


(15) *(16)*

4. Phosphinidenes from P_1-Compounds

Phosphinidene formation can be assumed for any conversion of a P_1-compound into the cyclophosphane. Thus, *Henderson*, *Epstein* and *Seichter*[6] discussed the intermediacy of a phosphinidene in the reaction that they discovered, in which dichlorophosphanes are converted into cyclophosphanes on reaction with metals, in particular with magnesium. Trapping experiments with cyclohexene, tolan, and butadiene were, however, unsuccessful.

Later, however, diethyl phenyldithiophosphonite *(1)* or the spirocyclic orthophosphonic ester *(16)* was isolated in very good yield following the addition of diethyldisulfane or benzil in the reaction of phenyldichlorophosphane with magnesium[8, 22].



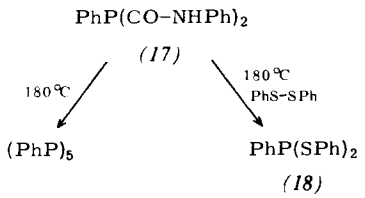
(1) *(16)*

The course of the reaction can be understood by assuming phenylphosphinidene as an intermediate, but it can be explained just as convincingly by primary formation of magnesium bis(ethanethiolate) or α,β-stilbenediolate, which then reacts with phenyldichlorophosphane to give *(1)* and *(16)*, respectively. There is, however, no sign of the formation of a thiolate or stilbenediolate, yet this cannot be excluded, at least on the surface of the metal. Production of phosphinidenes in the reaction of dichlorophosphanes is also indicated by the findings on polarographic two-electron reduction of phenyldichlorophosphane[30].

Gallagher and *Jenkins*[24] have formulated phenylphosphinidene as an intermediate in the formation of pentaphenylcyclopentaphosphane from phenylphosphonous anhydride. On addition of diethyldisulfane the phenyldithiophosphonous ester is formed this case too (however, the limitations mentioned in Section 3.2.1 apply also for this trapping reaction). If the reaction is allowed to proceed in the presence of benzil then a little *(16)* and a large amount of benzoin [the hydrolysis product of *(16)*] can be isolated.

Similar caution is necessary for the trapping reaction of phenylphosphinidene with diphenyldisulfane, yielding *(18)*, in the thermal formation of cyclophosphane from *(17)*[31]. In this reaction even at 180 °C it is necessary to take into

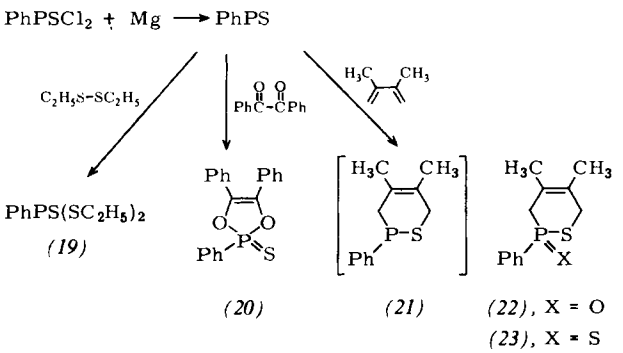
consideration possible cleavage of the cyclophosphane by phenylsulfur radicals from the disulfane.



Phosphinidine as an intermediate can be assumed in the reaction of phenylphosphane and carbonyldiimidazole forming pentaphenylcyclopentaphosphane[36].

5. Phosphinidene Oxide and Phosphinidene Sulfide

Japanese authors[32] have attempted to detect phenylphosphinidene oxide and sulfide in the reactions of $PhPOCl_2$ and $PhPSCl_2$ with magnesium. The trapping agents used were the disulfanes and benzil used previously by us in experiments with phosphinidenes. Although in the event *(19)* and *(20)* were found, the same limitations apply to the strength of the evidence about the mode of their formation as were discussed in Sections 3.2.1 and 4. In the reaction in the presence of dimethylbutadiene the heterocycles *(22)* and *(23)* were isolated. The critical reader will not be convinced by the explanation that compound *(21)* is formed primarily by cycloaddition and is converted into *(22)* and *(23)* by the action of atmospheric oxygen and $PhPSCl_2$, respectively[*].

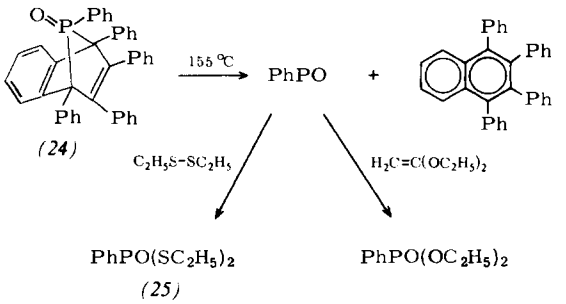


Tomioka et al.[34] obtained phenylphosphonous monoester on irradiation of 1-phenylphospholene oxide in alcohols. The reaction mechanism proposed involved insertion of PhPO into the O—H bond of the alcohol, which appears unlikely in view of the large dissociation energy of this bond.

Note should be taken of the attempts made by American authors[35] to trap the phenylphosphinidene oxide split off from the 7-phosphanorbornadiene derivative *(24)* at 155 °C with the formation also of tetraphenylnaphthalene. Experiments with alkynes and alkenes were unsuccessful. In the presence of diethyldisulfane the product *(25)* was isolated and its formation was interpreted by insertion of PhPO into the S—S bond.

[*] The sulfur compound *(23)* was obtained previously by cycloaddition of phenyldithiophosphinic anhydride to dimethylbutadiene [33]. It is possible that the formation of *(23)* in the reaction formulated above occurs by way of phenyldithiophosphonic anhydride formed from $PhPSCl_2$.

The objection raised above applies again here against the assumption that phenylphosphinidene oxide is inserted into the O—H bond of alcohols.



Drs. I. Boie, A. Ecker, C. Osterroht, and R. Schröer participated in our work. The mass-spectroscopic investigations were performed by Prof. H. Achenbach and Prof. H. F. Grützmacher. Financial assistance was kindly provided by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and later by the Österreichischer Fonds zur Förderung der wissenschaftlichen Forschung.

Received: December 2, 1974 [A 70 IE]
German version: Angew. Chem. 87, 535 (1975)
Translated by Express Translation Service, London

[1] *O. M. Nefedow* and *M. N. Manakow*, Angew. Chem. 78, 1039 (1966); Angew. Chem. internat. Edit. 5, 1021 (1966).
[2] *W. H. Atwell* and *D. R. Weyenberg*, Angew. Chem. *81*, 485 (1969); Angew. Chem. internat. Edit. *8*, 469 (1969).
[3] *H. E. Gunning* and *O. P. Strausz*, Advan. Photochem. *4*, 1 (1966).
[4] *U. Schmidt* and *Ch. Osterroht*, Angew. Chem. 77, 455 (1965); Angew. Chem. internat. Edit. *4*, 437 (1965); *U. Schmidt, K. Kabitzke, I. Boie*, and *Ch. Osterroht*, Chem. Ber. *98*, 3819 (1965).
[5] Review: *L. Maier*, Fortschr. Chem. Forsch. *8*, 1 (1967). The papers reported therein are not cited below.
[6] *W. A. Henderson Jr., M. Epstein*, and *F. S. Seichter*, J. Amer. Chem. Soc. *85*, 2462 (1963).
[7] *M. Baudler, K. Kipker*, and *H. W. Valpertz*, Naturwissenschaften *53*, 612 (1966).
[8] *U. Schmidt, I. Boie, Ch. Osterroht, R. Schröer*, and *H. F. Grützmacher*, Chem. Ber. *101*, 1381 (1968).
[9] *M. Baudler* and *M. Bock*, Z. Anorg. Allg. Chem. *395*, 37 (1973).
[10] *K. Issleib* and *E. Fluck*, Angew. Chem. *78*, 597 (1966); Angew. Chem. internat. Edit. *5*, 587 (1966).
[11] *U. Schmidt, R. Schröer*, and *H. Achenbach*, Angew. Chem. *78*, 307 (1966); Angew. Chem. internat. Edit. *5*, 316 (1966).
[12] *A. H. Cowley* and *R. P. Pinnel*, Inorg. Chem. *5*, 1459 (1966); *L. R. Smith* and *J. L. Mills*, J. C. S. Chem. Commun. *1974*, 808.
[13] *W. Kuchen* and *H. Buchwald*, Chem. Ber. *91*, 2296 (1958).
[14] *A. Ecker* and *U. Schmidt*, Chem. Ber. *106*, 1453 (1973).
[15] *J. M. Miller*, J. Chem. Soc. *A 1967*, 828.
[16] *B. Zeeh* and *J. B. Thomson*, Tetrahedron Lett. *1969*, 111.
[17] *H. F. Grützmacher, W. Silhan*, and *U. Schmidt*, Chem. Ber. *102*, 3230 (1969).
[18] *H. F. Grützmacher* and *J. Lohmann*, Liebigs Ann. Chem. *705*, 81 (1967).
[19] *E. Fluck* and *K. Issleib*, Z. Naturforsch. *21 b*, 736 (1966).
[20] *M. Baudler* and *E. Fluck*, private communication.
[21] Cf. [6], footnote 10.
[22] *U. Schmidt* and *Ch. Osterroht*, Angew. Chem. 77, 455 (1965); Angew. Chem. internat. Edit. *4*, 437 (1965).
[23] *A. H. Cowley*, J. Amer. Chem. Soc. *89*, 5990 (1967); *A. H. Cowley* and *D. S. Dierdorf, ibid. 91*, 6609 (1969).
[24] *M. J. Gallagher* and *I. D. Jenkins*, J. Chem. Soc. *C 1966*, 2176; *C 1971*, 593.
[25] Review: *W. Kirmse*: Carbene Chemistry. Academic Press, New York 1971, p. 439; *W. Ando, S. Kondo, K. Nakayama, K. Ichibori, K. Kohoda, H. Yamato, I. Imai, S. Nakaido*, and *T. Migita*, J. Amer. Chem. Soc. *94*, 3870 (1972).
[26] *R. D. Baechler, J. P. Hummel*, and *K. Mislow*, J. Amer. Chem. Soc. *95*, 4442 (1973).
[27] *A. Ecker* and *U. Schmidt*, Monatsh. Chem. *102*, 1851 (1971).
[28] *W. Mahler*, J. Amer. Chem. Soc. *86*, 2306 (1964).
[29] *U. Schmidt* and *I. Boie*, Angew. Chem. *78*, 1061 (1966); Angew. Chem. internat. Edit. *5*, 1038 (1966).

[30] *R. E. Dessy, T. Chivers*, and *W. Kitching*, J. Amer. Chem. Soc. *88*, 467 (1966).
[31] *H. Fritzsche, U. Hasserodt*, and *F. Korte*, Angew. Chem. *75*, 1205 (1963); Angew. Chem. internat. Edit. *3*, 64 (1964).
[32] *S. Nakayama, M. Yoshifuji, R. Okazaki*, and *N. Inamoto*, Chem. Commun. *1971*, 1186; J. C. S. Perkin I *1973*, 2065, 2069.
[33] *A. Ecker, I. Boie*, and *U. Schmidt*, Angew. Chem. *83*, 178 (1971); Angew. Chem. internat. Edit. *10*, 191 (1971); Monatsh. Chem. *104*, 503 (1973).
[34] *H. Tomioka, Y. Hirano*, and *Y. Izawa*, Tetrahedron Lett. *1974*, 1865.
[35] *J. K. Stille, J. L. Eichelberger, J. Higgins*, and *M. E. Freeburger*, J. Amer. Chem. Soc. *94*, 4761 (1972).

Methods for the Preparation of Bridgehead Olefins[**]

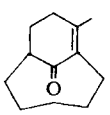
New synthetic methods (11)

By Reinhart Keese[*]

During the past eight years, bridgehead olefins have attracted rapidly increasing attention. In view of their significance with regard to the stereochemistry of alkenes, the study of certain reaction mechanisms, and the nature of the double bond, detailed research into this structural type appears highly desirable. Bridgehead olefins represent connective linkages between olefins in the ground state and species which can arise in the deactivation of photochemically excited alkenes and cycloalkenes and also contribute to our understanding of the structural conditions prevailing during *cis-trans* isomerization of alkenes.

1. Introduction

In the course of experimental work subsequent to the structural elucidation of (+)-camphor, *Bredt* noted that all the reactions in bicyclic ring systems which should lead to a bridgehead olefin either failed to take place or yielded other products. These findings, known as *Bredt*'s rule, played an important role in the structure determination of unsaturated bi- and polycyclic natural products. Furthermore, this rule prompted experimental work which led to a more precise knowledge of the size of bicyclic ring systems which are compatible with a bridgehead double bond. The synthesis of 8-methylbicyclo[5.3.1]undec-7-en-11-one and related studies by *Prelog* towards the end of the 1940's[1] represented a climax of this development.



In 1950 this period came to a rather abrupt end with a survey of the essential aspects of the Bredt rule by *Fawcett*[2]. Interest in bridgehead olefins[***] was only reawakened in 1956 when *Edwards*[3] found that lycoctonamic acid, which contains a 2-oxobicyclo[3.3.1]nonane-1-carboxylic acid as a structural component, undergoes ready decarboxylation This observation prompted *Miller* to study the decarboxylation of the corresponding unsubstituted β-keto acid[4]. After a brief induction period, a series of important studies were published from 1967 which led to the isolation of bicyclo[3.3.1]non-1-ene *(2)*[5, 6]; in 1971/72 it was proved that the classical bridgehead olefin 1-norbornene (bicyclo[2.2.1]hept-1-ene) *(106)* can exist as a reactive intermediate[7]. Very recently, intense research has been directed to this exciting area with a focus on problems of the stereochemistry of olefins and the structural course of certain reactions as well as on the electronic nature of highly strained double bonds. This article will deal with some general aspects of *Bredt*'s rule[*] and discuss methods and structural prerequisites for the preparation of bridgehead olefins.

The Bredt rule[8] may be briefly summarized[**] as follows: *In small bi- and polycyclic ring systems a normal* (usual) *double bond cannot emanate from the bridgehead.* A usual double bond is characterized geometrically by two doubly bonded carbon atoms and four ligands all of which lie in a common plane. Twisting and changes in bond lengths and angles lead to a geometrical distortion which is accompanied by strain[***]. Twisting and pyramidalization (= out of plane or wagging deformation) of the ligands produce a structure corresponding to the typical geometry of a bridgehead double bond in a Bredt olefin. To a first approximation it can be assumed that the strain is largely localized in the distorted double bond. Thus the maximum strain of a bridgehead olefin is given by the rotational barrier to *cis-trans* isomerization of an olefin (*ca.* 65 kcal/mol)[10]. However, if it is borne in mind that bi- or polycyclic systems are often also strained without even having a bridgehead double bond then it is conceivable that the overall strain of a bridgehead olefin makes it possible for it to decompose to a dicarbene. Insofar as the Bell-Evans-Polanyi principle[11] or the Hammond postulate[12] are valid, the Bredt rule applies to transition states of reactions in which highly strained bridgehead olefins are formed.

[*] Dr. Reinhart Keese
Laboratorium für organische Chemie,
Eidgenössische Technische Hochschule
CH-8006 Zürich (Switzerland)
Present address:
Institut für organische Chemie der Universität Bern
CH-3000 Bern 9, Postfach 89 (Switzerland)

[**] Based on the Habilitationsschrift of *R. Keese*, ETH Zürich 1974.

[***] The common structural feature of bridgehead olefins is a bi- or polycyclic skeleton with a double bond originating from the bridgehead. "Bredt olefins" are bridgehead olefins having a bridged structure such as *(2)* and *(7)*; they differ structurally (but not necessarily with regard to the magnitude of their strain energy) from those having annelated ring systems, *i.e.* with a "zero bridge" as in *(148)* and *(149)* (cf. Section 2.11, and also ref. [16]).

[*] Other review references are given in refs. [2, 9, 16, 32].

[**] A detailed discussion is given in *R. Keese*, Habilitationsschrift, ETH Zürich 1974.

[***] The concept of strain is based on comparison of energy with that of a standard molecule, whereas the energy of vibronically excited molecules is given relative to the vibronic ground state of the same species.

Thus, for example, elimination reactions initiated by rapid formation of a carbenium ion must possess a particularly high activation energy if strained bridgehead olefins are formed; the poor π-conjugation of a twisted double bond must manifest itself in the transition state of the reaction leading to its formation. This formulation is essentially identical to the stereoelectronic control[13] of such elimination reactions.

The stereoelectronic restrictions of the Bredt rule also extend to intramolecular 1,2-hydride shifts in bi- and polycyclic carbenium ions[14] and similar rearrangements (cf. Section 2.9). Concerted bimolecular eliminations of HX depend upon the dihedral angle between the hydrogen and the leaving group X. The reactions proceed most rapidly for syn- or antiplanar orientations, and least rapidly for a dihedral angle of 90°[15]. During formation of bi- and polycyclic bridgehead olefins by E_2 reactions it must be considered that conformational mobility of the rings, especially the ring bearing the leaving group, can in some circumstances affect the dihedral angle in a manner crucial to the course of reaction. Nevertheless, from the standpoint of the Bredt rule one must consider whether concerted bimolecular eliminations are possible at all if the bonds to be cleaved are mutually orthogonal.

Likewise, we are almost completely ignorant of stereoelectronic prerequisites of eliminations which are initiated by fast deprotonation of carbanion formation prior to the rate determining step (cf., however, Section 2.7).

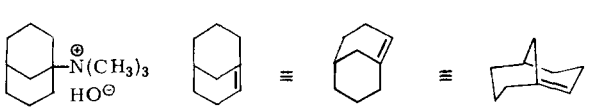
The Bredt rule also embraces bicyclic bridgehead olefins in which one or two heteroatoms of the first or second row of the Periodic Table participate in the double bond and the special class of "Bredt compounds", as defined by *Köbrich*[16], which are stable at room temperature [cf. *(148)* and *(149)* in Section 2.11]. Participation of second row elements leads, for instance, to bi- or polycyclic alkylidenephosphoranes and -sulfuranes (cf. Section 2.5). Replacement of carbon by elements of higher atomic number, especially those of the transition series, is particularly relevant to the nature of the double bond and must also be viewed in relation to problems of bonding in metal-carbene complexes[17].

2. Methods for Preparation of Bridgehead Olefins

2.1. Eliminations

The typical elimination reactions have considerably extended out knowledge about bridgehead olefins in which the double bond is formally located in a seven or preferably larger-membered ring.

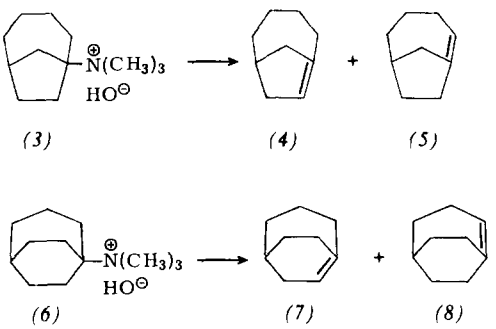
In particular, the Hofmann elimination has proved to be a powerful method for preparing bicyclo[3.3.1]non-1-ene *(2)* and its analogs in which the methylene bridge is replaced by a heteroatom[18].



(1) *(2)* *(2a)* *(2b)*

Degradation reactions have established beyond all doubt that *(2)* is indeed a bridgehead olefin. From a mechanistic point of view it would be important to establish whether or not *(2)* is formed by *syn* elimination from the less stable chair-boat conformation of *(1)*[19]; if so the E_2 reaction would be subject to stereoelectronic acceleration. Compound *(2)* must possess the quasi-boat-chair conformation *(2a)* for the bridgehead double bond to be *trans* in the eight-membered ring and *cis* in the six-membered ring. Predictably, *(2)* is an olefin exhibiting enhanced reactivity which appears to favor *syn* additions from the *exo* side.

Under comparable conditions the constitutionally isomeric bicyclic ammonium bases *(3)* and *(6)* undergo elimination to yield a mixture of the bridgehead olefins *(4)* and *(5)*, and *(7)* and *(8)*, respectively[20].



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

(6) *(7)* *(8)*

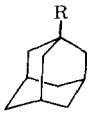
The preferential formation of the presumably less stable compound *(4)* [*(4)* and *(5)* are formed in the ratio of 5:1 respectively] during the thermolysis *(3)* is attributable to the stereoelectronically favored *syn*-elimination in the five-membered ring. The third possible olefin would be a derivative of *trans*-cyclohexene and as such would possess considerable strain energy. Thus its non-occurrence seems reasonable. The olefins *(7)* and *(8)*, which are comparable to *trans*-cycloheptene, possess a much lower thermal stability than *(4)* and *(5)*, corresponding to *trans*-cyclooctene. *(7)* and *(8)* dimerize so rapidly that all attempts to isolate the pure compounds have so far failed. In all cases of Hofmann eliminations cited the desired bicycloalkenes were accompanied by various amounts of the parent tertiary amines from which the quaternary ammonium salts had been prepared. Pyrolysis of *(9)* for example regenerates the tertiary amine *(10)* in up to 99% yield[21].

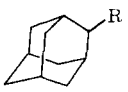
(9), R = $\overset{\oplus}{N}(CH_3)_3$ $OH^{\ominus}$
(10), R = $N(CH_3)_2$

(11), R = $\overset{\oplus}{N}(CH_3)_3$ $OH^{\ominus}$
(12), R = $\overset{\oplus}{N}(CH_3)_2O^{\ominus}$

Thermolysis of the homoadamantane derivatives *(11)* and *(12)* also predominantly afforded products most probably formed from nucleophilic substitution and Stevens or Meisenheimer rearrangement[22].

Nevertheless, in either case four additional saturated hydrocarbons were isolated, of which two can be regarded as direct dimerization products of 3-homo-1-adamantene *(131)* (cf. Section 2.9). It is hardly surprising then, that adamantene itself, which is comparable with *trans*-cyclohexene, is not formed either by Hofmann elimination from *(13)* or from *(16)*. Furthermore *(14)* merely rearranges to the dithiocarbonic ester *(15)* under the conditions of the Tschugaeff reaction[23] (cf. Sections 2.3 and 2.7).

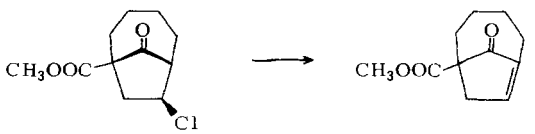




(13), R = $\overset{\oplus}{N}(CH_3)_3\ OH^{\ominus}$ *(16)*, R = $\overset{\oplus}{N}(CH_3)_3\ OH^{\ominus}$
(14), R = O–C(S)–S–CH_3
(15), R = S–C(O)–S–CH_3

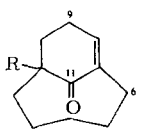
In this context it should also be mentioned that pyrolysis of *O*-bicyclo[3.3.1]non-1-yl *O*-*p*-tolyl thiocarbonate does not give the bridgehead olefin *(2)* but yields exclusively the more stable bicyclo[3.3.1]non-2-ene[24].

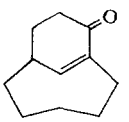
In certain cases however bridgehead olefins of this kind can be formed not only by Hofmann elimination but also by base-induced dehydrohalogenation. The 7-*exo*-chloro keto ester *(17)* affords a thermally labile bicyclic enone which has been assigned structure *(18)*[25].

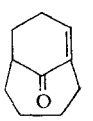


(17) *(18)*

If the stability of *trans*-cyclooctene and of bicyclo[3.3.1]non-1-ene are taken as a yardstick, then bicyclo[5.3.1]undecane is the smallest bicyclic ring system for which all three isomeric bridgehead olefins should be capable of isolation. 8-Methylbicyclo[5.3.1]undec-7-en-11-one has been prepared previously[1]; and *(19)*, *(20)*, and *(22)* have recently become accessible by base-catalyzed elimination[26].

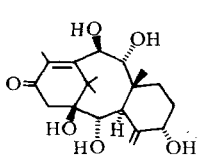


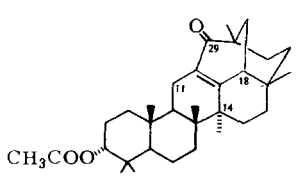




(19), R = $CO_2C_2H_5$ *(22)* *(23)*
(20), R = H
(21), R = CONH–C_6H_4Cl

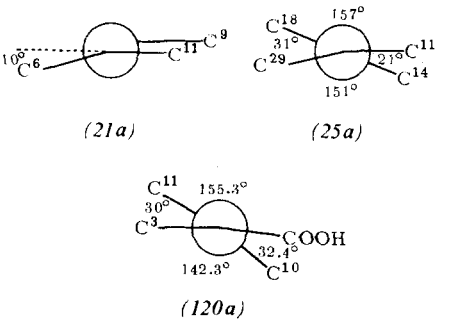
As expected, *(22)* is less stable than *(20)* and undergoes rapid dimerization at room temperature; in this respect it resembles the photochemically accessible *trans*-2-cyclooctenone[27] more than *trans*-cyclooctene. The diterpene taxicin I *(24)* also belongs to the family of bicyclo[5.3.1]undec-1-ene[28]. Compound *(23)*, which contains one ring member less than *(24)*, is formed on pyrolysis of 10-oxobicyclo[4.3.1]-dec-7-yl benzoate[29].





(24) *(25)*

The X-ray structure analysis of *(21)*[30], a modified precursor of *(20)*, illustrates the geometrical changes affecting a double bond in a bridgehead olefin discussed in the introduction. In addition to a torsional angle of *ca.* 32° between the carbonyl group and the double bond, twisting of the double bond is also observed, accompanied by pyramidalization and concomitant change of the bond angle [Fig. 1, formula *(21a)*]. A similar situation is encountered in the ketone *(25)* accessible from the triterpene catonic acid[31] and in the bridged decapentaene *(120)*. Apart from the specific effects of the carbonyl group a deformation of this kind must be a common feature of all strained bridgehead olefins [cf. Fig. 1, formulas *(25a)* and *(120a)*].

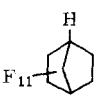


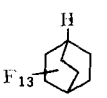
(21a) *(25a)*

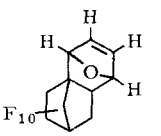
(120a)

Fig. 1. Concerning the structure of *(21)*, *(25)*, and *(120)*.

The specific and structural situation, of course, also affects the spectroscopic properties of bicyclic enones having a bridgehead double bond. These aspects have recently been the subject of a detailed discussion[32]. The presence of α-carbonyl groups is not absolutely essential for base-induced deprotonations at the bridgehead of bicyclic ring systems. Reaction apparently also proceeds after replacement of all methylene protons by fluorine (cf. also Section 2.5). The exceptional properties of the fluorine substituents increase the acidity to such an extent that *(26)* and *(27)* readily incorporate deuterium at the bridgehead in basic solution[33].







(26) *(27)* *(28)*

It is remarkable that *(27)* is merely deprotonated by methyllithium at room temperature, whereas under the same conditions *(26)* eliminates HF and in the presence of furan affords two apparently inseparable adducts for which the structure *(28)* has been postulated[32]. It would be interesting to know the minimum number and positions of the fluorine substituents necessary for deprotonation and elimination at the bridgehead of bicyclo[2.2.2]octane and bicyclo[2.2.1]heptane systems.

2.2. Bridgehead Olefins Having Adjacent Heteroatoms

Worthy of particular mention are olefins having the structure of bicyclo[3.3.1]non-1-ene *(2)* in which the methylene bridge has been replaced by heteroatoms. The compounds *(29)*, *(30)*, and *(31)*, accessible from 5-substituted cyclooctanones, undergo base-catalyzed reaction to give the bridge-

(29), X = N–CH_3, Y = Cl *(32)*, X = N–CH_3
(30), X = O, Y = OSO_2CH_3 *(33)*, X = O
(31), X = S, Y = OSO_2CH_3 *(34)*, X = S

head olefins *(32)*, *(33)*, and *(34)*, respectively[34]. They should belong to the *trans*-cyclooctene family and accordingly possess a quasi-boat-chair conformation.

Table 1 lists some spectroscopic data of these compounds. The NMR signal of the olefinic proton in the bicyclic compounds *(2)* and *(32)*—*(34)* is shifted downfield by varying amounts relative to standard values of corresponding open-chain olefins[35]. Attempts to parametrize these differences with the aid of simple models of conjugational interaction do not appear very conclusive.

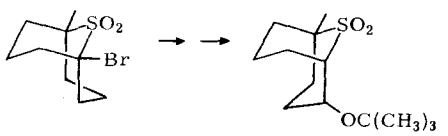
Table 1. Spectroscopic data of selected bridgehead olefins.

	IR	^{1}H-NMR		UV	
	ν_{max} [a] [cm^{-1}]	δ [b] [ppm]	J [Hz]	λ_{max} [c] [nm]	ε
(2)	1620 w [d]	5.62 t	7 [e]	206	7500
(32)	1620 m [d]	5.86 t	6 [f]	240	1667
				184 [g]	
(33)	1640 w [e]	5.74 t	6 [e]	190	6200
(34)	1600 w [e]	6.25 t	7 [e]	206	7500

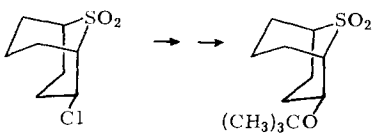
[a] C=C stretching frequency; w, weak; m, medium.
[b] Olefinic proton; t, triplet.
[c] In pentane; ε, molar extinction coefficient.
[d] Liquid.
[e] In carbon tetrachloride.
[f] In chloroform.
[g] End absorption.

The heteroatoms clearly influence the reactivity of the bridgehead double bonds. Thus addition of acetic acid to *(2)* at 25 °C is complete in less than two minutes while the half-reaction time with *(33)* is 68 h. The nonbonding electron pairs on the oxygen of *(33)* are apparently incapable of stabilizing adjacent carbenium ions by conjugation (cf. Section 2.6), as in the case of open-chain enol ethers.

Base-catalyzed dehydrohalogenation of *(35)* and *(37)* in *tert*-butyl alcohol unexpectedly affords products having differing configurations of the *tert*-butoxy groups[34b]. These surprising results are explained in terms of conformational differences.



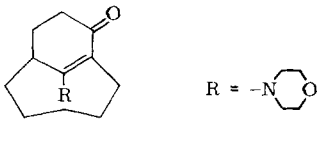
(35) *(36)*



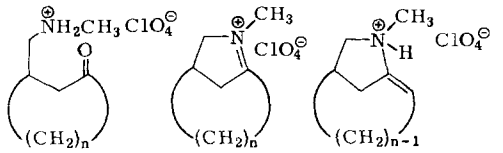
(37) *(38)*

Bicyclic enamine ketones with a bridgehead double bond are accessible by reaction of α,β-unsaturated acyl chlorides with medium and large ring enamines. Thus reaction of acryloyl chloride and *N*-(1-cyclooctenyl)morpholine affords *(39)*, which is considerably more stable than *(22)*. Enamines of cycloheptanone merely afford bicyclo[4.3.1]-decane-7,10-dione[36].

Bicyclic immonium salts having a carbon-nitrogen double bond at the bridgehead are formed by intramolecular condensation of type *(40)* if $n \geq 5$[37]. As in the case of the enamine ketones, ring size is again critical: the amino ketone *(40c)*



(39)

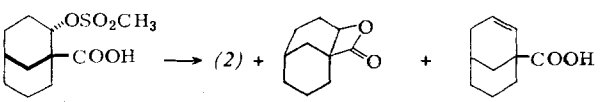


(40a), n = 9 *(41a)*, n = 9 *(42)*, n = 9
(40b), n = 5 *(41b)*, n = 5
(40c), n = 4

can no longer cyclize. The immonium salt *(41a)* undergoes base-induced reaction to give *(42)* whereas *(41b)* reacts in a different manner.

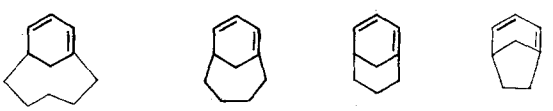
2.3. Fragmentations

It was mentioned in the introduction that *(2)* is accessible from *(1)* by Hofmann elimination. At about the same time *(2)* was also found to be formed by fragmentation reactions[38]. Thus the potassium or sodium salt of *(43)*, on heating in dimethyl sulfoxide, affords the strained olefin *(2)*, as well as the β-lactone *(44)* and the unsaturated carboxylic acid *(45)*. Since *(45)* is stable under the reaction conditions *(2)* must be formed directly from *(43)*. Presumably one of the less stable conformations of *(43)* undergoes fragmentation. The β-lactone *(44)* also decomposes above 260 °C to give *(2)* but is photochemically inert.



(43) *(44)* *(45)*

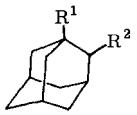
It is remarkable that the diene *(46)* is formed in good yield on reaction of 2-cyclooctenone with propenylidenetriphenylphosphorane in a one-pot, multistep process, terminated by an intramolecular Wittig reaction[39].

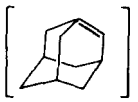


(46) *(47)* *(48)* *(49)*

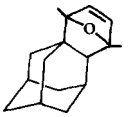
While *(47)* is still isolable at room temperature, *(48)* and *(49)* dimerize on formation. They can however be trapped by [4+2]-cycloaddition with 1,3-diphenylisobenzofuran or furan. It has recently also proved possible to prepare *(2)* by intramolecular Wittig reaction[40]. The long-sought adamantene *(53)*, which can be regarded as a methylene-bridged bicyclo[3.3.1]non-1(9)-ene having the double bond in the short bridge, definitely belongs to the *trans*-cyclohexene structural type. A first indication that it can exist was provided by the observation that thermally induced fragmentation of the di-*tert*-butyl ester of 1,2-adamantanediperoxycarboxylic acid *(50)*, in the presence of 2,5-dimethylfuran, affords products having the constitution *(54)*[41].

It would seem that the success of this fragmentation method is crucially dependent upon the comparable rates of cleavage of the two peroxy ester groups which are certainly frequently encountered in the formation of unstrained double bonds[42].





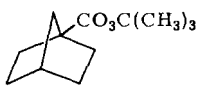
(53)



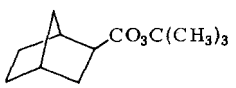
(54)

(50), $R^1 = R^2 = C(O)-O-O-C(CH_3)_3$
(51), $R^1 = O-C(O)-CH_2C_6H_5$, $R^2 = H$
(52), $R^1 = H$, $R^2 = O-C(O)-CH_2C_6H_5$

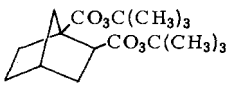
Preliminary measurements show that the fragmentation of the *tert*-butyl ester of 2-adamantaneperoxycarboxylic acid is about 10 times slower than that of 1-adamantaneperoxycarboxylic acid[41]. If the difference in reaction rate of the peroxy ester groups is even greater, as in the case of (55) and (56)[43],



(55)

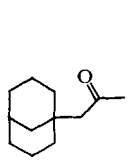


(56)

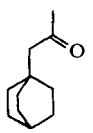


(57)

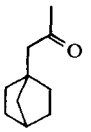
then no evidence for the expected bridgehead olefin 1-norbornene (106) is obtained from thermally induced fragmentation of the diester (57)[44]. Photochemically induced fragmentation of 1-adamantyl phenylacetate (51) and the 2-adamantyl ester (52) in monodeuteriomethanol gave 1% of 1-methoxyadamantane having comparable deuterium contents in both cases. Since only 1-substituted adamantane derivatives are formed on photolysis of 1- and 2-substituted adamantyl esters, a common intermediate is postulated, *i. e.* adamantene (53)[45] (cf. Sections 2.1 and 2.7).



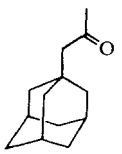
(58)



(59)



(60)

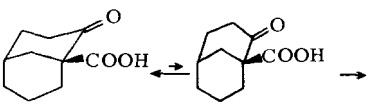


(61)

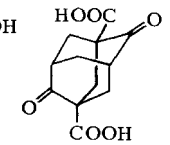
Attempts to generate bicyclic bridgehead olefins by Norrish type II cleavage have so far been unsuccessful. Only cyclobutanol derivatives can be detected on photolysis of the ketones (58)—(61)[46,47]. Apparently fragmentation of the 1,4-diradical formed by γ-H abstraction during the photolysis is a stereoelectronically highly demanding reaction.

2.4. Decarboxylations

All bi- and polycyclic β-keto acids which should form a bridgehead enol of the *trans*-cyclopentene or *trans*-cyclohexene series either fail to undergo decarboxylation or do so only with extensive modification of the carbon skeleton[32,48][*]. The limit imposed by ring size seems to be relatively clear-cut since all known homologs potentially capable of forming an enol of the *trans*-cycloheptene series readily eliminate carbon dioxide above 200 °C[49]. For stereoelectronic reasons β-keto acids have to undergo decarboxylation in a conformation having a dihedral angle between the carbonyl and the carboxyl group of the order of 90°. This arrangement is a prerequisite for maximum possible conjugational stabilization of the incipient carbanion by the π-system of the adjacent carbonyl group. If a conformational change of this kind is impossible, as in the case of (64), the corresponding enol is not formed[50]. It is therefore highly probable that (62) can only decarboxylate to (63) in the conformation (62b).

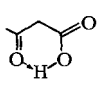


(62a) (62b) (63)

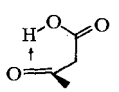


(64)

According to the generally accepted mechanism of decarboxylation of a β-keto acid, carbon dioxide is eliminated from the cyclic structure (65) having an intramolecular hydrogen bond to form the enol[51]. However, consideration of models reveals that a dihedral angle of 90° is only compatible with an intramolecular hydrogen bond involving the π-system of the carbonyl group, as in (66), and not the lone pair of the oxygen, as in (65). Moreover, such a hydrogen bond is also required for a Hückel aromatic transition state for decarboxylation.

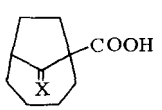


(65)

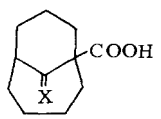


(66)

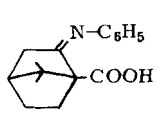
If the carbonyl group is replaced by an imino group, decarboxylation is accelerated so drastically that it has so far proved impossible to detect simple β-imino carboxylic acids. In contrast, β-imino carboxylic acids having a bicyclic skeleton can be isolated but decarboxylate about 10^6 times faster than comparable β-keto acids (Table 2)[52]. However, this effect is not pronounced enough to be able to induce the acids (69) and (70) to eliminate carbon dioxide.



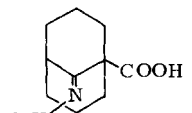
(67a), X = O
(67b), X = N–C_6H_5



(68a), X = O
(68b), X = N–C_6H_5



(69)



(70)

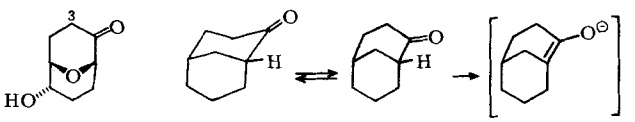
Table 2. Concerning the decarboxylation of bicyclic keto and imino acids.

	Ring size of the potential enol	Decarboxylation [°C]	$\Delta H^{\neq}$ [kcal/mol]
(67a)	7	150—220	38.7
(67b)	7	69—86	26.5
(68a)	7	130—150	36.7
(68b)	7	78—93	26.4
(69)	6	not below 300 °C	—
(70)	6	not below 300 °C	—

[*] Optically active 2,5-dioxobicyclo[2.2.2]octane-1,4-dicarboxylic acid racemizes on monodecarboxylation, thus ruling out intermediacy of the bridgehead enol.

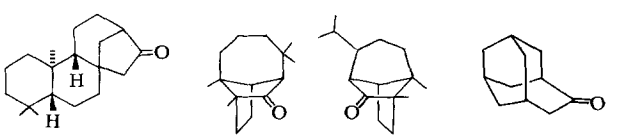
2.5. Deprotonations

On acid catalysis a ketone affords an enol which should be structurally and energetically identical to that formed from decarboxylation of the corresponding β-keto acids. Accordingly, the deprotonation of a ketone should be subject to the same conformational and stereoelectronic criteria as the elimination of carbon dioxide from β-keto acids. No systematic studies designed to support this relationship have been reported. Apart from an exceptional case which proceeds *via* a different mechanism[53], there appear to be no bicyclic ketones which undergo acid-catalyzed deuteration at the bridgehead if the carbon ring of the potential enol is eight-membered or smaller[54]. Acid catalyzed enolization of ketones (or at least that of bicyclic ketones) appears to be structurally more selective than base-induced deprotonation. Thus in acidic deuterium oxide *(71)* merely exchanges the two protons on C-3 whereas deuterium is also incorporated at the bridgehead in basic solution[55]. This difference can be attributed both to the comparatively slower acid-catalyzed reaction and to the formation of a more rigid enol[56].



(71) *(72a)* *(72b)* *(73)*

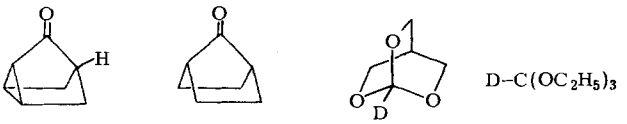
The minimum size of the carbocycle for which bridgehead enolization can still be observed is 7. Thus *ent*-17-norcauran-16-one *(74)*, longicamphor *(75)*, and especially copacamphor *(76)* can readily be deuterated at the bridgehead albeit under drastic basic conditions[57, 58].



(74) *(75)* *(76)* *(77)*

Deprotonation is affected not only by ring size but also by the conformation of the bicyclic skeleton, especially that of the carbonyl-containing ring. Although compounds having a bicyclo[3.3.1]nonane structure appear to prefer a double chair conformation in the crystalline state[59], formation of the bridgehead enolate ion of *(72)* is stereoelectronically favored only in the chair-quasi-boat geometry *(72b)* (cf. Section 2.4). The bridgehead enolate ion itself should largely retain the conformation *(73)* in the case of strong double bond character. Additional alkylene bridges which restrict the conformational mobility only slightly or hardly at all, do not interfere with base-induced bridgehead deprotonation. Presumably the ketones *(74)*—*(76)*, unlike *(77)*[60], can be deuterated at the bridgehead for this reason.

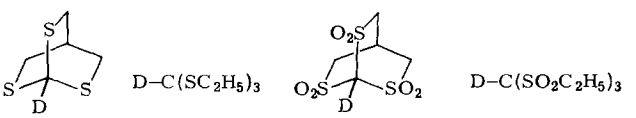
Hitherto it was tacitly assumed that an incipient carbanion at the bridgehead can be stabilized by a neighboring carbonyl group *via* π-delocalization. However, other effects can become dominant under certain conditions. An indication for this is provided by the observation that the ketone *(78)* not only undergoes the expected proton exchange of the cyclopropane ring under drastic conditions at 200 °C but is also partially deuterated at the bridgehead, although the carbonyl group is in a conceivably unfavorable position for π-conjugation with the potential bridgehead carbanion[61]. *(79)* is also partially deuterated at the bridgehead. Alternative mechanisms, such as exchange on ring-opened intermediates with subsequent recyclization, are regarded as incompatible with experimental findings.



(78) *(79)* *(80)* *(81)*

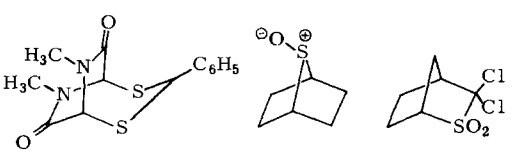
Not only carbonyl groups but also heteroatoms accelerate deprotonation at the bridgehead of bicyclic ring systems. A few noteworthy examples are cited.

The bicyclic trisulfide *(82)* is dedeuterated in the presence of alkoxides even faster than *(83)*, whereas the oxygen analogs *(80)* and *(81)* display no exchange[62]. If the relative rate of isotope exchange were to reflect the difference in pK_a values



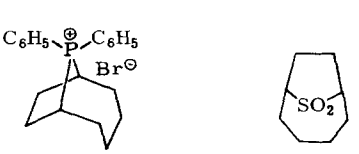
(82) *(83)* *(84)* *(85)*

of these compounds[63] then *(82)* would be more acidic than *(83)*. The converse applies to the trisulfones *(84)* and *(85)*: the open-chain *(85)* is the stronger acid[64]. The significance of bridgehead deprotonation for the successful synthesis of natural products in the gliotoxin and sporidesmin series has recently become apparent: bridged diketopiperazines of type *(86)* can be diastereoselectively deprotonated by *n*-butyllithium and thus readily substituted at the bridgehead[65]. Bicyclic compounds having just a single hetero substituent can likewise be deprotonated at the bridgehead Both the sulfoxide *(87)*[66] and the sulfone *(88)*[67] are subject to base-catalyzed deutera-



(86) *(87)* *(88)*

tion. These reactions should proceed *via* compounds having a C=S bond. Without exception, saturated and unsaturated bicyclic sulfones of type *(90)* apparently form bridgehead dianions on treatment with *n*-butyllithium since only the disubstituted derivatives can be isolated on subsequent treatment with deuterioacetic acid or methyl iodide[68].



(89) *(90)*

The bicyclic phosphonium salt *(89)* can also be easily deuterated in basic solution[69]. The reaction should proceed *via* an alkylidenephosphorane.

Attempts to interpret the acidity-enhancing effects of heteroatoms can be found in the more recent literature[66, 70].

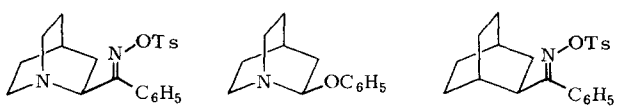
2.6. Solvolyses

The acceleration of a solvolysis by nonbonding electron pairs of α-heteroatoms is explained by conjugational stabilization of the incipient carbocation. Thus while open-chain α-halo ethers are generally isolable, they undergo extremely rapid solvolysis. On the other hand, the open-chain α-halo amines are isolable only as immonium salts. It therefore seems appropriate to investigate the solvolysis of corresponding bicyclic compounds, in order to establish whether intermediates having bridgehead double bonds are formed.

The aza compounds *(91)*, *(93a)*, and *(93b)* solvolyze more slowly than the carbocyclic compounds *(92)*, *(94a)*, and *(94b)* by a factor of 20, 10, and 2, respectively. However, on comparison with values estimated for a retarding σ-acceptor effect of the nitrogen they display an acceleration in the order of 10^3—10^8 which has been termed "π-acceleration"[71].

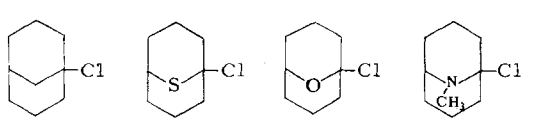
(91) *(92)* *(93a)*, X = OTs *(94a)*, X = OTs
(93b), X = Cl *(94b)*, X = Cl

Presumably, additional effects also play a role here since the α-chloro amine *(126b)* is in fact solvolyzed faster than 1-bromo-3,3-dimethylbicyclo[2.2.2]octane[72]. It should be mentioned in this context that *(95)*, in phenol, not only rearranges but also fragments to give *(96)*[73]. The fact that *(95)*



(95) *(96)* *(97)*

is solvolyzed two to four times faster than *(97)* is attributable not to a smaller activation energy but to a more positive activation entropy. A comparatively unusual acceleration of solvolysis has been observed for the α-chloro amine *(101)*[34d]. The k_{rel} values given have been extrapolated to 29.1 °C. No explanation has yet been offered for the striking difference in relative rates.



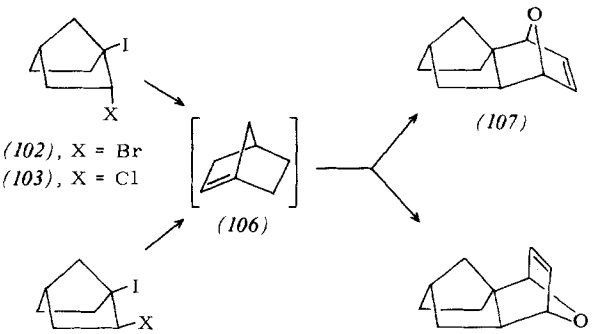
(98) *(99)* *(100)* *(101)*

k_{rel} 1 1.07×10^{-2} 0.323 8.06×10^6

2.7. Reductive Eliminations

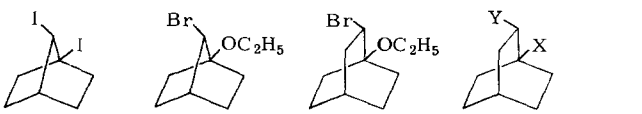
Of the many variants of reductive elimination used for the production of olefins only few have so far been applied to the generation of olefins having bridgehead double bonds. Bisdehalogenation of bicyclic 1,2-dihaloalkanes induced by alkyllithium plays a prominent role in this context. This method was first used in the case of 1,2-dihalonorbornanes and led to the classical bridgehead olefin 1-norbornene (bicyclo[2.2.1]hept-1-ene) *(106)* as intermediate[7].

On reaction of the diastereoisomeric pairs *(102)*/*(104)* and *(103)*/*(105)* with butyllithium in the presence of furan the intermediate *(106)* led to cycloadducts *(107)* and *(108)* in a constant ratio. The structures of *(107)* and *(108)* were established by oxidative degradation to bicyclo[2.2.1]heptane-1,2-*exo*-dicarboxylic acid, which in turn was synthesized by an independent route. The existence of *(106)* as a discrete intermediate in these reactions is substantiated by the constant adduct ratio and the finding that olefin formation is induced in each case by lithium-iodine exchange[7].



(102), X = Br
(103), X = Cl
(106)
(107)
(104), X = Br
(105), X = Cl
(108)

Attempts to bisdehalogenate *(109)* in the same manner gave no indication of the transient formation of bicyclo[2.2.1]-hept-1(7)-ene[74]. Both the magnesium and the lithium compound accessible from *(110)* are likewise stable up to 80 °C[75]. Furthermore, in the homologous series the reaction of *(111)* with an excess of *tert*-butyllithium under controlled conditions gave, *inter alia*, the compounds *(112a)* and *(112b)* which

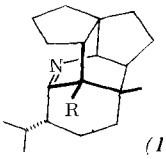


(109) *(110)* *(111)* *(112a)*, X = $C(CH_3)_3$, Y = H
(112b), X = H, Y = $C(CH_3)_3$

may be regarded as trapping products of bicyclo[2.2.2]oct-1-ene *(129)*[76]. As expected, bisdehalogenation becomes easier and more specific with increasing ring size: 1,2-dibromobicyclo[3.3.1]nonane is cleanly reduced by sodium in alcohol to the olefin *(2)*[77]. On reductive bisdehalogenation of 1,2-diiodo- and 1-bromo-2-iodoadamantane in the presence of furan only two saturated hydrocarbons were isolated which can be viewed as dimers of adamantene *(53)*[78]. However, if the reaction is carried out in butadiene the cycloaddition product is formed[79] (cf. Sections 2.1 and 2.3).

2.8. Oxidative Eliminations

In the course of structural elucidation of alkaloids it was observed that the methyl ester of homo-seco-daphniphyllic acid is oxidized to the bridgehead imine *(113)* by lead tetraacetate[80]. Other conceivable double bond isomers are ruled out partly for steric reasons and partly on the basis of the spectra. Rearrangement products are unlikely since *(113)* is reduced practically quantitatively to the original amino ester by $NaBH_4$ or on catalytic hydrogenation. The formation of *(113)*, a bicyclic analog of *trans*-1-azacyclooctene, is presuma-



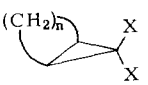
$R = CH_2 \diagdown\diagup CH_2 \diagdown\diagup COOCH_3$

(113)

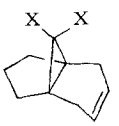
bly promoted by both the fixed boat-chair conformation of the 2-azabicyclo[3.3.1]nonane skeleton—which has been verified by X-ray structure analysis of the saturated compound—and by the absence of any alternative reactions. In any case, bicyclic bridgehead imines of the same type have hitherto not been isolated[81].

2.9. Rearrangements

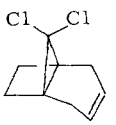
Bicyclic compounds of type *(114)* can easily isomerize to monocyclic dihalo olefins if $n \leqslant 3$. The propellanes *(115a)* and *(115b)* of analogous structure are considerably more stable since electrocyclic opening of the three-membered ring entails formation of bridgehead olefins.



(114), X = Cl, Br



(115a), X = Cl
(115b), X = Br

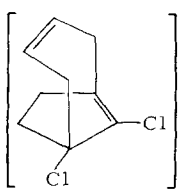


(116)

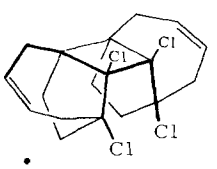
However, if the strain in the propellane increases more rapidly than in the bicyclic bridgehead olefin with decreasing ring size then the tendency to undergo rearrangement can again increase. Nevertheless it is rather surprising that *(116)* is unstable at room temperature and affords dimers which are formally derivable from a bridgehead olefin *(117)*[82].

As shown by X-ray structure analysis of the major product the predominant dimer formed from the twelve possible alternatives is the *meso* form *(118)*. Thus the dimerization formally corresponds to $[_\pi 2_s + _\pi 2_s]$-cycloaddition. It has been estimated for a strain of about 20 kcal/mol in *(116)* that isomerization of *(116)* to *(117)* is exothermic to the extent of about 10 kcal/mol.

It is to be expected that directed studies of the dimerization of reactive bridgehead olefins should lead to considerable refinement of the selection principles and mechanistic models of [2+2]-cycloadditions.



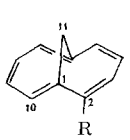
(117)



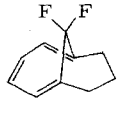
(118)

The rate of rearrangement of thermally stable dihalopropellanes of type *(115)* can be enhanced by acceleration of the ring-opening solvolysis step: both *(115b)* and the corresponding saturated propellane are rapidly hydrolyzed in the presence of silver ions. The products formed can be formulated in terms of intermediate bridgehead olefins[83].

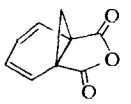
The bridged annulenes accessible from certain unsaturated propellanes can be classified as bridgehead olefins with conjugationally stabilized double bonds. The 1,6-bridged cyclodecapentaene *(119)* is cited as an example[84]. The structure of the carboxylic acid *(120)*, a derivative of *(119)*, is characterized by ready twisting of the partial bridgehead double bond, accompanied by pyramidalization[85] [Fig. 1, formula *(120a)*].



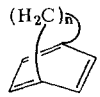
(119), R = H
(120), R = COOH



(121)



(122)

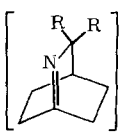


(123a), n = 7
(123b), n = 6

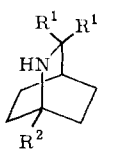
The equilibrium between the cycloheptatriene and norcaradiene structure of bridged compounds of type *(121)* and *(122)* must also be viewed in light of the Bredt rule[86-90].

Meta- and paracyclophanes having small bridges[91-93] such as *(123a)* and *(123b)*, which have only become available very recently and whose structure should prove particularly informative, will at last put discussions of the flexibility of aromatic rings on a firm basis.

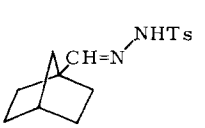
The rearrangement of carbenes and nitrenes is developing into a potent method for the preparation of highly reactive bridgehead olefins. Thus, for example, photolysis of 1-azidobicyclo[2.2.1]heptane in methanol affords the α-amino ethers *(126a)* and *(127)* which are formally derivable from the imines *(124a)* and *(125)*, respectively[94].



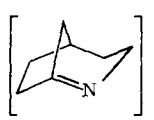
(124a), R = H
(124b), R = CH_3



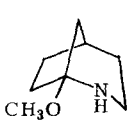
(126a), R^1 = H, R^2 = OCH_3
(126b), R^1 = CH_3, R^2 = Cl



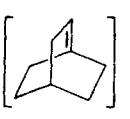
(128)



(125)

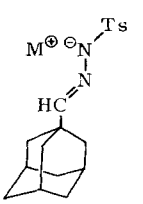


(127)

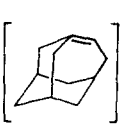


(129)

Products which could arise *via* bridgehead olefins are formed from carefully dried salts of tosylhydrazones only under conditions of flash pyrolysis. 3-Methylene-1,6-heptadiene, which is isolated on decomposition of the lithium salt of *(128)*, formally arises from bicyclo[2.2.2]oct-1-ene *(129)* by retro-Diels-Alder reaction[95].



(130a), M = Li
(130b), M = Na



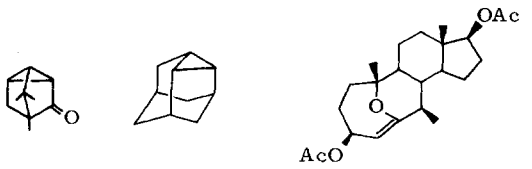
(131)

Pyrolysis of *(130a)* and *(130b)*, however, does not give unsaturated compounds but instead yields five hydrocarbons, of which three are regarded as direct dimerization products of 3-homo-1-adamantene *(131)*[96]. Apart from their configur-

ation it remains to be established which of the dimers are also formed on thermolysis of *(11)* and *(12)*[22a].

It should nevertheless be emphasized that potentially suitable carbenes only react to give bridgehead olefins if rearrangement is favored by stereoelectronic factors: thermolysis of α-diazocamphor does not give an olefin but instead the tricyclic ketone *(132)*, and pyrolysis of the lithium salt of adamantanone tosylhydrazone essentially affords 2,4-didehydroadamantane *(133)*[97]. In the $AlCl_3$-catalyzed reductive ring opening of 1-(*N*,*N*-dichloro)amino-7,7-dimethylbicyclo[2.2.1]heptane to give *(126b)*, it is conceivable that the strained imine *(124b)* or the corresponding bridgehead immonium ion is formed as an intermediate[98].

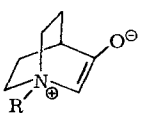
An unusual oxidative ring expansion was observed in the reaction of hydroxy-B-norsteroid with lead tetraacetate[99]. The bicyclic enol ether *(134)* having a 10-oxabicyclo[4.3.1]-dec-1-ene skeleton was formed as major product.



(132) *(133)* *(134)*

Sigmatropic rearrangements of order [2,3] are likewise subject to the stereoelectronic restrictions of the Bredt rule. The isolable ammonium enolate *(135)* isomerizes readily to the α-amino ketone *(137)*, which is assigned the configuration shown on the basis of mechanistic arguments and NMR spectroscopic data[100]. However, the corresponding Stevens rearrangement having the sigmatropic order [2,1] is apparently stereoelectronically much more demanding since heating of *(136)* merely affords a complex mixture of products.

(135), R = CH_2–C_6H_5 *(137)*
(136), R = CH_2–C_6H_5



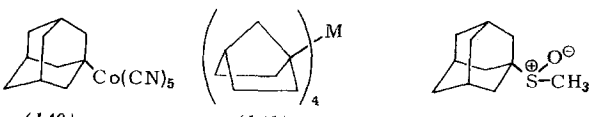
(138), R = CH_2–C_6H_5
(139), R = CH_2–C_6H_5

Since the torsional angle increases with decreasing bridge length it is hardly surprising that the ammonium enolates *(138)* and *(139)* are stable and no longer undergo sigmatropic rearrangement.

2.10. Robust and Labile Bridgehead-Substituted Bicyclic and Polycyclic Compounds

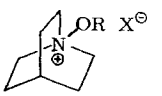
As already mentioned, a series of elimination reactions have been developed for preparing bridgehead olefins. In some studies less interest is attached to the strained double bond than to the functional group at the bridgehead. Since decomposition reactions such as β-eliminations, and nucleophilic substitutions of course, are kinetically hindered, if not completely suppressed, by the bi- or polycyclic system, the chemical and physical properties of certain functional groups become observable to study over a considerably greater temperature range.

Thus the kinetic stability of the metal complex *(140)* is comparable to that of pentacyanomethylcobalt(III) while the corresponding *tert*-butyl complex decomposes so readily that it has so far evaded isolation[101]. The transition metal compounds of type *(141)* also owe their stability, at least in part, to the lack of β-elimination[102].



(140) *(141)* *(142)*

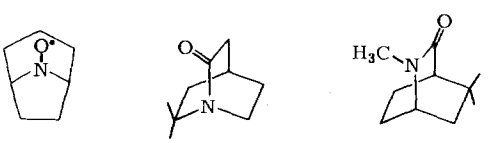
M = Hf, Zr, Ti, V, Cr, Mn, Fe, Co



(143a), R = COC_6H_5, X = Cl
(143b), R = $SO_2C_6H_4$, CH_3, X = $SbCl_6$

Since pyrolysis of alkyl sulfoxides with β-hydrogens entails ready *cis*-elimination to give olefins their racemization can only be investigated if the alkyl groups either bear no β-hydrogen or have a structure in which β-elimination is stereoelectronically hindered: the sulfoxide *(142)* racemizes without simultaneous elimination[103]. Dealkylation of tertiary amines according to *Polonovski*[104] is formulated as proceeding *via* unstable *N*-acyloxyammonium salts which are transformed rapidly into immonium ions on base catalysis, and afford secondary amines after hydrolysis. In contrast, the salts *(143a)* and *(143b)* accessible from quinuclidine *N*-oxide do not undergo elimination because formation of the bicyclic bridgehead immonium ion is largely suppressed[104].

Dialkylnitroxyls have long evaded any study of their physical properties because they rapidly decompose to nitrones and hydroxylamines. However, bicyclic nitroxyls possess adequate stability since formation of nitrones having a strained imine double bond is much slower. Thus *(144)* decomposes about 10^9 times more slowly than an acyclic dialkylnitroxyl[105–108]. The configuration of *(144)* is unknown.



(144) *(145)* *(146)*

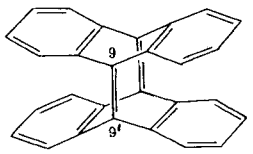
On the other hand, compounds which are normally stabilized by conjugation can become highly reactive if the functional groups are incorporated into a bi- or polycyclic skeleton in such a manner that π-delocalization is no longer possible. The effect of this conformational difference on the chemical and physical properties of the quinuclidones *(145)* and *(146)* is particularly striking. Thus *(145)* reacts with methanol in basic solution about 10^4 times faster than the bicyclic lactam *(146)*[109].

2.11. "Annelated" Bridgehead Olefins

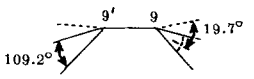
The strain in bridgehead olefins possessing a bridged polycyclic skeleton as common structural feature (Bredt olefins) is largely attributed to twisting[*]. "Annelated" bridgehead olefins, on the other hand, are predominantly strained for

[*] The extent of twisting is overemphasized by formulas and models having rigid bond angles.

reasons of bond angle deformation and pyramidalization. The polycyclic compound *(147)*[110] should be mentioned as a prototype since in this case both bond angle narrowing and pyramidalization are very pronounced [cf. formula *(147a)*].



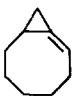
(147)



(147a)

Bicyclic compounds of type *(148)*, whose chemistry has recently been surveyed in detail[116], also belong to this class of bridgehead olefins, as do *(149)*[111]. For that matter, this class really also embraces cephalosporins[112] and penicillins.

(148)



(149)

3. Outlook

The methods presented by no means exhaust the arsenal for preparation of bridgehead olefins. Potential reactions include both those which have proved of value in the preparation of 1,2-dehydrobenzene[113] and those which are suitable for introduction of an additional double bond into cyclobutene[114].

Interest, however, will probably continue to be focused upon development of methods providing an entry to highly strained bridgehead olefins under conditions in which their physical and chemical properties can be directly determined. We can also expect the study of bridgehead olefins to make a significant contribution to our understanding of the photochemistry of simple alkenes[115, 116] and the reactivity of strained olefins[117, 118]. Moreover, Bredt olefins themselves will extend our knowledge about the structural course of thermal *cis-trans* isomerizations of simple alkenes.

From the vantage point of preparative organic chemistry, bridgehead olefins possess considerable interest whenever they afford products that are otherwise accessible only with difficulty. An impressive example is seen in the synthesis of dimethyl bicyclo[2.2.1]heptane-1,2-*exo*-dicarboxylate from norcamphor *via* 1-norbornene[7].

Received: September 2, 1974;
in abbreviated form: December 30, 1974 [A 72 IE]
German version: Angew. Chem. *87*, 568 (1975)

[1] *V. Prelog*, J. Chem. Soc. *1950*, 420.
[2] *F. S. Fawcett*, Chem. Rev. *47*, 219 (1950).
[3] *O. E. Edwards, L. Marion*, and *D. K. R. Stewart*, Can. J. Chem. *34*, 1315 (1956).
[4] *J. P. Ferris* and *N. C. Miller*, J. Amer. Chem. Soc. *85*, 1325 (1963).
[5] *J. A. Marshall* and *H. Faubl*, J. Amer. Chem. Soc. *89*, 5965 (1967).
[6] *J. R. Wiseman*, J. Amer. Chem. Soc. *89*, 5966 (1967).
[7] *R. Keese* and *E. P. Krebs*, Angew. Chem. *83*, 254 (1971); *84*, 540 (1972); Angew. Chem. internat. Edit. *10*, 262 (1971); *11*, 518 (1972).
[8] *J. Bredt*, Liebigs Ann. Chem. *437*, 1 (1924).
[9] *R. C. Fort, Jr.* and *P. v. R. Schleyer*, Advan. Alicyclic Chem. *1*, 364 (1966).
[10] *R. S. Rabinovitch* and *F. S. Looney*, J. Chem. Phys. *23*, 2439 (1955); cf. also *R. Hoffmann*, Tetrahedron *22*, 521 (1966).
[11] *M. J. S. Dewar*: The Molecular Orbital Theory of Organic Chemistry. McGraw Hill, New York 1969, pp. 284f.
[12] *G. S. Hammond*, J. Amer. Chem. Soc. *77*, 334 (1955).
[13] *E. J. Corey* and *R. A. Sneen*, J. Amer. Chem. Soc. *78*, 6269 (1956).
[14] a) *H. W. Geluk* and *J. L. M. A. Schlatman*, Tetrahedron *24*, 5361 (1968); b) *P. Vogel, M. Saunders, W. Thielecke*, and *P. v. R. Schleyer*, Tetrahedron Lett. *1971*, 1429.
[15] *C. H. DePuy, R. D. Thurn*, and *G. F. Morris*, J. Amer. Chem. Soc. *84*, 1314 (1962).
[16] *G. Köbrich*, Angew. Chem. *85*, 494 (1973); Angew. Chem. internat. Edit. *12*, 464 (1973).
[17] Cf. *inter alia E. O. Fischer*, Pure Appl. Chem. *30*, 353 (1972); Angew. Chem. *86*, 651 (1974).
[18] *J. R. Wiseman* and *W. A. Pletcher*, J. Amer. Chem. Soc. *92*, 956 (1970).
[19] *J. Sicher*, Angew. Chem. *84*, 177 (1972); Angew. Chem. internat. Edit. *11*, 200 (1972).
[20] *J. R. Wiseman, H.-K. Foon*, and *C. J. Ahola*, J. Amer. Chem. Soc. *91*, 2812 (1969); *J. R. Wiseman* and *J. A. Chong, ibid. 91*, 7775 (1969).
[21] *J. A. Chong* and *J. R. Wiseman*, J. Amer. Chem. Soc. *94*, 8627 (1972).
[22] a) *B. L. Adams* and *P. Kovacic*, J. Amer. Chem. Soc. *95*, 8206 (1973); b) *96*, 7014 (1974); c) *B. L. Adams, J.-H. Liu*, and *P. Kovacic*, Tetrahedron Lett. *1974*, 427; d) *J. L. Fry, M. G. Adlington, R. C. Badger*, and *S. T. McCullough, ibid. 1974*, 429.
[23] *H. G. Thomas*, Dissertation, Technische Hochschule Aachen 1965. I am indebted to Dr. *Thomas* for this information.
[24] *H. Gerlach, T. T. Huong*, and *W. Müller*, J. C. S. Chem. Comm. *1972*, 1215.
[25] *W. Carruthers* and *M. I. Qureshi*, J. Chem. Soc. *C 1970*, 2238.
[26] *G. L. Buchanan* and *G. Jamieson*, Tetrahedron *28*, 1123, 1129 (1972).
[27] *P. E. Eaton* and *K. Lin*, J. Amer. Chem. Soc. *86*, 2087 (1964).
[28] *J. W. Harrison, R. M. Scrowston*, and *B. Lythgoe*, J. Chem. Soc. *C 1966*, 1933; *1967*, 452.
[29] *B. G. Cordiner, M. R. Vegar*, and *R. J. Wells*, Tetrahedron Lett. *1970*, 2285.
[30] *A. F. Cameron* and *G. Jamieson*, J. Chem. Soc. *B 1971*, 1581.
[31] *W. E. Thiessen, H. A. Levy, W. G. Dauben, G. H. Beasley*, and *C. A. Cox*, J. Amer. Chem. Soc. *93*, 4312 (1971).
[32] *G. L. Buchanan*, Chem. Soc. Rev. *3*, 41 (1974).
[33] *S. F. Campbell, R. Stephens*, and *J. C. Tatlow*, Chem. Commun. *1965*, 134; Tetrahedron *21*, 2997 (1965); *S. F. Campbell, J. M. Leach, R. Stephens*, and *J. C. Tatlow*, Tetrahedron Lett. *1967*, 4269; J. Fluorine Chem. *1*, 85 (1971/72); *S. F. Campbell, J. M. Leach, R. Stephens, J. C. Tatlow*, and *K. N. Wood, ibid. 1*, 103 (1971/72); *W. B. Hollyhead, R. Stephens, J. C. Tatlow*, and *W. T. Westwood*, Tetrahedron *25*, 1777 (1969).
[34] a) *C. B. Quinn* and *J. R. Wiseman*, J. Amer. Chem. Soc. *95*, 1342 (1973); b) *95*, 6120 (1973); c) *C. B. Quinn, J. R. Wiseman*, and *J. C. Calabrese, ibid. 95*, 6121 (1973); d) *H. O. Krabbenhoft, J. R. Wiseman*, and *C. B. Quinn, ibid. 96*, 258 (1974).
[35] *L. M. Jackman* and *S. Sternhell*: Applications of Nuclear Magnetic Spectroscopy in Organic Chemistry. 2nd Edit., Pergamon Press, Oxford 1969, p. 185.
[36] *J. R. Hargreaves, P. W. Hickmott*, and *B. J. Hopkins*, J. Chem. Soc. *C 1969*, 592.
[37] *H. Newman* and *T. L. Fields*, Tetrahedron *28*, 4051 (1972).
[38] *J. A. Marshall* and *H. Faubl*, J. Amer. Chem. Soc. *92*, 948 (1970).
[39] *W. G. Dauben* and *J. Ipaktschi*, J. Amer. Chem. Soc. *95*, 5088 (1973).
[40] *K. B. Becker*, Chimia *28*, 726 (1974). I am grateful to Dr. *Becker* for communicating these results prior to publication.
[41] *A. H. Alberts, J. Strating*, and *H. Wynberg*, Tetrahedron Lett. *1973*, 3047.
[42] *E. N. Cain, R. Vukov*, and *S. Masamune*, Chem. Commun. *1969*, 98.
[43] a) *P. D. Bartlett, G. N. Fickes, F. C. Haupt*, and *R. Helgeson*, Accounts Chem. Res. *3*, 177 (1970); b) *R. C. Fort, Jr.* and *R. E. Franklin*, J. Amer. Chem. Soc. *90*, 5267 (1968).
[44] *R. Keese* and *E. P. Krebs*, unpublished.
[45] *J. E. Gano* and *L. Eizenberg*, J. Amer. Chem. Soc. *95*, 972 (1973).
[46] *R. R. Sauers, M. Gorodetsky, J. A. Whittle*, and *C. K. Hu*, J. Amer. Chem. Soc. *93*, 5520 (1971).
[47] *R. B. Gagosian, J. C. Dalton*, and *N. J. Turro*, J. Amer. Chem. Soc. *92*, 4754 (1970).
[48] *G. L. Buchanan*, personal communication (Jan. 8, 1974).
[49] For examples see ref. [18].
[50] *B. R. Vogt*, Tetrahedron Lett. *1968*, 1579.
[51] a) *J. Bredt*, Ann. Acad. Sci. Fenn., Ser. A2, *29*, 3 (1927); b) *K. J. Pedersen*, J. Amer. Chem. Soc. *58*, 240 (1936); c) *F. H. Westheimer* and *W. A. Jones, ibid. 63*, 3283 (1941).
[52] *K. Taguchi* and *F. H. Westheimer*, J. Amer. Chem. Soc. *95*, 7413 (1973).
[53] *H. O. House* and *H. Müller*, J. Org. Chem. *27*, 4436 (1962).
[54] a) *A. J. Sisti*, Tetrahedron Lett. *1967*, 5327; b) *J. P. Schaefer* and *L. M. Honig*, J. Org. Chem. *33*, 2655 (1968); c) *C. D. Gutsche* and *T. D. Smith*, J. Amer. Chem. Soc. *82*, 4067 (1960); d) *E. W. Warnhoff, C. M. Wong*, and *W. T. Tai*, J. Org. Chem. *32*, 2664 (1967).
[55] *C. Ganter* and *R. O. Duthaler*, unpublished; cf. *R. O. Duthaler*, Dissertation, ETH No. 5108 (1973).

[56] *A. F. Thomas*: Deuterium Labeling in Organic Chemistry. Appleton-Century Crafts, Educational Division, New York 1971, p. 185.
[57] *D. H. Bowen* and *J. MacMillan*, Tetrahedron Lett. *1972*, 4111.
[58] *K. W. Turnbull*, *S. J. Gould*, and *D. Arigoni*, J. C. S. Chem. Comm. *1972*, 597.
[59] a) *M. Dobler* and *J. D. Dunitz*, Helv. Chim. Acta *48*, 695 (1964); b) *P. D. Cradwick* and *G. A. Sim*, J. Chem. Soc. *B 1971*, 2218.
[60] *P. v. R. Schleyer*, *E. Funke*, and *S. H. Liggero*, J. Amer. Chem. Soc. *91*, 3965 (1969).
[61] *P. G. Gassman* and *F. V. Zalar*, J. Amer. Chem. Soc. *88*, 3070 (1966).
[62] *S. Oae*, *W. Tagaki*, and *A. Ohno*, J. Amer. Chem. Soc. *83*, 5036 (1961).
[63] *D. J. Cram* and *W. D. Kollmeyer*, J. Amer. Chem. Soc. *90*, 1791 (1968).
[64] *W. v. E. Doering* and *L. K. Levy*, J. Amer. Chem. Soc. *77*, 509 (1955).
[65] *Y. Kishi*, *T. Kukuyama*, and *S. Nakatsuka*, J. Amer. Chem. Soc. *95*, 6490, 6492 (1973); *Y. Kishi*, *S. Nakatsuka*, *T. Fukuyama*, and *M. Havel*, *ibid. 95*, 6493 (1973).
[66] *F. Montanari*, cited by *S. Wolfe*, *A. Rauk*, *L. M. Tel*, and *I. G. Csizmadia*, J. Chem. Soc. *B 1971*, 138.
[67] *C. R. Johnson*, *J. E. Keiser*, and *J. C. Sharp*, J. Org. Chem. *34*, 860 (1969).
[68] *L. A. Paquette*, *R. H. Meisinger*, and *R. Gleiter*, J. Amer. Chem. Soc. *95*, 5414 (1973).
[69] *E. W. Turnblom* and *T. J. Katz*, J. Amer. Chem. Soc. *95*, 4292 (1973).
[70] a) *S. Wolfe*, *A. Rauk*, and *I. G. Csizmadia*, J. Amer. Chem. Soc. *91*, 1567 (1969); b) *R. Hoffmann*, *D. B. Boyd*, and *S. Z. Goldberg*, *ibid. 92*, 3929 (1970); c) *A. Streitwieser*, *Jr.* and *D. Holtz*, *ibid. 89*, 692 (1967); d) *A. Streitwieser*, *Jr.*, *A. P. Marchand*, and *A. H. Pudjaatmaka*, *ibid. 89*, 693 (1967).
[71] *P. G. Gassman*, *R. L. Cryberg*, and *K. Shudo*, J. Amer. Chem. Soc. *94*, 7600 (1972).
[72] *R. D. Fisher*, *T. D. Bogard*, and *P. Kovacic*, J. Amer. Chem. Soc. *94*, 7599 (1972).
[73] *C. A. Grob* and *A. Sieber*, Helv. Chim. Acta *50*, 2531 (1967).
[74] *R. Keese* and *H. Dubas*, 1974, unpublished.
[75] *H. H. Grootveld*, *C. Blomberg*, and *F. Bickelhaupt*, Tetrahedron Lett. *1971*, 1999; *H. H. Grootveld*, Dissertation, Amsterdam 1973.
[76] *H. H. Grootveld*, *C. Blomberg*, and *F. Bickelhaupt*, J. C. S. Chem. Comm. *1973*, 542.
[77] See ref. [18], footnote 25a.
[78] a) *D. Grant*, *M. A. McKervey*, *J. J. Rooney*, *N. G. Samman*, and *G. Step*, J. C. S. Chem. Comm. *1972*, 1186; b) *D. Lenoir*, Tetrahedron Lett. *1972*, 4049. I am grateful to Dr. *Lenoir* for communicating these results prior to publication.
[79] *W. Burns* and *M. A. McKervey*, J. C. S. Chem. Comm. *1974*, 858.
[80] *M. Toda*, *Y. Hirata*, and *S. Yamamura*, Chem. Commun. *1970*, 1597; Tetrahedron *28*, 1477 (1972).
[81] *M. Toda*, *H. Niwa*, *K. Tenaga*, and *Y. Hirata*, Tetrahedron Lett. *1972*, 335.
[82] *P. Warner*, *R. LaRose*, *C. Lee*, and *J. C. Clardy*, J. Amer. Chem. Soc. *94*, 7607 (1972).
[83] *C. B. Reese* and *M. R. D. Steebles*, J. C. S. Chem. Comm. *1972*, 1231.
[84] *E. Vogel* and *H. D. Roth*, Angew. Chem. *76*, 145 (1964); Angew. Chem. internat. Edit. *3*, 228 (1964).
[85] *M. Dobler* and *J. D. Dunitz*, Helv. Chim. Acta *48*, 1429 (1965). I am grateful to Dr. *H.-B. Bürgi* for additional information and an instructive discussion.
[86] *E. Vogel*, *W. Wiedemann*, *H. D. Roth*, *J. Einer*, and *H. Günther*, Liebigs Ann. Chem. *759*, 1 (1972).
[87] *H. J. Scholl*, Dissertation, Universität Köln 1969. I am indebted to Dr. *K. Müllen* for drawing my attention to this work.
[88] *R. Darms*, *T. Threlfall*, *M. Pesaro*, and *A. Eschenmoser*, Helv. Chim. Acta *46*, 2893 (1963).
[89] *G. E. Hall* and *J. D. Roberts*, J. Amer. Chem. Soc. *93*, 2203 (1971).
[90] *E. Ciganek*, J. Amer. Chem. Soc. *93*, 2207 (1971).
[91] *W. E. Parham*, *D. C. Egberg*, and *W. C. Montgomery*, J. Org. Chem. *38*, 1207 (1973).
[92] *N. L. Allinger*, *T. J. Walter*, and *M. G. Newton*, J. Amer. Chem. Soc. *96*, 4588 (1974).
[93] a) *A. D. Wolf*, *V. V. Kane*, *R. H. Levin*, and *M. Jones*, *Jr.*, J. Amer. Chem. Soc. *95*, 1680 (1973); b) *V. V. Kane*, *A. D. Wolf*, and *M. Jones*, *Jr.*, *ibid. 96*, 2643 (1974).
[94] *J. O. Reed* and *W. Lwowski*, J. Org. Chem. *36*, 2864 (1971).
[95] *A. D. Wolf* and *M. Jones*, *Jr.*, J. Amer. Chem. Soc. *95*, 8209 (1973).
[96] *M. Fărcasiu*, *D. Fărcasiu*, *R. T. Conlin*, *M. Jones*, *Jr.*, and *P. v. R. Schleyer*, J. Amer. Chem. Soc. *95*, 8207 (1973).
[97] *A. C. Udding*, *J. Strating*, *H. Wynberg*, and *J. L. M. A. Schlatmann*, Chem. Commun. *1966*, 657.
[98] *R. D. Fisher*, *T. D. Bogard*, and *P. Kovacic*, J. Amer. Chem. *94*, 7599 (1972).
[99] *D. Rosenthal*, *C. F. Leffler*, and *M. E. Wall*, Tetrahedron *23*, 3583 (1967).
[100] *S. Mageswaran*, *W. D. Ollis*, *I. O. Sutherland*, and *Y. Thebtaranonth*, Chem. Commun. *1971*, 1494.
[101] *S. H. Goh* and *L.-Y. Goh*, J. Organometal. Chem. *43*, 401 (1972).
[102] *B. K. Bower* and *H. G. Tennent*, J. Amer. Chem. Soc. *94*, 2512 (1972).
[103] *D. R. Rayner*, *A. J. Gordon*, and *K. Mislow*, J. Amer. Chem. Soc. *90*, 4854 (1968).
[104] *R. Huisgen* and *W. Kolbeck*, Tetrahedron Lett. *1965*, 783.
[105] *R.-M. Dupeyre* and *A. Rassat*, J. Amer. Chem. Soc. *88*, 3180 (1966).
[106] *G. D. Mendenhall* and *K. U. Ingold*, J. Amer. Chem. Soc. *95*, 6390, 6395, 8610 (1973).
[107] *I. Morishima*, *K. Yoshikawa*, *K. Bekki*, *M. Kohno*, and *K. Arita*, J. Amer. Chem. Soc. *95*, 5815 (1973).
[108] *G. D. Mendenhall* and *K. U. Ingold*, J. Amer. Chem. Soc. *94*, 7166 (1972).
[109] *H. Pracejus*, *M. Kehlen*, *H. Kehlen*, and *H. Matschiner*, Tetrahedron *21*, 2257 (1965).
[110] *R. L. Viavattene*, *F. D. Greene*, *L. D. Cheung*, *R. Majeste*, and *L. M. Trefonas*, J. Amer. Chem. Soc. *96*, 4342 (1974).
[111] *A. S. Kende*, J. C. S. Chem. Comm. *1974*, 383.
[112] *R. M. Sweet* and *L. F. Dahl*, J. Amer. Chem. Soc. *92*, 5489 (1970).
[113] *R. W. Hoffmann*: Dehydrobenzene and Cycloalkynes. Verlag Chemie, Weinheim, and Academic Press, New York 1967, Chapter 1.
[114] *G. Maier*, Angew. Chem. *86*, 491 (1974); Angew. Chem. internat. Edit. *13*, 425 (1974).
[115] *D. Scharf*, Fortschr. Chem. Forsch. *11*, 216 (1968/69).
[116] Cf., *e.g.*, *P. J. Kropp*, J. Amer. Chem. Soc. *95*, 4611 (1973).
[117] *T. J. Traylor*, Accounts Chem. Res. *2*, 152 (1969).
[118] *N. S. Zefirov* and *V. I. Sokolov*, Russ. Chem. Rev. *36*, 87 (1967).

Microencapsulation

By Wolfgang Sliwka[*]

Microencapsulation is the enveloping of liquid droplets or fine solid particles to form microscopic capsules 1 to 5000 μm in diameter. For the fabrication of such capsules special techniques have been developed which take into account the substance to be encapsulated and the intended use of the capsules. The envelopes, consisting of natural or synthetic polymers, may be made permeable, semipermeable, or impermeable. Thus, there are several possibilities for controlled release of an encapsulated reactive substance, for example by destruction of the envelope or by permeation: alternatively, reactions can be allowed to take place within the microcapsules. Microencapsulation facilitates delivery of many substances to their site of utilization in a novel form of preparation and novel mode of dosage, the solids being dispersed very finely and having a very large surface area.

1. Introduction

Microencapsulation is the name given to a novel technique for the preparation of substances, the development of which began about 20 years ago.

Numerous processes and their products—microcapsules—have been described, largely in patent literature. A few surveys are available[1–5]. In what follows an attempt is made to review the field of microcapsules, their preparation, their properties and their uses and potential applications.

Since life began nature has been utilizing the envelopment of systems for their protection or for providing particular reaction spaces, the enveloping wall displaying in addition specific membrane functions. The abundance of examples available is quite overwhelming and extends from arboreal fruits and plant seeds to spores, from the hen's egg and its shell to the cell and its cell wall. The principle is found in nature from the macroscopic down to the microscopic range.

In the macroscopic range the enclosing of active ingredients in capsules, for example of medical preparations in the familiar gelatin capsules, has long been practised. Powdered active principles are offered in sausage-shaped hard capsules, liquid or pasty ones are brought between two soft gelatin ribbons which are then shaped and welded together by special machines to form spherical capsules. Encapsulation improves the dosability, but principally it serves to protect the active principles against light and oxygen. Release of the active principle is postponed until the capsule has entered the organism, for example, after dissolution of the capsule wall within the stomach or the intestine.

The technique of microencapsulation aims at enveloping gases, liquids, or solids present in finely dispersed form. In general, the mean particle diameters can be varied between about 1 and 5000 μm; natural or synthetic polymers are used for the walls of the capsules. The external form of the capsules depends on the core material and the deposition of the material of the wall. Thus, microcapsules may appear as smooth spherical globules, as grape-like clusters, or as irregular structures with a smooth or folded surface. They can be readily investigated by means of scanning electron microscopy (SEM) (Fig. 1)[*].

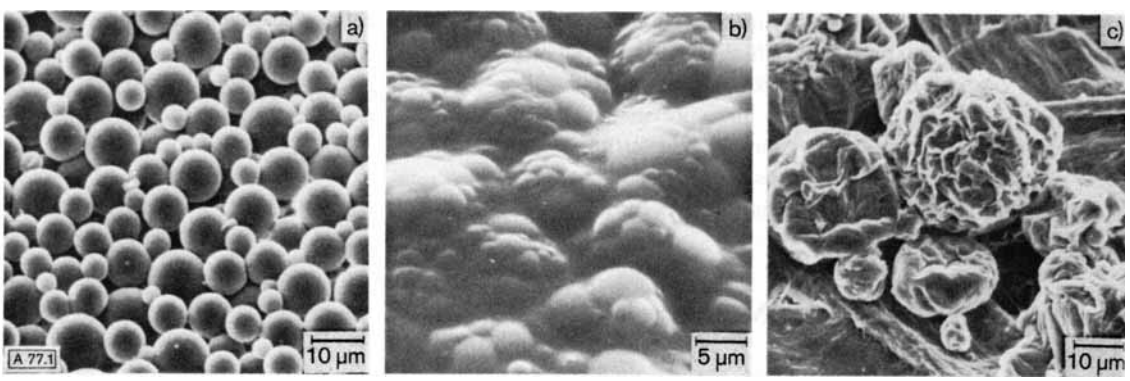


Fig. 1. a) Polyacrylate capsules prepared by a phase-separation technique. b) Complex coacervate capsules on a paper base. c) Polyamide capsules prepared by rapid interfacial condensation (despite the folds the capsules are impermeable). SEM photomicrographs.

The nature of the polymers and the wall thickness determine the ability of the microcapsule (the capsule envelope) to isolate the contents and to release them selectively. Some examples of the possibilities are given below.

The capsule wall seals off the capsule contents from the external surroundings, and to release them it must be opened. This may be effected mechanically from outside, *i.e.* by shearing or crushing, or from inside *e.g.* by heating above the boiling point of the core material, and by dissolution, melting, or burning of the wall material (Figs. 2a and b).

The capsule wall can be semipermeable, for example impermeable to the core material but permeable to low-molecular

[*] Dr. W. Sliwka
Kunststofflaboratorium der BASF AG
67 Ludwigshafen (Germany)

[*] This and the following SEM photomicrographs were taken by Dr. *Hendus* in the Hauptlaboratorium, BASF AG (Ludwigshafen, Germany).

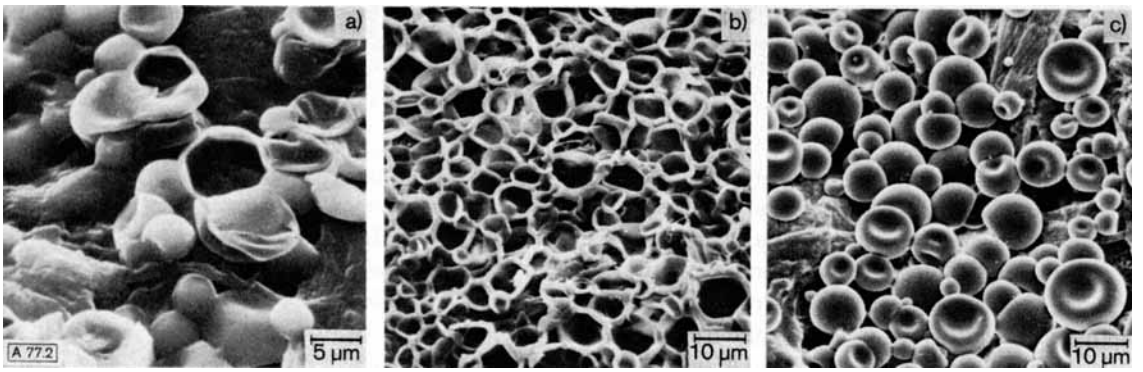


Fig. 2. a) Polyacrylate microcapsules on a paper base: mechanically opened, b) opened by melting at 220 °C, c) with dents formed as a result of the loss of volatile solvent as core material. (SEM photomicrographs.)

liquids coming in from outside. Provided these liquids exhibit no tendency to mix with the core material, the contents remain enclosed. Otherwise the liquid entering by diffusion builds up an osmotic pressure which threatens to burst the capsule from within. Microcapsules which resist the osmotic pressure can be used as exchangers. They take up substances from the environment and release them again on being introduced into a different medium. Microcapsules which do not resist the osmotic pressure burst and release the capsule contents.

The capsule wall can be permeable to the core substance. Release of the core material is regulated by the thickness and pore width of the wall (Fig. 2c). In contrast to the case of destruction of the capsule, the contents do not emerge all at once but slowly (sustained release). In this way a certain concentration of core material can be maintained in the surroundings for a prolonged period, which is often desired, *e.g.* for therapeutic purposes.

The permeability of the capsule wall also depends on the surrounding medium. Thus, if an impermeable microcapsule is introduced into a liquid in which the wall material will swell, then the polymer network expands. As a result the capsule may become permeable to the core material, and in this way the core constituents—for example, fertilizers and drugs—are dissolved out of the capsules.

Such properties open up many possible uses for microcapsules.

2. Influencing the Properties of Microcapsules

According to Fick's diffusion law, the quantity dm/dt [mole/s] that diffuses through the wall of a microcapsule is proportional to the surface area A of the capsule shell, the concentration gradient dc/dw (dc is the concentration drop across the wall thickness dw), and the diffusion coefficient D [cm²/s]:

$$\frac{dm}{dt} = -D \cdot A \cdot \frac{dc}{dw} \tag{1}$$

The diffusion coefficient D embraces the specific properties of the envelope material, such as its physicochemical constitution, its interaction with the surroundings (*e.g.* the swelling power), and the temperature dependence of these interactions. D/dw is the permeability coefficient or the permeability [cm/s].

On the basis of this equation, the capsule surface area, the wall thickness, and the physicochemical constitution of the wall material in relation to the physicochemical constitution of its environment are the important parameters.

2.1. Capsule Dimensions

For the sake of simplicity we shall confine our discussion here to spherical microcapsules, such as are normally formed during the encapsulation of liquids.

During the encapsulation operation a definite ratio by weight of the core material k to the wall material w is weighed out and the capsule diameter is then adjusted in a dispersing stage. Assuming that all capsules display this ratio, the capsule diameter then unambiguously establishes the wall thickness.

Starting from a wall and core material of the same density ($\rho_w = \rho_k$) we obtain the relationship between the wall thickness $dw = r_2 - r_1$ and the ratio of the weight of the wall material W_w to that of the core material W_k:

$$\frac{W_w}{W_k} = \frac{(4/3)\pi(r_2^3 - r_1^3)\cdot\rho_w}{(4/3)\pi r_1^3 \cdot \rho_k} \tag{2}$$

which, after rearranging, gives

$$dw = (r_2 - r_1) = \left[\left(\frac{W_w}{W_k} + 1\right)^{1/3} - 1\right] r_1 \tag{3}$$

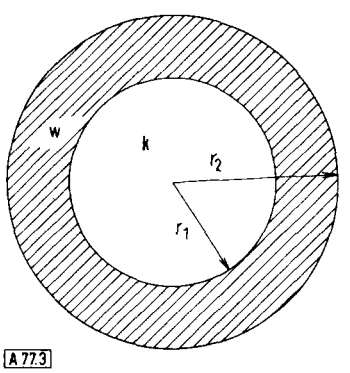


Fig. 3. Cross-section of an idealized microcapsule. r_2 = capsule radius, r_1 = radius of core material, k = core material, w = wall material.

For the usual $W_k/(W_w + W_k)$ ratios of 0.50 to 0.95 the linear increase in wall thickness with increasing capsule diameter shown in Fig. 4 is obtained.

In practice the results will be affected by the capsule diameter distribution that is always present, and by the percentage wall material distribution on individual capsules.

The linear dependence of release of diffusible core material on the thickness of the capsule, expected according to eq. (1), has essentially been confirmed by experiment (examples: phenobarbital/gelatin[6]; eprazinone/gelatin[7]).

Table 1. Storage characteristics of some liquids in gelatin microcapsules (after [1]).

Encapsulated liquid	As fraction of total capsule weight [%]	Mean capsule diameter [μm]	Storage time [d]	Liquid loss at 25 °C and 50 % RH [%]
Benzene	85.5	500	198	0.5
Toluene	90.6	480	400	0.1
Xylene	90.2	500	730	0.2
Hexane	70.8	35	730	0.1
Carbon tetrachloride	82.8	500	602	0.3
Chloroform	78.9	420	730	0.1
Trichloroethylene	87.2	500	400	1.0
Perchloroethylene	87.9	500	600	0.1

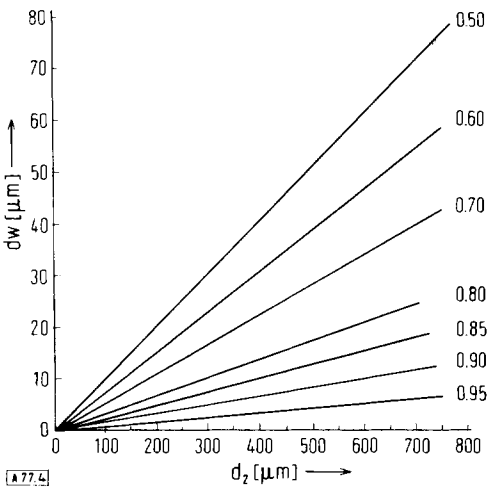


Fig. 4. Wall thickness dw as a function of capsule diameter d_2 for various $W_k/(W_w + W_k)$ ratios.

With the small diameter of the microcapsules, and the consequently limited thickness of the capsule wall, complete impermeability with respect to gases or liquids, and especially solvents, cannot be obtained. However, the durability of the core material can be optimized by suitable choice of the capsule dimensions and the wall materials (cf. Table 1).

2.2. Capsule Wall Material

The wall material is as decisive for the permeability properties of the capsule wall as are the capsule dimensions. In the selection of a suitable wall material it is helpful to refer to Hildebrand's solubility parameters[8] (Table 2). For the preparation of impermeable capsules a wall material with a solubility parameter as different as possible from that of the core material should be chosen. In this way it is possible to carry out a preliminary selection, also taking into consideration, the diffusion coefficients of the core material and of the substances surrounding the wall.

Results of investigations on the permeability of wall materials are reproduced in Figures 5—7[9, 11]. As expected the permeability decreases with increasing molecular weights of the permeating materials[10]. The state of the polymeric wall material also influences the permeability. Thus the rate of release of sulfamerazine from gelatin microcapsules diminishes sharply with increasing degree of crosslinking in the gelatin[11].

2.3. Mode of Preparation of the Microcapsules

Capsules may be prepared in dispersion, for example in water, or as dry capsules, for example, in the form of a free-flowing powder. The suitable form will always depend on the subsequent use. The surrounding medium is of decisive importance as regards the stability of the capsules and especially of their contents.

Table 2. Hildebrand's solubility parameter δ [(cal/cm³)$^{1/2}$] for some solvents and polymers [8]. As a rule two solvents are miscible if their solubility parameters δ do not differ by more than 2—3 units. For polymers the δ range is given: 0 denotes insolubility in solvents of this group.

δ	Solvents with poor H-bonding
0	Nylon 8
0	Poly(vinylformal)
7.0	*n*-Pentane
8.3	Polyethylene
8.9	Toluene
9.3	Chloroform
9.3 ± 1.3	Polystyrene
9.6	Chlorobenzene
9.6 ± 1.5	Ethylcellulose, N 22
10.2 ± 0.9	Vinyl chloride-vinyl acetate copolymer
10.8 ± 1.2	Polymethyl methacrylate
11.8	Acetonitrile
11.9 ± 0.8	Nitrocellulose SS 0.5 s, dry

δ	Solvents with moderate H-bonding
0	Nylon 8
7.4	Diethyl ether
8.5	*n*-Butyl acetate
8.8 ± 1.0	Ethylcellulose N 22
9.0 ± 0.9	Polystyrene
9.1	Ethyl acetate
9.4	Dibutyl phthalate
10.0	Acetone
10.6 ± 2.8	Vinyl chloride-vinyl acetate copolymer
10.9 ± 2.4	Polymethyl methacrylate
11.5 ± 1.6	Polyvinylformal
11.9 ± 0.8	Nitrocellulose SS 0.5 s, dry
13.3	Propylene carbonate
14.7	Ethylene carbonate

δ	Solvents with strong H-bonding
0	Polymethyl methacrylate
0	Polyvinylformal
0	Polystyrene
9.5	2-Ethylhexanol
10.9	*n*-Pentanol
11.0 ± 3.6	Ethylcellulose N 22
12.6 ± 1.6	Nylon 8
12.7	Ethanol
13.9	Ethylene glycol
14.5	Methanol
14.5	Nitrocellulose SS 0.5 s, dry
16.5	Glycerol
23.2	Water

3. Microencapsulation Techniques

Microencapsulation can be carried out in two ways: (i) physicomechanically and (ii) chemically.

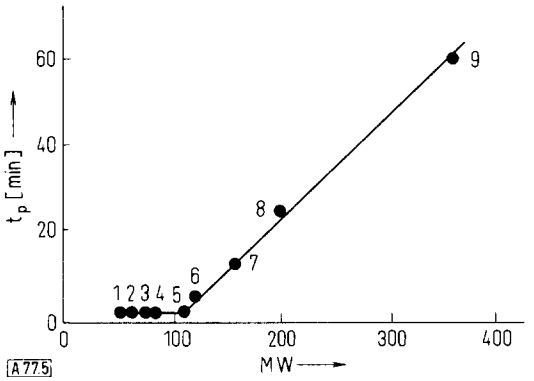


Fig. 5. Reciprocal permeability (t_p) of nylon microcapsules as a function of the molecular weight (MW) of the permeating substance. 1 = acetone, 2 = urea, 3 = ether, 4 = thiourea, 5 = creatinine, 6 = L-cysteine, 7 = DL-methionine, 8 = D-dextrose, 9 = D-sucrose (after [9]).

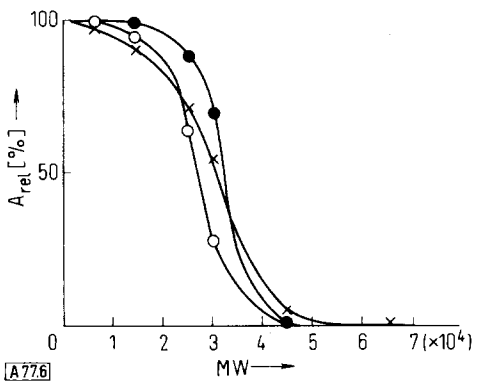


Fig. 6. Permeability of microcapsules (wall materials: o — o ethylcellulose, ● - ● cellulose acetate and × — × polyvinylformal) as a function of the molecular weight (MW) of the permeating substances methylene blue, tuberactinomycin, polymyxin B, insulin, lysozyme, α-chymotrypsin, semi-alkaline protease, pepsin, ovalbumin, serum albumin, and γ-globulin; measured as their relative adsorption on activated charcoal as core material (after [10]).

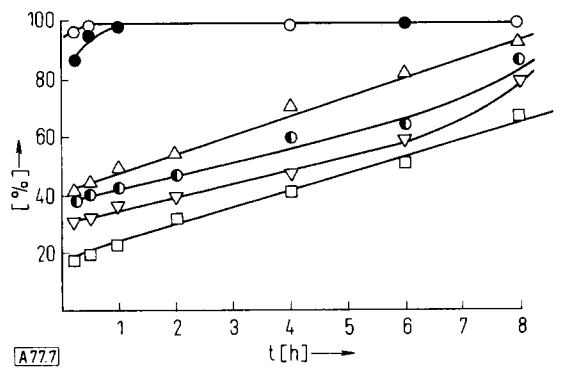


Fig. 7. Rate of release of sulfamerazine from microcapsules made of gelatin with various degrees of crosslinking; gelatin/sulfamerazine 8:4; solution medium: acid pepsin solution B.P.; temperature 37 °C. o Sulfamerazine crystals, ● noncrosslinked gelatin envelope. Gelatin envelope treated with formaldehyde for △ 15 min, ◐ 1 h, ▽ 3 h, □ 6 h; after [11].

In the physicomechanical procedures liquid and solid particles are encapsulated in the gas phase. The chemical encapsulation techniques make use of the liquid phase, *i. e.* the process is carried out in emulsion or dispersion. Deposition of the wall material on the interface between the liquid core material and the liquid surrounding medium represents the chief problem here. Not only must a third phase be precipitated, but it must also appear in the right place, namely at the boundary between the two other phases.

3.1. Physicomechanical Microencapsulation Techniques

3.1.1. Spray Drying

One microencapsulation process of very general application consists in the spraying of an emulsion or dispersion in a stream of hot inert gas. A film-forming polymer is dissolved in the continuous phase which surrounds the core material particles inside the sprayed droplets. The drying process causes this solution to shrink into a pure polymer envelope firmly enclosing the core material. The resulting capsules are obtained as free-flowing, dry powder.

For the preparation of capsules containing dye solutions and pigment dispersions for copying papers, for example, a dispersion of carbon black in oil is emulsified in a large excess of a solution of film-forming polymer, *e. g.* hydroxyethylcellulose in water. The emulsion is then atomized and the water volatilized. Free-flowing microcapsules 1 to 10 μm in diameter are obtained[12]. A wide range of solid particles have been encapsulated by means of this procedure from an organic solution of a film former[13].

Preformed microcapsules can be obtained as powder by spraying from their dispersion. This procedure is also used for putting a second or third wall layer around the capsules and thus for altering the wall permeability[14].

3.1.2. Dipping or Centrifuging Techniques

The principle of these techniques is based on passing the core material particles or droplets at high speed through a thin film of the liquid envelope material. The particles entrain the wall material and are enveloped by it. Microcapsules are formed when the wall material film sets, for example in a hardening bath. The technique gives relatively large capsules, with diameters of up to 8 mm, and the size uniformity is very good.

A special embodiment is the centrifuge process proposed by *Sommerville*[15, 16].

The core material atomized from a rotating disk strikes a row of the numerous orifices on the periphery of the centrifuge bowl. A film of the wall material is stretched over the orifices and is constantly renewed by fresh wall material solution.

In one example kerosene as core material is enveloped with a solution of polyvinyl alcohol and sodium alginate in water/glycerol. The wall material is hardened in 20 % $CaCl_2$ solution.

3.1.3. Multiple Nozzle Spraying

In multiple-nozzle processes the core material emerges from an inner nozzle and the wall material from a concentric ring nozzle slit. When the stream tears outside the nozzle, droplets consisting of core and envelope are formed. Water or aqueous solutions are enveloped in a shell of paraffin and other waxes. The capsule diameters vary from fractions of a millimeter to a few millimeters.

The capsule wall is hardened either by cooling and allowing it to set or in a hardening bath[16–18].

3.1.4. Fluidized Bed Coating

Finely divided solid core material is held suspended by a vertical current of air and sprayed with the wall material

solution. Following evaporation of the solvent a solid skin of the wall material is deposited around each particle.

This technique lends itself to coating solid particles with diameters from 40 μm up to tablet size. Smaller particles agglomerate. Pharmaceuticals, chemicals, seeds, and foodstuffs above all are encapsulated in this way. The list of wall materials used stretches from sugar through gelatin, resins, and waxes to cellulose derivatives and synthetic polymers.

A special embodiment is the process known as the Wurster process in the American literature[19–21]. It is carried out in chambers with batches of up to 450 kg. The chambers are fitted with a fixed vertical pipe, around which the core material carried by the ascending air current is made to circulate. It moves upward through the interior of the vertical pipe section while being sprayed and descends outside the pipe section while the coating dries. Each time the particles pass through the encapsulating zone they receive an extra coating. This process is repeated until the desired thickness of the coating is achieved, depending on the intended use of the capsule.

3.1.5. Electrostatic Microencapsulation

Liquids can be encapsulated by atomizing the core material and molten wall material and charging the two kinds of droplets with opposite polarity. The droplets are then mixed in a collision chamber where they combine. To obtain the capsule shape the particles are allowed to dwell as a suspension in a thermostated space and are then cooled to give capsules in powder form[22].

3.1.6. Vacuum Encapsulation

The principle of this process consists in enveloping solid nonvolatile core materials under high vacuum. The wall material is volatilized in vacuum and condensed on the colder particles, which are in rotary motion. Paraffins, waxes, metals, oxides, and the like are used as the wall materials.

Various types of apparatus can be used for this purpose. In one of them the core material particles are cooled in a reservoir vessel and are allowed to fall onto a vibrating chute under vacuum where they are struck by a jet of vaporized wall material and coated. Capsules of 10 μm to 25 mm can be produced[1, 4, 23].

In another type of apparatus the evaporator is situated in the center of a drum, which rotates at a speed such that the particles adhere to the inner wall. The particles are turned by a scrabber. This arrangement is used predominantly for the coating of acetate flocks, silicon carbides, ceramic compositions, and metal powders with a wide variety of metals[24].

3.2. Chemical Encapsulation Techniques

Over the years many chemical encapsulation techniques have been developed. The capsule wall can be formed by polyreactions from monomeric or oligomeric starting materials, or from preformed polymeric wall material.

3.2.1. Wall Formation from Monomeric or Oligomeric Starting Materials by Polycondensation and Polyaddition

A very well known encapsulation technique is based on the principle of interfacial polycondensation[25]. One monomer component, for example ethylenediamine, is dissolved in water, and this solution is covered with the solution of the other component, for example, terephthalic acid dichloride in toluene. The result is the instantaneous formation of a film of polyamide, insoluble in either phase, at the interface between the mutually immiscible phases. *Ruus*[14] and later *Vandegaer*[26] modified this process by dispersing a toluene solution of terephthalic acid dichloride, with vigorous stirring, in an excess of water containing polyvinyl alcohol as protective colloid. An aqueous solution of ethylenediamine is then added slowly to this emulsion. To neutralize the liberated acid, the aqueous diamine solution contains an appropriate quantity of caustic soda. The two monomers react at once on the interface between the toluene droplets and water to form solid polyamide. Capsules are obtained, which in this case contain toluene as the core material (Fig. 8).

The procedure is very simple in principle. The reaction very quickly affords a capsule wall whose thickness tends to a limiting value determined by the resistance offered by the wall to diffusion of the components. This process is especially suitable for laboratory encapsulations and for studying the preparation of capsules in terms of capsule diameter, wall permeability, and the charge on the capsule as a function of the core materials[27, 25]. The reactivity of the monomers sets limits on the choice of the core material and the surrounding medium.

The properties of the polymers used for the capsule wall can be varied by suitable selection of the diamines or acid dichlorides, for example, hexamethylenediamine, sebacoyl chloride, phosgene, and many others. Triamines lead to crosslinking and thus enable reduction of the permeability of the capsule wall.

This technique can be used, for example, for the production of capsules containing water as the core liquid by spraying an aqueous diethyltriamine solution into a terephthalic acid dichloride solution in petrol.

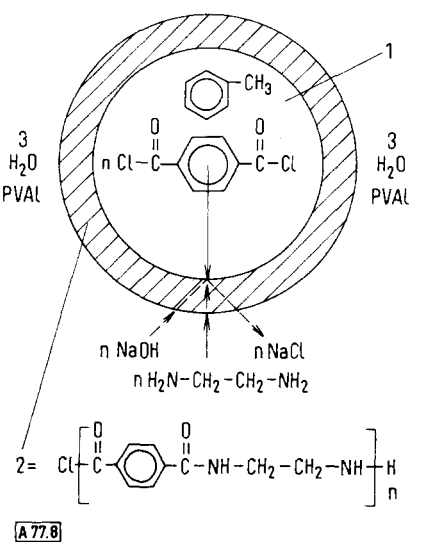


Fig. 8. Encapsulation of toluene by the interface polycondensation technique. 1 = inner or core phase consisting of toluene and terephthalic acid dichloride, 2 = capsule envelope of polyamide, 3 = continuum consisting of water, polyvinyl alcohol (PVAL), ethylenediamine, NaOH, and NaCl.

Isocyanates, or polyisocyanates may be used for the encapsulation in place of the acid chlorides[28, 29]. In some cases they are used in combination with the acid chlorides.

A different procedure starts from urea-formaldehyde precondensates. The core material is dispersed in an aqueous solution

of the precondensate and curing of the precondensate is initiated by acidification. The resin, which becomes more and more insoluble as the condensation progresses, precipitates on the core material particles and microcapsules 1—500 μm in diameter are obtained[30].

A procedure is also known in which monomeric styrene dissolved in the core phase is insolubilized by polymerization and subsequently forms an envelope around the remaining components[31].

3.2.2. Wall Formation in the Presence of Polymeric Wall Material

Many microencapsulation techniques of this type are known. Most of them have in common the fact that the polymeric wall material is dissolved and the solution is added to the core phase or, more frequently, to the continuous phase. The core material is dispersed to the desired particle size in the continuous phase and the polymeric wall material is then deposited on the interface as a third phase by gradual precipitation of the polymer. This is achieved either by the use of precipitants, by changes in temperature, or by removal of the solvent by dilution or distillation. The state of division of the core material must not be altered. Thus, encapsulation is achieved by phase separation, in special cases by coacervation or complex coacervation. Subsequently the wall material is deposited on the core material/surrounding medium interface when its solubility parameter[8] (cf. Table 2) lies between that of the core material and the surrounding medium.

A water-soluble solid, *e.g.* ammonium dichromate powder, may be encapsulated by dispersing it in a solution of ethylcellulose in toluene/ethanol (4:1) and heating the whole to 70 °C. Slow addition of a petroleum fraction causes the ethylcellulose phase to separate and deposit on the particles. After addition of petroleum fraction in excess the capsules can be obtained by decantation[32].

Further examples are the encapsulation of ammonium nitrate with ethylcellulose[33] or with nitrocellulose[34]. Activated charcoal[10] and phenobarbital[35] have also been encapsulated in this way.

Water or glycerol droplets can be encapsulated with a partially saponified ethylene-vinyl acetate copolymer. A stirred solution of the wall material in toluene is warmed and treated with a solution of polydimethylsiloxane in toluene (1:1) and with the glycerol to be encapsulated. Three phases are formed: the continuous phase with polydimethylsiloxane in toluene, the glycerol phase as the microcapsule core, and a solution of the wall polymer in toluene. After cooling and crosslinking of the wall material the microcapsules are separated with toluene diisocyanate[36].

In a technically reliable microencapsulation technique[37] a copolymer is used consisting of hydrophilic and hydrophobic monomer units. It is insoluble both in the core material (for example hydrocarbons) and in water. The copolymer of various acrylic and methacrylic acid derivatives is dissolved in a low-boiling solvent, *e.g.* chloroform and isopropyl alcohol, and added to an emulsion of the core material in water with vigorous stirring. The water as the external phase contains a protective colloid, for example polyvinylpyrrolidone. On dispersion the polymer solution is distributed over and around the core material droplets. Depending on solubility, the organic solvents at once become distributed over the core phase, the water phase, and the wall material phase. The change in the solvent composition produces separation of the wall material phase in highly viscous form. Distillation removes the low-boiling components leading to solvent-free deposition of the wall. The wall material may subsequently be crosslinked with formaldehyde, dialdehydes, or diamines. A 16 to 30% capsule dispersion is obtained, which consists for example, of individual capsules 6—12 μm in diameter (cf. Fig. 1a).

3.2.2.1. Coacervation

During conversion of a lyophilic colloid from the sol state into that of a solid precipitate by insolubilization an intermediate state can arise. This state is characterized in that the previously uniformly distributed colloid or polymer precipitates in a second, still liquid, solvent-containing phase. *Bungenberg de Jong* and *Kruyt*[38] called this process coacervation (Latin "acervus", heap).

The coacervation, triggered off by the addition of a salt or precipitant, by dilution, or by a change in pH, begins with the precipitation of very fine coacervate droplets accompanied by clouding of the previously almost clear sol (microcoacervation).

As the coacervation continues the fine coacervate droplets coalesce into larger ones (macrocoacervation), until a coherent coacervate phase is formed which contains practically all of the polymer. The coacervate droplets display a tendency toward enclosing solid particles, such as dyes, present in the sol.

Green[39] used this phenomenon for microencapsulating very finely dispersed dye precursor solutions, which he divided and dispersed in the polymeric solution before carrying out the coacervation (Fig. 9).

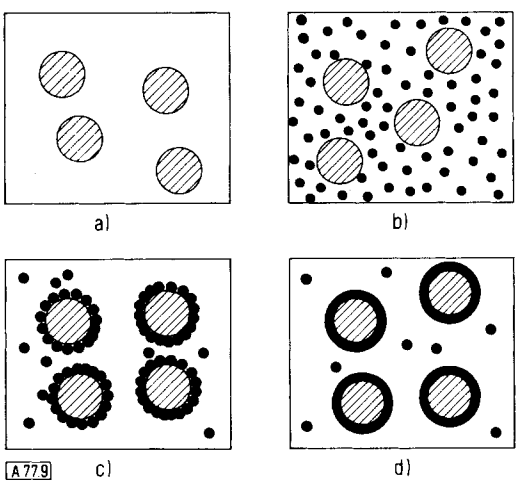


Fig. 9. Schematic representation of microencapsulation by coacervation. a) Dispersed core material droplets in gelatin/gum arabic solution; b) beginning of coacervation by precipitation of fine-particle microcoacervate from the solution; c) gradual precipitation of the microcoacervate on core material droplets; d) coalescence of the microcoacervate of the wall material phase.

3.2.2.2. Encapsulation by Complex Coacervation

Complex coacervation is the mutual precipitation of two oppositely charged sols or polymers in solution to form a complex coacervate. A gelatin solution is mixed with a gum arabic solution at, for example, pH 4.5 and is then diluted (Fig. 10), or the pH of the diluted solution is slowly adjusted to pH 4.5. Gelatin is an amphoteric polymer with an isoelectric

point at pH 8. On acidification of the solution the polymer becomes positively charged and interaction with the always negatively charged gum arabic takes place. Since gelatin solutions gel at room temperature, the complex coacervation is carried out above the gelation temperature of 37 °C.

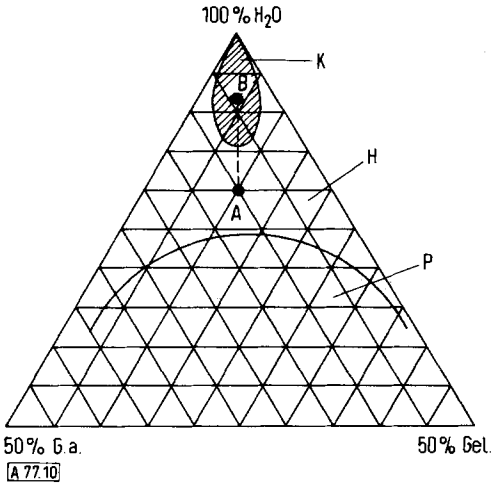


Fig. 10. Three-component diagram for complex coacervation of gelatin (Gel.) and gum arabic (G.a.) by dilution with water at pH 4.5; dilution proceeds along the line from A to B; K = complex coacervate region (both polymers are in the coacervate); H = homogeneous solution region; P = phase separation region in which the two polymers are present in different phases (after [39]).

Industrial scale microencapsulation is carried out as follows: The solution of the gellable hydrophilic polymer gelatin is placed in a stirred vessel and the core material, *e.g.* the solution of dye precursor, is emulsified in it until the desired particle size of say 2—5 µm has been obtained. Gum arabic solution is then added. Coacervation occurs, the system being constantly stirred. Subsequently the composition is cooled from 50 °C to 5—10 °C and the gelatin-gum arabic complex coacervate which has precipitated around the core phase is allowed to gel. It is hardened by the addition of glutaraldehyde or formaldehyde and slow adjustment of the pH to 9—10 with caustic soda.

This process is used, for example, for the production of microcapsules used in the manufacture of carbonless copy paper (Sections 4.1.1 and 4.1.2). The microcapsules obtained by this method are to a greater or lesser extent cluster aggregates (cf. Fig. 1b). By taking suitable measures the agglomeration can be prevented[40].

3.2.2.3. Encapsulation by Chemical Reaction of the Polymer

The solution of hydrolyzable cellulose derivative is dispersed in the core material, *e.g.* a solution of the aniline dye Ceres Blue GN^R in a mixture of 68 parts of cyclohexanone and 25 parts of diphenoxyethylformal in water containing caustic soda and some dispersant. The dissolved cellulose derivative is saponified, which leads to the precipitation of a water- and core-material-insoluble cellulose film on the core material as a third phase. Capsules 30—50 µm in diameter are formed and can be isolated after washing with water[41].

4. Applications of Microcapsules

4.1. Capsules with Impermeable Envelopes

4.1.1. Carbonless Copy Paper

In the past copies of writing were produced solely by inserting a sheet of carbon or copying paper between the original and the intended copy. The impression was obtained through the transfer of carbon, by virtue of the writing pressure, from the layer on carbon paper onto the sheet underneath. This technique is simple but has certain drawbacks. The inserted carbon paper makes the paper assembly thicker. Parts of the assembly shift readily out of register and the whole is therefore difficult to manipulate. The carbon paper tends to soil the fingers and the copy. The copy itself is not rubproof. Environmental problems arise during destruction of the papers.

These adverse factors soon prompted a search for an improved, "cleaner" method of copying. The work undertaken to this end led to a number of novel mechanically and chemically reacting copying paper. The latter has become known in the English-speaking countries as carbonless copy paper or simply carbonless paper. It is estimated that 500000 tons of carbonless copy paper was used in 1974 in the Western hemisphere, including Japan: this corresponds to 50000 tons of microcapsules. The proportion of carbonless paper in the copy paper market varies between 7 and 40 %[42].

In these carbonless papers the carbon is replaced by a solution of dye precursor which is transferred to a specially prepared surface of the copying sheet underneath, on which the dye develops.

Initially, the back of the top sheet was for this purpose provided with a type of foam coating, in the voids of which the dye precursor solution was located. However, this arrangement was not very successful[43]. It was not until *Green*[39] produced microcapsules by successfully enveloping very fine droplets of dye precursor solution with gelatin by means of coacervation that the breakthrough for carbonless copy paper arrived. Microencapsulation began to develop at the same time.

4.1.2. Makeup and Mode of Action of Carbonless Copy Papers

How are carbonless copy papers made today? Let us take a look at a simple set of invoice forms, or a transfer requiring two copies. The top or CB (coated-back) sheet carries the microcapsule layer on the back. Underneath lies a middle or CFB (coated front and back) sheet, carrying the developer layer on the front and the capsule layer on the back. Below this is the bottom or CF (coated front) sheet with the developer layer on top.

The individual layers can be reproduced with the aid of scanning electron microscopy (SEM). Fig. 11a shows the surface of untreated paper, Fig. 11b the same paper coated with the active adsorbent, the developer or acceptor layer (7—8 g/m^2). The developer layer consists of activated inorganic pigments such as attapulgite, Fuller's earth, silica gel, and sodium aluminum silicates[44], which are fixed together with a binder, *e.g.* a polymer dispersion. Recently, organic substances such as phenolic resins[45] and salts of salicyclic acid derivatives have been used as developers.

Fig. 11c shows a layer of microcapsules on the back of the top or CB sheet (5 g capsules/m^2). The botryoidal aggregation of gelatin capsules is embedded in a binding material. The cellulose cuttings, which are added to the layer of capsules as a spacer, prevent premature destruction of the capsules. Starch and other powders have recently been employed as spacers.

Fig. 11d shows a layer of single microcapsules on the back of a top or CB sheet. The wall of the capsules manufactured

by the phase separation process consists of an acrylate copolymer. Fig. 11e shows these capsules after the sheet has been used for copying, *i.e.* after the writing process.

Black copies can be obtained by combining suitable color formers, for example blue, red, and yellow, or green-blue and red[50].

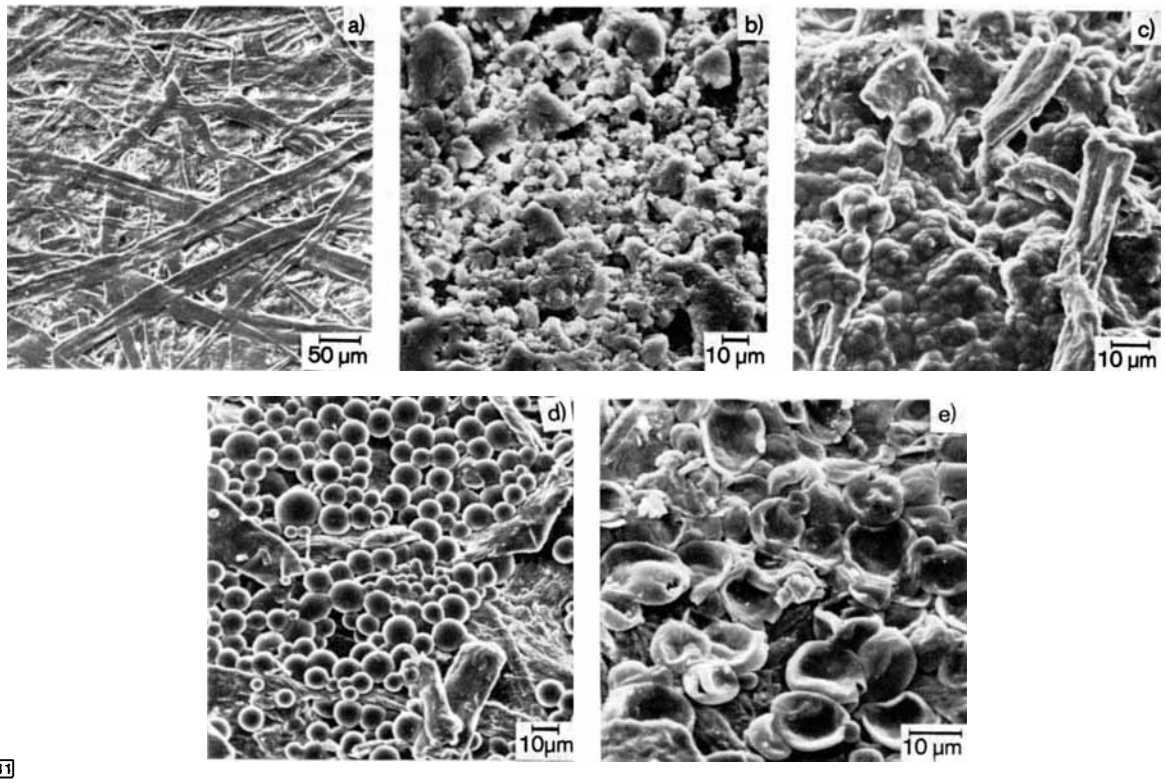


Fig. 11. a) Untreated paper surface. b) Carbonless copy paper; with bottom or CF sheet coated with activated clay as developer. c) Gelatin microcapsules (filled with dye precursor solution) on the back of the top or CB sheet. The capsules were manufactured by complex coacervation. Cellulose cuttings as spacer. d) Individual acrylate-copolymer microcapsules (filled with dye precursor solution) on the back of the top or CB sheet. The capsules were manufactured by the phase separation process. Cellulose cuttings as spacer. e) The capsules shown in Fig. 11d after the writing process. (SEM micrographs.)

In most commercially available papers the capsule content consists of two dye precursors: 3,3-bis(*p*-dimethylaminophenyl)-6-dimethylaminophthalide (crystal violet lactone) (see Fig. 12) and *N*-benzoylleukomethylene blue (see Fig. 13). The two color formers are dissolved in high-boiling hydrocarbons such as polyphenyl derivatives[46], alkylnaphthalenes[47], and alkylbenzenes[48] alone or mixed with high-boiling petroleum fractions (4—6 % solutions).

The weight ratio of the wall material to the core material is 20—30 parts of wall material to 60—90 parts of core material (coloring solution).

Crystal violet lactone develops a blue color on the adsorbent within a few seconds. Like all triphenylmethane dyes, it is not very stable and fades with time, especially on exposure to light. *N*-Benzoylleukomethylene blue slowly develops a blue-green color over a period of weeks, which is substantially more lasting. By combining the two color formers an initially blue and later a stable blue-green copy is obtained.

The development of the color from crystal violet lactone occurs as a result of the opening of the lactone ring on the solid activated surface following chemisorption of the molecule[*] (Fig. 12).

The color from *N*-benzoylleukomethylene blue develops by hydrolysis and photooxidation on the activated adsorbent[49].

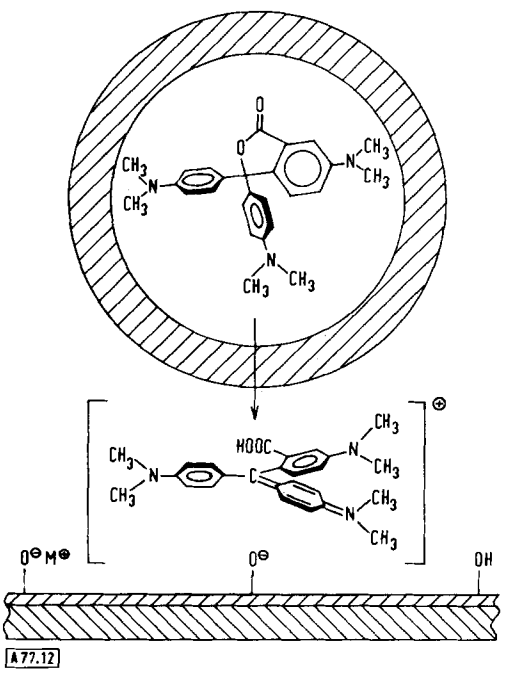


Fig. 12. Development of color from crystal violet lactone in the leuko form (top) by formation of the blue pigment ion on the developer layer (bottom).

By applying capsules and active adsorbent (developer) together on the front of a sheet of paper a so-called "self-contained paper" is obtained. Since the capsules are present next

[*] *H. Feichtmayr*, Farbenforschungslaboratorium, BASF AG, private communication.

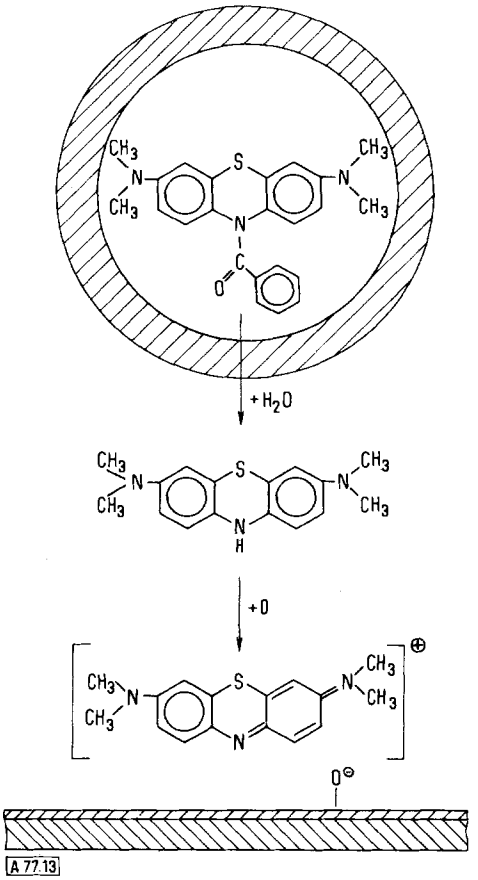


Fig. 13. Development of color from *N*-benzoylleukomethylene blue (top) by slow hydrolysis to leukomethylene blue (center) and its rapid photooxidation to the pigment ion on the developer layer (bottom).

to activated pigment, any site where the capsules are destroyed at once produces a mark caused by the color former developing on adjacent pigment. Thus, these papers furnish copies even when used in combination with unprepared paper.

4.1.3. Additional Uses of Microcapsules with Impermeable Envelopes

Liquid crystals of the cholesterol ester type are protected from UV light, moisture (hydrolysis), and impurities by microencapsulation in capsules 10—30 μm in diameter[51]. In this form they can be easily utilized. Their property of changing color with temperature is used in medical diagnosis for determining skin temperature characteristics[52, 53] and in other fields[54].

For producing lightweight papers an attempt was made to use hollow spheres with a diameter of 25—28 μm as lightweight pigment[55]. They are manufactured by emulsion polymerization[56] of vinylidene chloride and subsequent formation of hollow microcapsules by expansion of the polymer particles containing isobutane as a blowing agent.

The irritant action of flame-retardant substances on the skin and mucosa, above all of halogenated organic compounds, can be reduced substantially by microencapsulation. The compatibility of the encapsulated substances with polymeric systems is increased, thus improving their blendability. In case of fire the capsule opens as a consequence of the rise in temperature and releases the flame-retardant[57].

Microencapsulation of adhesives, above all two-component adhesives, also offers many advantages. In the case of unsaturated polyesters, and especially epoxides, the liquid components are encapsulated[58]. The capsules (25—150 μm in diameter) are processed together with the binder and the second component. In aircraft[60] and automobile[61] construction *e.g.* they are applied onto screws[59] or rivets; the capsule contents are released on riveting or screwing, and the result is a metal-to-metal bond plus an anticorrosive effect.

After the encapsulation of liquid curing agents such as triethylenetetramine and hexamethylenetetramine and mixing with epoxides, a slow outward diffusion and reaction cannot be avoided. All the same, the time needed for setting to take place after mixing increases to 10 days to 8 weeks. The contents are released by heating[62].

The use of microencapsulated flavors, leaveners for bakery goods, fermentation agents, oils, and fats has become widespread in the food industry, especially where liquid substances must be converted into solids for dry mixes or where an improved durability or reduced volatility is desired. The active content of the capsules is 50—90%. Release is by heat, by pressure (chewing gum) or by dissolution of the wall (above 40 °C). Natural or synthetic polymers tested and approved by the American FDA are used as wall materials. Examples are gelatin, gum arabic, and cellulose derivatives.

In the marine feedstuffs sector efforts are being devoted to developing feeds sufficiently finely divided for freshly hatched fish; however, no suitable composition has as yet been discovered[63]. Feeding of encapsulated unsaturated vegetable fats to cattle leads to the production of milk containing a higher proportion of unsaturated fats. The capsule walls protect the unsaturated fats from enzymatic hydrogenation during the passage through the stomach and open only later, in the acidic intestinal portion of the digestive tract, where the fats hydrolyze[64]. The encapsulation of vitamins and hormones to protect them against oxidation and degradation is also known in the feedstuffs industry.

Brighteners in household detergents have been encapsulated (to provide protection against bleaching agents), as have also bleaching agents and odoriferants[65].

An attempt is being made to encapsulate certain rodenticides in order to neutralize their taste. The amounts ingested by rats are indeed increased, but the mortality rates achieved give conflicting results. It is probable that the release mechanism has not yet been adequately mastered[66].

To combat fire ants Mirex capsules have been developed. By encapsulating the insecticide the applied dose is reduced to one-half or one-quarter[67, 68].

4.2. Microcapsules with Controlled Release of the Contents

The enveloping of readily soluble fertilizers[69] has long been of interest to agriculture. Waxes, resins, asphalt, and also plastics made of urea-formaldehyde resins, polystyrene, polyethylene, and even polyepoxides and polyurethanes, have been employed for enveloping. A uniformly diminished dissolution rate is obtained both by multiple coating—*e.g.* of ammonium nitrate, aiming at a decrease in the hydrophilic properties of the wall material toward the outer layers[70]—and by single coating of compound fertilizers. Fig. 14 demonstrates the release of the nitrogen component of a compound fertilizer encapsulated with 1—10% by weight polybutadiene, which is active up to a complete growth period of 6—9 months[71]. The combination of aminoplast resins with a very wide range of polymers gives similar results[72]. Urea envel-

oped in sulfur[73] and a wax-capsulated fertilizer solution[74] intended for small gardens have recently been developed.

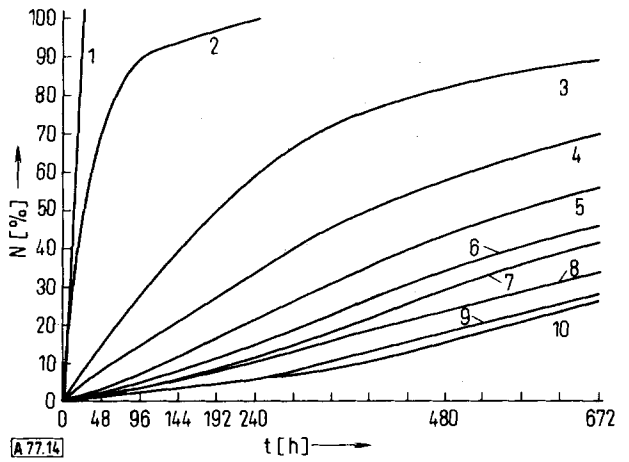


Fig. 14. Fertilizer release (in % nitrogen) with time t following the water immersion of a compound manure (13 N/13 P_2O_5/21 K_2O) particle size 2—4 mm, enveloped in 1—10 wt-% polybutadiene (after [71]).

Encapsulation avoids a high local fertilizer concentration and reduces the number of applications required. With small amounts of the coating material, for example less than about 1% polybutadiene on 2—4 mm fertilizer grains, nondusting and noncaking materials are obtained[75].

Encapsulation of the sown crops retards germination to such an extent that summer grain can be sown as early as the fall. The result is a very early appearance of the crops in the spring[76].

The insecticide methyl parathion has been encapsulated with polyamide[26], whose degree of crosslinking determines the rate of release. Methyl parathion [*O,O*-dimethyl-*O*-(*p*-nitrophenyl)thiophosphate] has a short persistence of several hours to some days and is very toxic. Encapsulation to give a diameter of 30—50 μm allowed the persistence to be increased and the toxicity to be reduced to 1/9th. The slow release by diffusion and the greater persistence allow smaller doses and fewer applications to be used[77, 68]. This type of product has been approved for cultures of cotton, lucerne, and sweet corn by the FDA in the United States since 1974.

Copper sulfate is encapsulated to act as a water herbicide (algicide)[68]. The capsules, 1600 μm in diameter, cannot be sprayed. They sink to the bottom in water and slowly liberate the copper sulfate by diffusion through micropores or after biological degradation of the capsule wall. Field trials are being conducted on encapsulated insect sexual stimulants and pheromones[63].

In pharmacology an attempt is being made to achieve a depot effect by slow release of the therapeutic agent from the microcapsules and to prevent an overdose immediately after administration[78, 79, 11, 6, 35]. Here masking the taste[80, 81] protection against oxidation[82] are also of vital importance. Gelatin, gum arabic, hydroxystearyl alcohol, glyceryl monostearate, sodium alginate, ethylcellulose, and carboxymethylcellulose are used as the capsule wall materials.

In the cosmetic industry, the release of deodorants, perfumes[65, 83], and antitranspirants[84] can be controlled by microencapsulation, *i.e.* their action can be sustained.

4.3. Microcapsules with a Semipermeable Envelope

Semipermeable microcapsules offer a sound prerequisite for separating substance systems. As packings in columns they are simple and clean in use. Their very small dimensions give them an extremely high area-to-volume ratio, while their very thin membrane-like envelope is very stable. Thus, they allow a high rate of exchange.

Kondo et al.[85] have determined the permeability constants of 24 different, encapsulated electrolytes. The capsule walls were prepared by interfacial condensation from diethylenediamine and terephthaloyl dichloride. The permeability constant of the 2 μm capsules was very small (10^{-8} cm/s). Diffusion obeyed Fick's law.

Thies et al. used water-containing microcapsules for the liquid/liquid extraction of monoethylamine, triethanolamine, and triethylenetetramine in chloroform or toluene[86]. The capsules were prepared by a special procedure[36], with walls of partially hydrolyzed ethylenevinyl acetate copolymers and were crosslinked with isocyanate. They were used in a normal chromatographic column. Up to a certain limiting value the capsules absorb the amines completely.

Microencapsulated activated charcoal[10] (see Fig. 6) has been used, *inter alia*, for the preparation and purification of kanamycin, tuberactinomycin from its mother liquor, lysozyme from protein, and decolorization of protease solution.

Microcapsules with semipermeable envelopes are equivalent to natural biological cells and mitochondria. *Chang*[9, 87] has prepared a series of microcapsules of varying selectivity (see Fig. 5) and reactivity ("artificial cells"). The envelopes were generally obtained by interfacial condensation. Selection and combination of a wide range of monomers enabled very different envelopes to be produced, capable of withstanding considerable internal pressures. Individual enzymes and enzyme combinations were encapsulated. Urease, carboanhydrase, trypsin, catalase, aspariginase, lipase, lactase, and the hemolyzate of red blood cells are active in the encapsulated form. At high protein concentrations the stability of encapsulated enzymes is better than that of free enzymes[87].

Chang is attempting to use the artificial cells for building up artificial organs, for the treatment of liver and kidney failure and in treating cases of drug poisoning. In order to make the microcapsules compatible with blood they are coated with albumin.

Microencapsulated urease selectively converts urea into ammonia[88] and blood urea can thus be transformed in an exchange chamber located outside the body. The ammonia formed must be bound by a special adsorbent[89]. Microencapsulated asparaginase enables asparagine to be removed selectively and, in this way, the growth of asparagine-containing tumors is suppressed. Uremic toxins can be removed with microencapsulated activated charcoal. The adsorption is very fast[88].

An artificial kidney has been developed which has been in clinical use for the past 4 years. Inside the small apparatus 300 ml of large microcapsules (about 200 μm in diameter) have a surface area of 2.25 m^2, which is twice that of the membrane of a standard artificial kidney (1 m^2). As a result of the very thin membranes (0.05 μm) a 200 times faster transport rate is obtained, and the patient-treatment time can be reduced from 6—12 h to 2 h[87].

5. Concluding Remarks

In the initial stages of the development of microencapsulation impermeability of the capsules was the main concern. Under these circumstances the core substance can be released and *e.g.* made available for a reaction only by destruction of the capsule wall. This procedure has rapidly gained major economic importance, notably for encapsulating color-former solutions for carbonless copy papers. At first the encapsulation was carried out by depositing gelatin envelopes onto liquid droplets of an aqueous emulsion, but with the course of development new techniques and new natural and above all synthetic polymers began to be used as the wall materials. As a result, the increasing variation in the possible core materials was accompanied by a variation in the properties of the envelope.

At the present time envelopes making possible a slow release of the core substance are being investigated. Drugs, fertilizers, and plant-protection agents are being studied as the core materials. The aim is to obtain a uniform release of the active principle over a prolonged period and to avoid harmful overdoses at the commencement of use. The developing environmental consciousness has led to new tasks being posed in respect of plant-protection agents for which microencapsulation too is being employed in various laboratories. Extensive experiments are required to obtain official authorization to use the encapsulated active principles. An encapsulated insecticide has already been approved for certain crops.

Microcapsules with semipermeable envelopes can be produced and used for separation processes. Their use in biochemistry and medicine is of special interest. Here enzymes and enzyme systems in addition to adsorbents can now be given a stable encapsulation. These microcapsules are the equivalent of artificial cells. Packed in columns, they can perform the function of organs; an artificial kidney of very small dimensions (about the size of a football) is already undergoing clinical trials.

Much work remains to be done in matching the properties of the capsules to the circumstances and to exhaust the possibilities offered by microencapsulation. Future development of microencapsulation commands great interest.

Received: June 5, 1975 [A 77 IE]
German version: Angew. Chem. *87*, 556 (1975)
Translated by Express Translation Service, London

[1] *J. A. Herbig* in Kirk-Othmer: Encyclopedia of Chemical Technology, 2nd Ed. Wiley, New York 1967, Vol. 13, 436.
[2] *C. A. Anderson et al.*: Microencapsulation. Management Reports, Boston 1963.
[3] *M. Gutcho*: Capsule Technology and Microencapsulation. Noyes Data Corp., Park Ridge, N. J. 1972.
[4] *L. A. Luzzi*, J. Pharm. Sci. *59*, 1367 (1970).
[5] *D. F. Müller*, Verfahrenstechnik *6*, 409 (1972).
[6] *P. L. Madan, J. C. Price*, and *L. A. Luzzi*, 166th ACS-Meeting, Chicago, 33 No. 2, 589 (1973).
[7] *L. Si-Nang, P. F. Carlier, P. Delort, J. Gazzola*, and *D. Lafont*, J. Pharm. Sci. *62*, 452 (1973).
[8] *J. H. Hildebrand*, J. Am. Chem. Soc. *57*, 866 (1935); *J. Hildebrand* and *R. Scott*: The Solubility of Nonelectrolytes, 3rd Ed. Reinhold, New York 1949; *H. Burrell*, Off. Dig. Fed. Soc. Paint Technol. *27*, 726 (1955); VI. Fatipec-Kongress, 21 (1962); *C. M. Hausen*, J. Paint Technol. *39*, 104 (1967).
[9] *T. M. S. Chang*: Artificial Cells. Charles C. Thomas, Springfield, Ill. 1972.
[10] *M. Morishita, M. Fukushima*, and *Y. Inaba*, 166th ACS-Meeting, Chicago, 33 Nr. 2, 603 (1973).
[11] *J. R. Nixon, S. A. H. Khalil*, and *J. E. Carless*, J. Pharm. Pharmacol. *20*, 528 (1968).
[12] *N. Macaulay*, US-Pat. 3016308 (1957). Moore Business Forms.
[13] *P. I. Wilson* and *F. R. Johnston*, DAS 1294932 (1965), Dunlop Rubber Co.
[14] *H. Ruus*, DOS 1444415 (1962), US-Pat. 3429827 (1962), Moore Business Forms.
[15] *G. R. Sommerville*, US-Pat. 3015128 (1960), Southwest Research Institute, Texas.
[16] *J. T. Goodwin* and *G. R. Sommerville*, 166th ACS-Meeting, Chicago, 33 No. 2, 611 (1973).
[17] *J. T. Goodwin* and *G. R. Sommerville*, Chemtech *4*, 623 (1974).
[18] *R. P. Arens* and *N. P. Sweeny*, US-Pat. 3423489 (1966), Minnesota Mining and Manufacturing Co.
[19] *D. E. Wurster*, US-Pat. 2648609 (1949), 2799241 (1949, 1953), Wisconsin Alumni Research Foundation.
[20] *T. M. Hinkes* and *H. Hall*, 166th ACS-Meeting, Chicago 33 Nr. 2, 545 (1973).
[21] *T. M. Hinkes*, Lecture at Microencapsulation Course, Dec. 1972, Wisconsin Alumni Research Foundation, Madison, Wis.
[22] *G. Langer* and *G. Yamate*, US-Pat. 3159874 (1962), IIT Research Inst.
[23] *H. Skrobek*, Verfahrenstechnik *4*, 395 (1970).
[24] *C. A. Baer* and *R. W. Steeves*, US-Pat. 2846971 (1956), National Research Corp.
[25] *P. W. Morgan*, Soc. Plast. Eng. J. *15*, 485 (1959).
[26] *J. E. Vandegaer*, US-Pat. 3577515 (1963), Pennwalt Corp.; *J. E. Vandegaer*, DAS 1519925 (1963), Wallace & Tiernan Inc.; *J. E. Vandegaer* and *F. G. Meier*, US-Pat. 3575882 (1965), Pennwalt Corp.
[27] *Y. Shigeri, M. Koishi, T. Kondo, M. Shiba*, and *S. Tomioka*, Kolloid-Z. Z. Polym. *249*, 1051 (1971); *M. Shiba, Y. Kawano, S. Tomioka, M. Koishi*, and *T. Kondo*, *ibid. 249*, 1056 (1971); *Y. Shigeri, M. Tomizawa, K. Takahashi, M. Koishi*, and *T. Kondo*, Can. J. Chem. *49*, 3623 (1971); *M. Shiba, S. Tomioka, M. Koishi*, and *T. Kondo*, Chem. Pharm. Bull. *18*, 803 (1970); *M. Koishi, M. Fukuhara*, and *T. Kondo*, *ibid. 17*, 804 (1969); *S. Suzuki, T. Kondo*, and *S. G. Mason*, *ibid. 16*, 1629 (1968); *Y. Shigeri, M. Koishi*, and *T. Kondo*, Can. J. Chem. *48*, 2047 (1970).
[28] *H. W. Mackinney*, French Pat. 1278621 (1959), IBM Corp.
[29] *H. B. Scher*, DOS 2312059 (1972), Stauffer Chemical Co.
[30] *G. W. Matson*, Can. Pat. 742643 (1961, 1962), DAS 1290799 (1962), Minnesota Mining and Manufacturing Co.
[31] DBP 1096038 (1958), National Cash Register Co.
[32] Brit. Pat. 920866 (1960), National Cash Register Co.
[33] Austrian Pat. 227664 (1960), National Cash Register Co.
[34] *J. A. Herbig* and *J. F. Hanny*, DOS 1909385 (1968), National Cash Register Co.
[35] *N. N. Salib*, Pharm. Ind. *34*, 671 (1972).
[36] *R. G. Bayless, C. P. Shank, R. A. Botham*, and *D. W. Werkmeister*, US-Pat. 3674704 (1971), National Cash Register Co.
[37] *G. Baum, R. Bachmann*, and *W. Sliwka*, DOS 2119933 (1971), BASF; *G. Baum, R. Bachmann, D. Ludsteck*, and *W. Sliwka*, DOS 2237503 (1972), BASF.
[38] *H. G. Bungenberg de Jong* and *H. R. Kruyt*, Kolloid-Z. *50*, 39 (1930).
[39] *B. K. Green*, US-Pat. 2800458 (1953); *B. K. Green* and *L. Schleicher*, US-Pat. 2800457 (1953), Austrian Pat. 199206 (1953), all National Cash Register Co.
[40] DAS 1082282 (1957), Belg. Pat. 695911 (1966), National Cash Register Co; *T. Tada*, DOS 2261189 (1971), Kanzaki Paper Manufacturing Co.
[41] *L. Harbort*, DOS 1519930 (1966), Günther Wagner, Pelikan-Werke.
[42] *N. Yamanohe*, Kami-Pulp Gijutzu Times (Paper & Pulp Technical Times), March 1975.
[43] DAS 1010822 (1953), National Cash Register Co.
[44] DP 851806 (1948), DP 871604 (1944), National Cash Register Co.; *L. Harbort*, US-Pat. 3293060 (1956), Günther Wagner, Pelikan-Werke.
[45] *R. E. Miller* and *P. S. Phillips*, US-Pat. 3672935 (1964, 1968), *B. W. Brockett, R. E. Miller*, and *M. L. Hinkle*, DOS 2228430 (1971), National Cash Register Co.
[46] *J. K. Sears*, DOS 2251350 (1971), DOS 2306454 (1972), both Monsanto Co.
[47] *A. Konishi, M. Takahashi, F. Kimura*, and *T. Toguchi*, DOS 2134326 (1970, 1971), Kureha Kagaku Kogyo Kabushiki Kaisha; *P. S. Phillips, Jr.*, US-Pat. 3627581 (1970), National Cash Register Co.
[48] *W. Sliwka, W.-J. Gaefke, T. Korth*, and *H. Hartmann*, DOS 2213755 (1972), BASF.
[49] *H. A. Potts* and *A. H. Wood*, J. Appl. Chem. Biotechnol. *22*, 651 (1972).
[50] Brit. Pat. 1222418 (1967), National Cash Register Co.
[51] *D. Churchill, J. V. Cartmell, R. E. Miller*, and *P. D. Bouffard*, DOS 1698092 (1967), US-Pat. 3732119 (1966), US-Pat. 3697297 (1966), National Cash Register Co.
[52] *T. W. Davison et al.*, Cancer *29*, 1123 (1972).
[53] *Bassini*, Rivista medicoscientificia. Milano, Vol. XV, fascicolo 1—4 (1970).
[54] *S. Kubo*, 166th ACS-Meeting, Chicago, 33 No. 2, 549 (1973).
[55] *D. L. Kenaga*, Tappi *56*, 157 (1973).
[56] *D. S. Morehouse, Jr.* and *R. S. Tetreault*, US-Pat. 3615972 (1971), DOS 1495485 (1963), Dow Chemical Co.
[57] *D. Müller*, DOS 2113470 (1971), Omnitechnic GmbH.
[58] *D. F. Müller*, Z. Werkstofftech./J. Mater. Technol. *4*, 50, 227 (1973).
[59] *J. Esser*, VDI-Nachr. *26*, No. 16, 13 (1972).

[60] Development of Multipurpose Capsular Adhesives. Picatinuy Arsenal, US Government Report Nr. DAAA-21-68c-0581.
[61] *G. O. Fanger*, Chemtech *4*, 399 (1974).
[62] *M. Bank, R. Bayless, R. Botham*, and *P. Shank*, Mod. Plast. 50, No. 11, p. 84 (1973).
[63] *R. Bayless*, Chem. Eng. News *52*, 16 (August 12) (1974).
[64] *J. Bitman, T. R. Wrenn, L. P. Dryden, L. F. Edmondson*, and *R. A. Yoncoskie*, 166th ACS-Meeting, Chicago, 33 Nr. 2, 568 (1973).
[65] *J. Veronese*, Seifen-Öle-Fette-Wachse *100*, 281 (1974).
[66] *P. B. Cornwell*, Lecture at the Third British Pest Control Conference, Third Session, Paper No. 7; *J. H. Greaves, F. P. Rowe, R. Redfern*, and *P. Ayres*, Nature *219*, 402 (1968).
[67] *G. P. Markin* and *S. O. Hill*, J. Econ. Entomol. *61*, 1 (1971).
[68] Chem. Eng. News *50*, 68 (June 5) (1972).
[69] *R. Powell:* Controlled Release Fertilizers. Noyes Development Corp., London 1968, p. 102ff.
[70] *L. I. Hansen*, US-Pat. 3223518 (1961), DBP 1254162 (1959), Archer-Daniels-Midland Co.
[71] *O. Detmer, J. Jung, H. Müller*, and *H. Seibt*, DBP 1270579 (1962), BASF; US-Pat. 3365288 (1962), BASF.
[72] *H. Diekmann, K. Opp, O. Detmer, J. Jung, B. Lehmann*, and *H. Pohlemann*, DBP 1248687 (1962), BASF; *O. Detmer, J. Jung, H. Pohlemann, B. Lehmann, H. Heel*, and *M. Wendt*, DBP 1250456 (1962), BASF; *G. Daumiller, H. Pohlemann, B. Lehmann, K. Opp*, and *O. Detmer*, DBP 1467383 (1963), BASF.
[73] *D. W. Rindit, G. M. Blouin*, and *J. G. Getsinger*, J. Agr. Food Chem. *16*, 773 (1968); *L. H. Davies*, Sulphur Inst. J., 6 (Summer, 1974).
[74] *G. O. Fanger*, Chemtech *4*, 400 (1974); *R. P. Arens* and *N. P. Sweeny*, US-Pat. 3423489 (1966), Minnisota Mining and Manufacturing Co.
[75] *O. Detmer, K. Opp, H. Müller*, and *H. Seibt*, DOS 1467381 (1963), BASF; DOS 1467385 (1964), BASF; *H. Pohlemann, E.-G. Kasting, K. Opp, O. Detmer*, and *B. Lehmann*, DOS 1467386 (1964), BASF.
[76] *K. Schreiber* and *J. Lucks*, US-Pat. 3545129 (1967), Ca. Patents Developm. Ltd.; *K. Bronstert, K. Buchholz, A. Buchner, F. Hofher, H. Lang, A. Wagenknecht*, and *G. Wurl*, DOS 1767996 (1968), BASF.
[77] *E. E. Jvy*, 166th ACS-Meeting, Chicago, 33 No. 2, 554 (1973).
[78] *G. Levy, J. R. Leonards*, and *J. A. Procknall*, J. Pharm. Sci. *54*, 1719 (1965).
[79] *H. C. Caldwell* and *E. Rosen*, J. Pharm. Sci. *53*, 1387 (1964).
[80] *J. L. Anderson, G. L. Gardner*, and *N. H. Yoshida*, US-Pat. 3341416 (1967).
[81] *R. E. Miller* and *J. L. Anderson*, US-Pat. 3155590 (1964), National Cash Register Co.
[82] *J. C. Hecker* and *O. D. Hawks*, US-Pat. 3137630 (1964).
[83] Riechst., Aromen, Korperpflegem. *23*, 231 (1973).
[84] *H. Gottschalk, V. Böllert, P. Schönefeld*, and *M. Zimmermann*, DOS 2158463 (1971), Hans Schwarzkopf GmbH.
[85] *K. Takamura, M. Koishi*, and *T. Kondo*, Kolloid-Z. Z. Polym. *248*, 929 (1971).
[86] *M. Wingard, D. Werkmeister*, and *C. Thies*, 166th ACS-Meeting, Chicago, 33 No. 2, 575 (1973).
[87] *T. M. S. Chang*, Chemtech *5*, 80 (1975).
[88] *T. M. S. Chang*, Science *146*, 524 (1964).
[89] *T. M. S. Chang*, Trans. Amer. Soc. Artif. Intern. Organs *12*, 13 (1966).

COMMUNICATIONS

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

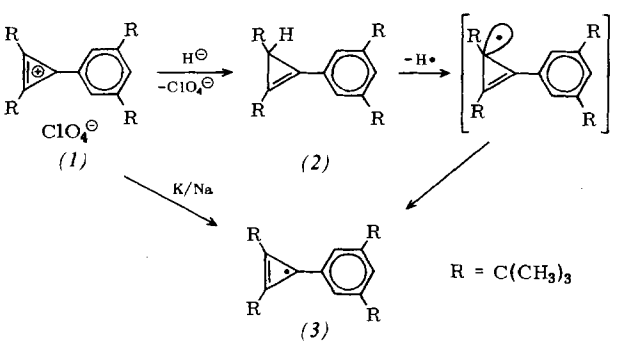
ESR Proof of the Antiaromaticity of a Cyclopropenyl Radical[1]

By *Kurt Schreiner, Wilhelm Ahrens*, and *Armin Berndt*[*]

Dedicated to Professor K. Dimroth on the occasion of his 65th birthday

The simplest representatives of previously known antiaromatic[2] compounds are the 4π-electron systems cyclobutadiene and the cyclopropenyl anions bearing substituents that force the carbanion center to adopt a planar configuration. Calculations by the electron gas method[3] and MO calculations with consideration of overlap integrals[4] lead to the expectation that even a cyclopropenyl radical with 3π-electrons has antiaromatic character[5].

By known methods[6] we have prepared di-*tert*-butyl-(3,5-di-*tert*-butylphenyl)cyclopropenylium perchlorate *(1)* and from this by means of $LiAlH_4$ 1,3-di-*tert*-butyl-2-(3,5-di-*tert*-butylphenyl)cyclopropene *(2)*. Photolysis of a solution of *(2)* in di-*tert*-butyl peroxide[7] at −30 °C affords a radical *(3)* whose



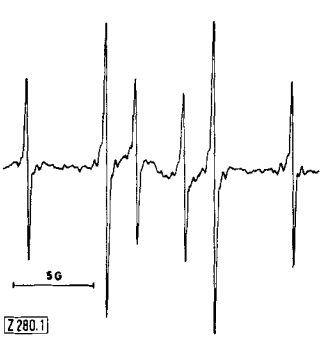


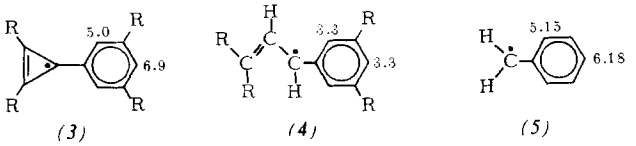
Fig. 1. ESR spectrum of the di-*tert*-butyl-(3,5-di-*tert*-butylphenyl)cyclopropenyl radical *(3)* in di-*tert*-butyl peroxide at −30 °C.

[*] Prof. Dr. A. Berndt, Dr. K. Schreiner, and Dipl.-Chem. W. Ahrens
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

ESR spectrum is shown in Fig. 1. The same radical is formed, although in distinctly lower concentration, when a benzene solution of *(1)* is shaken with K/Na alloy at room temperature.

The constitution of the radical *(3)* as di-*tert*-butyl-(3,5-di-*tert*-butylphenyl)cyclopropenyl follows from the splitting pattern of the ESR spectrum (doublet of triplets) and the *g* factor of 2.0029. The π nature of the radical is shown by the large coupling constants of the *o*- and *p*-protons which, being 5.0 and 6.9 gauss, are characteristic of π-radicals; σ-radicals are characterized by very small splitting constants of these protons[8].

For comparison of the delocalization of *(3)* with that of its open-chain analog we have prepared the phenylallyl radical 3-*tert*-butyl-1-(3,5-di-*tert*-butylphenyl)-4,4-dimethyl-2-pentenyl *(4)* (a^H=12.1 and 4.5 G for each 1H and 3.3 G for 3H) from the corresponding allyl bromide[9] and trimethyltin radicals. The allylic delocalization in *(4)* can be recognized, as expected, in the coupling constants of the *o*- and *p*-protons of the phenyl ring which are much smaller than for the benzyl radical *(5)*[7].



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

R = $C(CH_3)_3$

The considerably greater coupling constants of the phenyl protons in the phenylcyclopropenyl radical *(3)* as compared to those in the phenylallyl radical *(4)* prove that delocalization of the unpaired electrons in the cyclopropenyl ring is smaller than in the allylic portion of the open-chain analog. Thus antiaromaticity has for the first time been demonstrated for a cyclic conjugated 3π-electron system. Whereas previously antiaromaticity has been detected by measuring properties such as increased reactivity or decreased acidity, which are *consequences* of the lower delocalization, here the lower delocalization is detected itself.

The slightly greater sum of the coupling constants of the phenyl ring in *(3)* as compared to *(5)* shows that the unpaired electron resides to a greater extent in the phenyl ring of *(3)* than in that of *(5)*, from which it must be concluded that the unpaired electron is forced out of the three-membered ring by *destabilizing* interaction with the π-electrons of the conjugated double bond. *(3)* is therefore antiaromatic also by the more restrictive definition of antiaromaticity which requires destabilization as a consequence of electronic interaction.

Received: June 23, 1975 [Z 280 IE]
German version: Angew. Chem. 87, 589 (1975)

CAS Registry numbers:
(2), 56008-37-8; *(3)*, 56008-38-9; *(4)*, 56008-39-0

[1] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the Studienstiftung des Deutschen Volkes and the Chemische Werke Hüls.
[2] *R. Breslow*, Accounts Chem. Res. *6*, 393 (1973).
[3] *W. D. Hobey*, J. Org. Chem. *37*, 1137 (1972).
[4] *N. C. Baird*, J. Org. Chem. *40*, 624 (1975), and literature cited therein.
[5] The unsubstituted cyclopropenyl radical being a σ-radical has only 2π-electrons: *G. Cirelli, F. Graf*, and *Hs. H. Günthard*, Chem. Phys. Lett. *28*, 494 (1974).
[6] *J. Ciabattoni* and *E. C. Nathan*, J. Am. Chem. Soc. *91*, 4766 (1969).
[7] Method of *P. J. Krusic* and *J. K. Kochi*, J. Am. Chem. Soc. *90*, 7155 (1968).
[8] For example, the benzoyl radical: $a^H_{o,p}<0.2$; *P. J. Krusic* and *T. A. Rettig*, J. Am. Chem. Soc. *92*, 722 (1970).
[9] *K. Wieser* and *A. Berndt*, unpublished work.

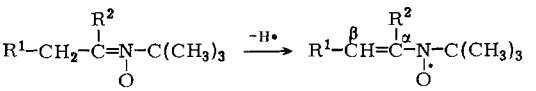
Vinylaminyl Oxides (Vinyl Nitroxides) with High Spin Density in the Vinyl Group[**]

By *Hans Günter Aurich, Klaus Hahn*, and *Karl Stork*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 65th birthday

We have now succeeded in preparing the first vinylaminyl oxides *(2)* with a proton on the β C-atom which show considerable delocalization of the unpaired electron in the vinyl group.

The nitrones *(1a)*—*(1c)* were prepared by known methods[1]. The radicals *(2)*, which we could detect ESR spectroscopically, were obtained by oxidation of *(1a)* and *(1b)* with nickel peroxide in chloroform and, in the case of *(1c)*, with lead dioxide in ether. The half-lives of *(2a)* and *(2c)* in solution are about 2 h; a half-life of about 10 min was found for *(2b)*.



(1) *(2)*

	R^1	R^2
(a)	C_6H_5—SO_2	H
(b)	C_6H_5—SO_2	C_6H_5
(c)	CO_2CH_3	CO_2CH_3

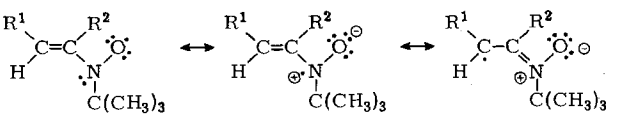
Table 1. Coupling constants of the radicals *(2)* and *(3)* (in gauss).

	a^N	a^H_β	a^H_α	a^H_X	*g*-Factor
(2a)	8.2	7.3	1.65	—	2.0057 ± 0.0002
(2b)	10.8	5.2	—	—	2.0057 ± 0.0002
(2c)	8.6	6.5	—	0.45 (3H) [a]	2.0060 ± 0.0002

	a^N	$a^H_{R^3}$		a^H	$a^H_{R^2}$
(3a)	10.45	2.7 (3H)	0.95 (2H)	2.4	0.4
(3b)	10.55	2.6 (3H)	0.9 (2H)	5.2	—
(3c)	13.6	—		2.1	—

[a] Protons of a methoxycarbonyl group.

The measured coupling constants (Table 1) indicate the presence of vinylaminyl oxides with considerable delocalization of the unpaired electron in the vinyl group[2]. The spin density at the β C-atom can be determined from the values for a^H_β. Thus, for *(2a)* $\rho_{\beta\text{-}C}=0.27$[3], a value which is indicative of this radical having a planar structure. Also in the case of the α-substituted radicals *(2b)* ($\rho_{\beta\text{-}C}=0.19$) and *(2c)* ($\rho_{\beta\text{-}C}=0.24$), only a slight distortion of the vinyl group can be assumed. We conclude therefore that the radicals are present in the conformation shown here.



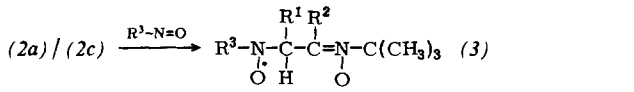
(2)

The vinylaminyl oxides *(2)* owe their stability to the electron acceptor substituent R^1, which decisively lowers the reactivity at the β C-atom[4]. Thus, *(2a)* reacts only with the more reactive nitrosobenzene with formation of the radical *(3a)*, while *(2c)* affords radicals of the structure *(3b)* and *(3c)*,

[*] Prof. Dr. H. G. Aurich, Dipl.-Chem. K. Hahn, and Dr. K. Stork
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

[**] Aminyl Oxides, Part 22.—This work was supported by the Fonds der Chemischen Industrie. Part 21: *H. G. Aurich* and *W. Weiss*, Tetrahedron, in press.

respectively, both with nitrosobenzene and with 2-methyl-2-nitrosopropane (see Table 1).



	R^1	R^2	R^3
(3a)	C_6H_5—SO_2	H	C_6H_5
(3b)	CO_2CH_3	CO_2CH_3	C_6H_5
(3c)	CO_2CH_3	CO_2CH_3	$C(CH_3)_3$

Received: May 28, 1975 [Z 274 IE]
German version: Angew. Chem. 87, 590 (1975)

CAS Registry numbers:
(1a), 55990-93-7; *(1b)*, 55990-94-8; *(1c)*, 55990-95-9; *(2a)*, 55990-96-0; *(2b)*, 55990-97-1; *(2c)*, 55990-98-2; *(3a)*, 55990-99-3; *(3b)*, 55991-00-9; *(3c)*, 55991-01-0; nitrosobenzene, 586-96-9; 2-methyl-2-nitrosopropane, 917-95-3

[1] *J. A. Saunders, K. Hovius*, and *J. B. F. N. Engberts*, J. Org. Chem. *39*, 2641 (1974); *E. Winterfeldt, W. Krohn*, and *H. U. Stracke*, Chem. Ber. *102*, 2346 (1969). Correct C,H,N analyses were obtained for *(1a)* and *(1b)*. The spectroscopic properties (NMR, IR, and mass spectra of *(1a)*—*(1c)* confirm all three compounds as being monomeric nitrones. We thank Frl. *G. Bach* for her assistance with the preparation of the starting compounds.

[2] a^N and a_2^N of *(2a)* are in good agreement with the corresponding values obtained for the comparable azomethineaminyl oxides; *H. G. Aurich* and *F. Bär*, Chem. Ber. *101*, 1770 (1968).

[3] Determined with the value $a^H = -27\,\rho_c$ for the McConnell relationship.

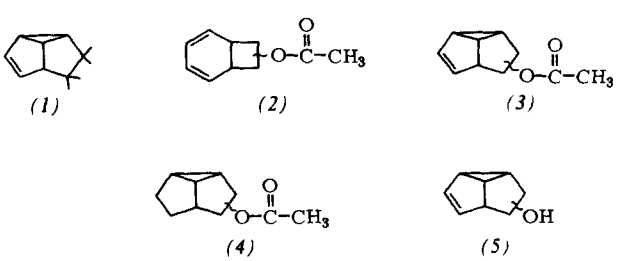
[4] On attempting to prepare *(2)*, $R' = CH_3$, $R^2 = H$, from 1-propenyl radicals and [D_9]-2-methyl-2-nitrosopropane, *Perkins et al.* could only detect the corresponding secondary radical (3): *C. M. Camaggi, R. J. Holman*, and *M. J. Perkins*, J. C. S. Perkin II *1972*, 501.

Photoaddition of Vinyl Acetate to Benzene

By *Andrew Gilbert* and *Mohd. Wahid bin Samsudin*[*]

1,3-Photoaddition ($\lambda = 254$ nm) of unconjugated olefins to benzene[1]—potentially a facile entry into dihydrosemibullvalenes *(1)*—has hitherto been restricted to hydrocarbons and vinyl ethers as olefinic components[2]. Furthermore, with such systems *(1)* is frequently accompanied by substantial amounts of other 1:1 adducts[2a, 3, 4]. The photoaddition of vinyl acetate to benzene is now reported and leads to a convenient synthesis of tricyclic compounds *(1)* functionalized in the 6 or 7 position.

Irradiation ($\lambda = 254$ nm, 20 °C, air or N_2) of an equivolume solution of benzene and vinyl acetate gave four products in the initial ratio of 1.0:1.4:25.4:3.4 (GLC elution sequence on Carbowax 20M), which changed to the steady value of 1.0:1.4:87.0:1.0 on further irradiation. The two shortest retention time products had molecular weights of 134[5] while the other two components of the mixture were 1:1 adducts ($M^+ = 164$, mass spectrum) of the starting materials. The minor 1:1 adduct ($\Phi = 0.027$) is assigned the 1,2-cycloadduct structure *(2)* on the basis of its thermal and photo-labilities, its fragmentation in the mass spectrometer[4], and its reaction with dienophiles.



The major adduct ($\Phi = 0.2$) was obtained in >95% purity from preparative experiments which yielded *ca.* 1 g of product from 65 ml of solution after 18 h irradiation. This yield can be increased if the heavy polymer film produced during irradiation is periodically removed from the quartz surface. Further purification of the adduct can be achieved by treatment of the crude product with maleic anhydride followed by distillation. From the spectroscopic data of such a sample and their comparision with those of adducts of known structure[2a], the major 1:1 adduct of benzene and vinyl acetate is assigned the 1,3-cycloadduct structure *(3)*[6]. The four possible isomers of *(3)* could not be separated even under conditions which allow separation of the four 1,3-cycloadducts of benzene and 4-penten-2-ol and the four ketones derived therefrom[7]. Controlled pyrolysis of 1,3-adducts leading to bicyclo[3.3.0]octa-2,7-dienes as a source of stereochemical information[8], indicated the 7-*endo* isomer to constitute *ca.* 20% of *(3)*.

Catalytic hydrogenation (10% Pd/C) of *(3)* occurs in two clearly defined steps giving *(4)* and bicyclo[3.2.1]octyl acetates respectively. Both *(3)* and its reduction products are essentially stable to 254 nm radiation (and 206 nm in the case of *(3)*): in particular no semibullvalene formation is observed from *(3)*, but all acetates show facile loss of 60 mass units in the mass spectrometer, presumably *via* a McLafferty rearrangement[9].

The mixture of adducts *(3)* was readily hydrolyzed by basic reagents to the alcohols *(5)* which were separated by GLC on Carboway 20M. The structure of the alcohols was assigned on the basis of the IR, UV, NMR, and mass spectra. Attempts to dehydrate *(5)* led to product mixtures of which a hydrocarbon of molecular weight 104 constituted only a minor fraction.

The 1,3-photoaddition of vinyl acetate to benzene provides a convenient route for the functionalization of dihydrosemibullvalenes and has been extended to anisole, toluene, the xylenes, and fluorobenzene as the aromatic compound.

Received: January 13, 1975;
supplemented: March 12, 1975 [Z 214 IE]
German version: Angew. Chem. 87, 540 (1975)

CAS Registry numbers:
Vinyl acetate, 108-05-4; benzene, 71-43-2; *(2)*, 23373-82-2; *exo-(3)* (6 isomer), 55759-44-9; *endo-(3)* (6 isomer), 55821-05-1; *exo-(3)* (7 isomer), 55759-45-0; *endo-(3)* (7 isomer), 55821-06-2; *exo-(4)* (6 isomer), 55759-46-1; *endo-(4)* (6 isomer), 55821-07-3; *exo-(4)* (7 isomer), 55821-08-4; *endo-(4)* (7 isomer), 24221-98-5; *exo-(5)* (6 isomer), 55759-47-2; *endo-(5)* (6 isomer), 55821-09-5; *exo-(5)* (7 isomer), 55759-48-3; *endo-(5)* (7 isomer), 55821-10-8

[1] *K. E. Wilzbach* and *L. Kaplan*, J. Am. Chem. Soc. *88*, 2066 (1966); *D. Bryce-Smith, A. Gilbert*, and *B. H. Orger*, Chem. Commun. *1966*, 512.

[2] a) *D. Bryce-Smith, A. Gilbert, B. H. Orger*, and *H. M. Tyrrell*, J. C. S. Chem. Comm. *1974*, 334; b) for example, *R. Srinivasan*, J. Am. Chem. Soc. *94*, 8117 (1972); J. Phys. Chem. *76*, 15 (1972); *V. Y. Merritt, J. Cornelisse*, and *R. Srinivasan*, J. Am. Chem. Soc. *95*, 8250 (1973); *D. Bryce-Smith*, Pure Appl. Chem. *34*, 193 (1973), and references therein; c) see *E. L. Allred* and *B. R. Beck*, J. Am. Chem. Soc. *95*, 2393 (1973), for the 1,3-photoaddition of 3,4-dichlorocyclobutene to benzene.

[3] *R. Srinivasan*, IBM J. Res. Dev. *15*, 34 (1971); *D. Bryce-Smith, B. E. Foulger, A. Gilbert*, and *P. J. Twitchett*, Chem. Commun. *1971*, 794; *D. Bryce-Smith, A. Gilbert*, and *B. E. Foulger*, *ibid.* *1972*, 664, 769.

[4] *K. E. Wilzbach* and *L. Kaplan*, J. Am. Chem. Soc. *93*, 2073 (1971).

[5] The nature and derivation of these products is still under investigation, but from their mass spectral fragmentation patterns, their structures differ significantly.

[6] The ratio of 1,2- to 1,3-addition of 0.135 approximates to that to be expected for benzene with such an olefin as vinyl acetate (ionization potential 9.19 eV) [2a].

[7] *A. Gilbert*, unpublished observations.

[8] *R. Srinivasan*, Tetrahedron Lett. *1971*, 4551.

[9] *F. W. McLafferty*, Anal. Chem. *28*, 306 (1956); *31*, 82 (1959).

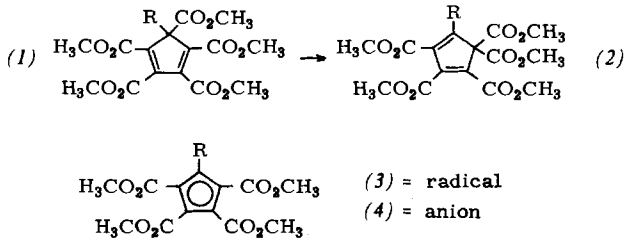
[*] Dr. A. Gilbert and M. Wahid bin Samsudin
Department of Chemistry, University of Reading
Whiteknights, Reading RG6 2AD (England)

Substituent Effect on a [1,5] Sigmatropic Ester Shift[**]

By *Jutta Backes, Reinhard W. Hoffmann,* and *Friedrich W. Steuber*[*]

Dedicated to Professor Karl Dimroth on the occasion of his 65th birthday

In his treatise on pericyclic reactions *Epiotis*[1] discusses substituent effects on sigmatropic rearrangements. These are assumed to be determined by the position of the HOMO in the two formally interacting radicals. We report here pronounced substituent effects on the sigmatropic [1,5] ester shift in the pentamethyl cyclopentadienepentacarboxylate system *(1)*→*(2)*[2,3]. The rates of the rearrangements have been followed by ^{1}H-NMR spectroscopy in the temperature range of 45 to 190 °C depending on the nature of the substituent R.



(1) *(2)*

(3) = radical
(4) = anion

Table 1. Relative rates for the rearrangement *(1)*→*(2)* at 400 K (measured or extrapolated) and longest wavelength absorption of *(4)* in CH_3OH.

R	k_{rel} [s^{-1}]	λ [nm]
CH_3S	0.28	(296.3) [b]
Cl	0.33	—
CH_3	1.0 [a]	305.9
C_6H_5	1.9	302.2
CH_3OCOCH_2	2.1	302.2
CH_3O	12.0	300.0
NC	15.5	300.2
C_6H_5NH	125	—
$(CH_3)_2N$	260	291.2

[a] Corresponds to $k = 2.26 \times 10^{-4}\ s^{-1}$ at 400 K; $\Delta H^{\neq} = 26.9 \pm 2.1$ kcal mol^{-1}; $\Delta S^{\neq} = -8.6 \pm 2.8$ cal $K^{-1}\ mol^{-1}$.
[b] Value could not be determined accurately.

The data recorded in Table 1 show that electron-releasing substituents increase the reaction rate: In attempts to generate *(1)* with $R = NH_2$ or $NHCH_3$ rearrangement to *(2)* occurred even at about 20 °C. The effect of $R = C_6H_5$ or CN is conspicuous in increasing the rate relative to $R = CH_3$, whereas substituents from the second row of the periodic table ($R = Cl$ or SCH_3) somewhat decrease the rate[4]. This unusual sequence of substituent effects neither follows Hammett's σ values nor *Hine*'s D_x-parameters[5]. In order to test *Epiotis*'s concept, we prepared the anions *(4)*[3], since they have the same HOMO as the radicals *(3)*. In Table 1 are given the UV data for the longest wavelength absorption of the anions *(4)* obtained. According to Hückel calculations the substituent R is situated at a position with a large coefficient in the HOMO, whereas in the LUMO it is at a node. Therefore the changes in the UV absorption should reflect mainly changes in the position of the HOMO.

[*] Dipl.-Chem. J. Backes, Prof. R. W. Hoffmann, and Prof. F. W. Steuber
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)
[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Verband der Chemischen Industrie and the Max-Buchner-Forschungsstiftung.

A diagram of $\log k_{rel}$ against $\tilde{\nu}$ suggests that the rate for the rearrangement *(1)*→*(2)* is indeed a function of the relative energy of the HOMO of *(3)*. Moreover the change in free

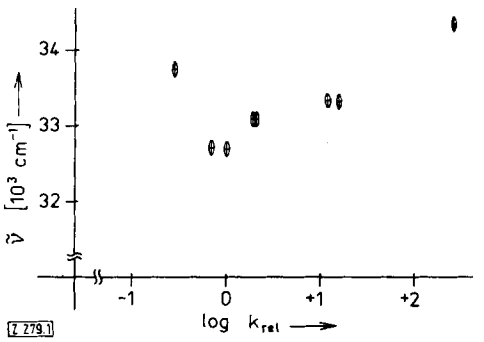


Fig. 1. Relation between $\log k_{rel}$ and $\tilde{\nu}$ (see Table 1 and text).

activation enthalpy of the rearrangement effected by the substituents (4.7 kcal mol^{-1}) is close to the change in the transition energy in the anions *(4)* (≈5 kcal mol^{-1}).

Received: June 30, 1975 [Z 279 IE]
German version: Angew. Chem. 87, 587 (1975)

CAS Registry numbers:
(1), R = CH_3S, 56008-90-3; *(1)*, R = Cl, 16691-62-6;
(1), R = CH_3, 16691-60-4; *(1)*, R = C_6H_5, 16691-61-4;
(1), R = CH_3OCOCH_2, 38135-77-2; *(1)*, R = CH_3O, 56008-91-4;
(1), R = NC—, 56008-92-5; *(1)*, R = C_6H_5NH, 56008-93-6;
(1), R = $(CH_3)_2N$, 56008-94-7; *(2)*, R = CH_3S, 56008-95-8;
(2), R = Cl, 56008-96-9; *(2)*, R = CH_3, 56008-97-0;
(2), R = C_6H_5, 56008-98-1; *(2)*, R = CH_3OCOCH_2, 38135-79-4;
(2), R = CH_3O, 56008-99-2; *(2)*, R = NC—, 56009-00-8;
(2), R = C_6H_5NH, 56009-01-9; *(2)*, R = $(CH_3)_2N$, 56009-02-0

[1] *N. D. Epiotis*, Angew. Chem. *86*, 825 (1974); Angew. Chem. internat. Edit. *13*, 751 (1974).
[2] *P. Schmidt, R. W. Hoffmann,* and *J. Backes*, Angew. Chem. *84*, 534 (1972); Angew. Chem. internat. Edit. *11*, 513 (1972).
[3] For the synthesis of the compounds see *J. Backes*, Dissertation, Universität Marburg 1975.
[4] The sequence of the substituent effects encountered here corresponds only roughly with the sequence found for the [1,5] H-shift in substituted cycloheptatrienes; *A. P. ter Borg, E. Razenberg,* and *H. Kloosterziel*, Rec. Trav. chim. Pays-Bas *84*, 1230 (1965). These effects encompass also a conformational factor.
[5] *J. Hine* and *N. W. Flachskam*, J. Am. Chem. Soc. *95*, 1179 (1973).

C—N Hyperconjugation in a π Radical Twisted through 90°

By *Elmar Krumbholz* and *F. W. Steuber*[*]

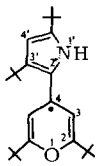
Dedicated to Professor Karl Dimroth on the occasion of his 65th birthday

To our knowledge no detailed experimental study has yet been performed on the C—N hyperconjugation[1] in a π radical twisted through 90°.

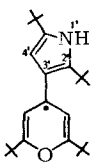
In order to investigate this interaction and to establish a relation between the magnitude of the nitrogen coupling constant and the angle of twist, we synthesized the radical

[*] Dipl.-Chem. E. Krumbholz and Prof. Dr. F. W. Steuber [+]
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)
[+] To whom correspondence should be addressed.

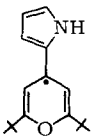
2,6-di-*tert*-butyl-4-(3,5-di-*tert*-butyl-2-pyrrolyl)pyryl *(1)* by reduction of the pyrylium salt. Owing to the steric effect of the 3-*tert*-butyl group the plane of the pyrrole ring in *(1)* is twisted by about 90° relative to the plane of the pyryl ring.



(1)



(2)



(3)

(4)

For sake of comparison we studied the radical *(2)*, likewise twisted through 90°, the coplanar radical *(3)*, and 2,4,6-tri-*tert*-butylpyryl *(4)*[2].

No p_π-p_π interaction between the pyryl and the pyrrole ring can occur in the twisted radicals *(1)* and *(2)* because the p orbitals are mutually orthogonal. Any hyperfine splitting that may still be observed in the ESR spectrum due to the atoms of the pyrrole ring can only be explained in terms of π-σ delocalization. We calculated the spin densities in position 4 of the pyryl rings (ρ_4, Table 1) from the ^{13}C-4 coupling constants according to the method of *Karplus* and *Fraenkel*[3] and using their parameters. The spin density at C-3 required in this calculation were obtained from the corresponding ^{1}H coupling constants with $Q^H_{C-H} = -27$ gauss according to *McConnel*[4]. In accord with a McLachlan calculation, we assumed this spin density to have a negative sign.

The coupling constants obtained from the ESR spectra (Table 1) could be assigned with aid of *tert*-butyl-, triphenylmethyl-, and deuterium-substituted derivatives.

Table 1. ESR coupling constants, assignment, and calculated spin densities ρ for C-4 (ρ_4) of *(1)*, *(2)*, *(3)*, and *(4)*.

		(1)	*(2)*	*(3)*	*(4)*
H-3	(2H)	1.57	1.68	1.53	1.80
C-4	(1C)	19.32 [a]	19.74 [a]	17.89 [a, b]	21.40 [a]
N-1′	(1N)	2.89	0	1.02	
H-1′	(1H)	0.69	0	1.01	
H-3′	(1H)			4.07	
H-4′	(1H)	0.55	0.90	0.47	
H-5′	(1H)			3.19	
H-tBu	(9H)				0.28 [c]
	ρ_4	0.579 [d]	0.587 [d]	0.533 [d]	0.638 [d, e]

[a] Determined for samples having natural isotopic abundance.
[b] Measured for 2.6-di-*tert*-butyl-4-(5-*tert*-butyl-4-deuterio-2-pyrrolyl)pyryl.
[c] γ-Coupling of the 4-*tert*-butyl group.
[d] Calculated neglecting the low spin density due to spin polarization at the C atom of the 4 substituent adjacent to C-4.
[e] Calculated using $Q^C_{C-C(CH_3)_3} = 16$ gauss [6].

The spin density ρ_4 of *(1)* and *(2)* is greater than that of *(3)*, which can be explained by the twisting of *(1)* and *(2)* and the resulting impairment of delocalization. We attribute the finding that ρ_4 for *(1)* and *(2)* is nevertheless smaller than ρ_4 of *(4)* to a fixing of the pyrrole rings of *(1)* and *(2)* in an orientation that is particularly favorable for hyperconjugation. Thus they can withdraw more spin through hyperconjugation than can the freely rotating 4-*tert*-butyl group of *(4)*.

In *(1)* hyperconjugation gives rise to a much larger nitrogen coupling constant than p_π-p_π interaction in *(3)*. However, the coupling constant of the proton on the nitrogen is lower in *(1)* than in *(3)*, apparently because no spin delocalization takes place in the pyrrole ring; the latter coupling can be explained by homohyperconjugation. A similarly large coupling constant was found for a corresponding proton in a benzyl radical twisted through 90°[5].

As a result of π-σ delocalization the coupling in position 4′ of *(1)* is larger than in *(3)*. Once again, the corresponding proton in a twisted benzyl radical has a very similar coupling constant[5].

No C—N hyperconjugation can occur in the twisted radical *(2)*. Accordingly, no nitrogen splitting was found in its ESR spectrum. The 4′ proton of *(2)* corresponds to the proton attached to nitrogen in *(1)* with regard to its position relative to the 4 p_z orbital; the coupling due to homohyperconjugation is expectedly of about the same size.

Similar reasoning suggests that the NH proton of *(2)* should have a coupling constant comparable with that of the 4′ proton of *(1)*. However, we found no such coupling in the ESR spectrum of *(2)* with its relatively large line width of 0.3 gauss. The experimental data yield a value of $a^N = 5.0$ gauss for the nitrogen coupling arising solely by hyperconjugation in a radical twisted through 90° if the spin density on the C atom located β to the nitrogen is $\rho^C = 1$.

Received: April 21, 1975 [Z 236 IE]
German version: Angew. Chem. *87*, 588 (1975)

CAS Registry numbers:
(1), 55702-06-2; *(2)*, 55702-07-3; *(3)*, 55702-08-4; *(4)*, 55702-09-5

[1] *A. Berndt*, Tetrahedron *25*, 37 (1969).
[2] Synthesis of *(1)*—*(4)*: *E. Krumbholz* and *F. W. Steuber*, to be published.
[3] *M. Karplus* and *G. K. Fraenkel*, J. Chem. Phys. *35*, 1312 (1961).
[4] *H. McConnell* and *D. B. Chesnut*, J. Chem. Phys. *28*, 107 (1958).
[5] *K. Schreiner* and *A. Berndt*, Angew. Chem. *86*, 131 (1974); Angew. Chem. internat. Edit. *13*, 144 (1974).
[6] *M. Broze* and *Z. Luz*, J. Chem. Phys. *51*, 749 (1969).

Twist and Chair Conformation of the Diphenyl Esters of, respectively, *cis*- and *trans*-Dithiodihydrazidodimetaphosphoric Acid[**]

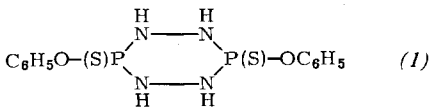
By *Udo Engelhardt* and *Hans Hartl*[*]

Saturated six-membered carbocycles and heterocycles generally favor the chair conformation[1] in which the sterically demanding substituents assume preferentially the equatorial

[*] Prof. Dr. U. Engelhardt [+] and Prof. Dr. H. Hartl
Institut für Anorganische Chemie FB-21, WE-1 der Freien Universität 1 Berlin 33, Fabeckstrasse 34—36 (Germany)
[+] To whom correspondence should be addressed.

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

positions[2]. Stable twist and boat forms are generally observed only if exocyclic double bonds, fused-on rings, hydrogen bonds, or direct bridges are present[3]. It has proved possible only in a few exceptional cases to confirm expectations that the twist conformation could be stabilized also in simple saturated cyclohexane analogs if, *e.g.* by 1,4-*cis*-substitution, one of the sterically demanding substituents is forced to assume the unfavorable axial position in the chair conformation[3a, 4].



(1)

By X-ray diffraction methods applied to single crystals we have found that *cis*-dithiodihydrazidodimetaphosphoric acid diphenyl ester, *cis-(1)*[5], exists in the twist (Fig. 1a) and the *trans*-isomer, *trans-(1)*[5], in the chair conformation (Fig. 1b).

Both compounds form monoclinic crystals. *cis-(1):* space group C2/c; $a=18.559\pm0.007$, $b=7.334\pm0.002$, $c=13.073\pm0.005$ Å, $\beta=113.24\pm0.03°$; $Z=4$; 1345 observed reflections; $R=3.7\%$. The molecules have a two-fold axis of symmetry and are chiral. The unit cell contains two of each enantiomer. *trans-(1):* space group $P2_1/c$; $a=7.605\pm0.002$; $b=5.773\pm0.002$; $c=18.538\pm0.007$ Å; $\beta=104.68\pm0.03°$; $Z=2$; 1358 observed reflections; $R=4.2\%$. The molecules have a center of symmetry. The sulfur atoms assume the equatorial, and the phenoxy groups the axial positions.

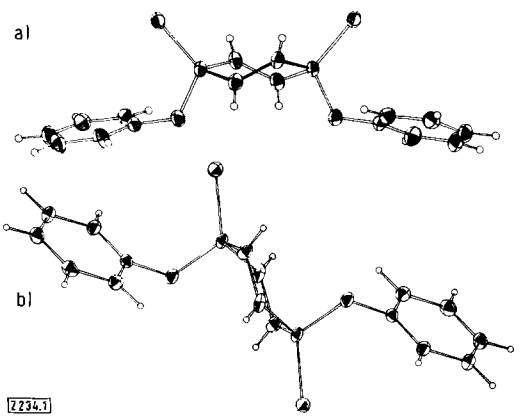


Fig. 1. a) Molecular structure of *cis*-dithiodihydrazidodimetaphosphoric acid diphenyl ester, *cis-(1)*; b) molecular structure of the isomer *trans-(1)*.

As expected, bond lengths and bond angles are very similar in the two isomers. The bond lengths are equal within the standard deviations, except for the N—N bonds which are relatively short for single bonds [*cis-(1):* 1.400 ± 0.003 Å; *trans-(1):* 1.422 ± 0.004 Å]. They accord with expectations, being r_{PN} between 1.645 and 1.662 Å and mean lengths $r_{PS}=1.910$, $r_{PO}=1.600$ and $r_{CO}=1.413$ Å. In both isomers each pair of opposing symmetry-equivalent nitrogen atoms has a bond angle of *ca.* 120° [*cis-(1):* $120.3\pm0.3°$; *trans-(1):* $120.9\pm0.2°$], whilst the angles at the other two nitrogen atoms are only 116.5 ± 0.3 or $115.6\pm0.3°$ severally. In both compounds the phosphorus atoms are in slightly distorted tetrahedral environments.

The torsional angles show that the chair conformation of *trans-(1)* is flattened ($\tau_{PN}=\pm41.9$ and $\pm44.5°$, $\tau_{NN}=\pm47.9°$; cyclohexane: $\pm54.5°$). The torsional angles of *cis-(1)*, however, correspond closely to those of a hypothetical twist conformation of cyclohexane ($\tau_{PN}=+33.0$ and $+27.1°$, $\tau_{NN}=-63.0°$; cyclohexane: $+31$, $+31$, and $-65°$, respectively). The maximal torsional angle ϕ_{max} amounts to 62°, and the pseudorotation parameter Δ to $-56.8°$[6].

Received: April 16, 1975 [Z 234 IE]
German version: Angew. Chem. *87*, 541 (1975)

CAS Registry numbers:
cis-(1), 28831-66-5; *trans-(1)*, 28941-59-5

[1] *F. R. Jensen* and *C. H. Bushweller*, Advan. Alicyclic Chem. *3*, 139 (1971); *F. G. Ridell*, Quart. Rev. Chem. Soc. *21*, 364 (1967); *P. L. Durette* and *D. Horton*, Advan. Carbohyd. Chem. Biochem. *26*, 49 (1971); *C. Romers*, *C. Altona*, *H. R. Buys*, and *E. Havinga*, Top. Stereochem. *4*, 39 (1969).

[2] *A. Hirsch*, Top. Stereochem. *1*, 199 (1967); *E. L. Eliel*, Angew. Chem. *77*, 784 (1965); Angew. Chem. internat. Edit. *4*, 761 (1965); *H. Feltkamp* and *N. C. Franklin*, Angew. Chem. *77*, 798 (1965); Angew. Chem. internat. Edit. *4*, 774 (1965); *E. L. Eliel*, Angew. Chem. *84*, 779 (1972); Angew. Chem. internat. Edit. *11*, 739 (1972).

[3] a) *G. M. Kellie* and *F. G. Ridell*, Top. Stereochem. *8*, 225 (1974); b) *U. Müller*, Z. Anorg. Allg. Chem. *382*, 110 (1971); c) *B. Hesper*, *H. J. Geise*, and *C. Romers*, Rec. Trav. Chim. Pays-Bas *88*, 871 (1969); d) *J. A. Heitmann*, *G. F. Richards*, and *L. R. Schroeder*, Acta Crystallogr. *B 30*, 2322 (1974).

[4] *A. Haaland* and *L. Schäfer*, Acta Chem. Scand. *21*, 2474 (1967); *C. H. Bushweller*, J. Amer. Chem. Soc. *91*, 6019 (1969); *A. Kobayashi*, *F. Marumo*, and *Y. Saito*, Inorg. Nucl. Chem. Lett. *7*, 777 (1971).

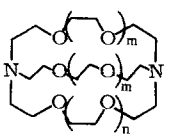
[5] *U. Engelhardt*, Z. Naturforsch. *24b*, 1486 (1969); *28b*, 357 (1973).

[6] *H. R. Buys* and *H. J. Geise*, Tetrahedron Lett. *1968*, 5619; *R. Bucourt*, Top. Stereochem. *8*, 159 (1974).

Selective Transport of Alkali Metal Cations through a Liquid Membrane by Macrobicyclic Carriers[1]

By *Michèle Kirch* and *Jean-Marie Lehn*[*]

Cations are known to be transported through lipid membranes by antibiotics or synthetic macrocyclic polyethers. We now report that macrobicyclic ligands *(cryptands) (1)—(4)* forming *cryptate*-type inclusion complexes with metal cations[2] may function as selective carriers for the transport of Na^+, K^+, and Cs^+ ions through liquid membranes (chloroform). Such synthetic ligands, which may in principle be modified at will, offer the possibility of studying the transport process and selectivity as a function of ligand structure[2].



(1), $m = n = 1$ [2.2.2]
(2), $m = 1$, $n = 2$ [3.2.2]
(3), $m = n = 2$ [3.3.3]
(4), $m = 1$, third bridge = $-(CH_2)_8-$ [2.2.C_8]

The alkali metal picrates used were transported with the aid of the cryptands *(1)—(4)*[2] from an IN to an OUT aqueous phase through a bulk liquid chloroform membrane. The picrate ion is more soluble in chloroform than, *e.g.*, the chloride ion and thus favors distribution into the membrane as cryptate-picrate ion pair (cf. ref. [3]). When the carrier is added to the membrane the alkali metal picrate (from the IN aqueous phase) distributes into the chloroform and the cation and picrate concentrations are found to increase in the OUT aqueous phase.

Table 1 lists data concerning the rate and selectivity of cation transport[4]. The results can be interpreted as follows:

1) Cryptands *(1)—(4)* function as cation carriers by dissolving the alkali metal picrate into the membrane as a 1:1 cryptate-picrate ion pair and releasing it at the OUT membrane-water interface. Transport occurs by carrier-mediated *facili-*

[*] M. Kirch and Prof. Dr. J. M. Lehn
Institut Le Bel, Universite Louis Pasteur
4, Rue Blaise Pascal, F-67 Strasbourg (France)
ERA 265 du CNRS.

Table 1. Rates and selectivities of alkali metal cation transport *via* cryptate complexes [4]. The cation concentrations in the membrane were measured at the end of the experiments and may be somewhat ($\leq 5\%$) lower than the initial concentrations because of the slight pH change (about 0.1—0.2 pH units).

Carrier	Cation	log K_s [mol^{-1}] [a]	Cation conc. in membrane [µmol/l] [b]	Carrier saturation [%] [c]	Initial transport rate [µmol/h]	Transport selectiviy $K^+:Na^+$	$Cs^+:K^+$
(1)	Na^+	7.2 [d]	1400	95	0.6	1:20	1:0.01
	K^+	9.7 [d]	$\geq$1400	$\geq$95	0.03		
	Cs^+	4.4	130	20	2.9		
(2)	Na^+	5.0	750	60	2.4	1:3.5	1:1.25
	K^+	7.0 [d]	1100	75	0.7		
	Cs^+	7.0 [d]	$\geq$1450	$\geq$95	0.6		
(3)	Na^+	2.7	110	10	1.5	1:0.55	1:0.9
	K^+	5.4	950	65	2.7		
	Cs^+	5.9	1250	85	3.0		
(4)	Na^+	3.5	140	15	1.6	1:0.45	1:50
	K^+	5.2	850	80	3.6		
	Cs^+	2.7	7	0.7	0.07		

[a] K_s = stability constant of cryptate complex in methanol [2].
[b] K^+, Cs^+: $\pm 5\%$; Na^+: $\pm 10\%$.
[c] For the weakest complexes, the cation and picrate concentrations in the membrane may differ significantly because of competition of cation extraction with ligand protonation. The carrier saturation has been calculated with respect to unprotonated carrier in the membrane. The amount of protonated carrier is equal to the difference between the amounts of picrate (UV) and cation (atomic absorption) in mol.
[d] These values are for methanol containing 5% water. Somewhat higher values are expected for pure methanol (about ± 0.5 log K_s).

tated diffusion down the concentration gradient of the salt. No transport is detectable in the absence of carrier.

2) Carrier-cation pairs forming very stable cryptate complexes display efficient *extraction* of the salt into the organic phase.

3) The *rate of transport* strongly depends on both the cation and the carrier (anion effects are not considered here). It is of the same order of magnitude as observed for antibiotic-mediated transport across a bulk liquid membrane[6].

4) The *transport selectivities* differ widely for each of the carriers *(1)*—*(4)*. However, they are all lower than the complexation selectivities in methanol.

5) In contrast to observations for antibiotic-mediated transport the *relative transport rates* are not proportional to complex stability and extraction efficiency. In the case of *(1)* they are actually opposite to each other. Thus 12 µmol of *(1)*, whose K^+ cryptate is very stable, transports only 3 µmol of potassium picrate in 100 h! The rate of transport is determined either by a diffusional step or by the rate of heterogeneous reaction at the interfaces[8].

6) Under the present conditions there is an *optimum stability* of the cryptate complex for efficient transport: log $K_s \approx 5$. Thus *(2)* and *(3)* display the same complexation selectivity for Na^+ and K^+ but opposite transport selectivity. Interestingly, this value amounts to 4.9 for the efficient natural K^+ carrier valinomycin (in methanol[7]).

7) Finally, comparison of the carrier properties of *(1)* and *(4)* shows the effect of a simple structural modification on the sequence of stability constants and transport rates. *(4)* carries Na^+ and K^+ much faster than *(1)*; also the very high Cs^+/K^+ stability of *(4)* surpasses that found for most antibiotics[9]. This may simply be rationalized by the fact that *(4)* retains the same intramolecular cavity size as *(1)* but removal of two oxygen binding sites lowers all stability constants and places the cryptate complex of K^+ and *(4)* in the optimal stability range for efficient transport. This structural modification transforms a specific K^+ *receptor (1)* into a specific K^+ *carrier (4)*. The same principle may be used for the design of other specific carriers.

Received: April 18, 1975 [Z 235 IE]
German version: Angew. Chem. *87*, 542 (1975)

CAS Registry numbers:
(1), 23978-09-8; *(2)*, 31255-22-8; *(3)*, 31255-19-3;
(4), 31250-03-0; Na, 7440-23-5; K, 7440-09-7; Cs, 7440-46-2

[1] Transport in Organic Chemistry, Part 3.—Part 2: *J. M. Lehn, A. Moradpour*, and *J. P. Behr*, J. Amer. Chem. Soc. *97*, 2532 (1975).
[2] *J. M. Lehn*, Struct. Bonding *16*, 1 (1973); *B. Dietrich, J. M. Lehn, J. P. Sauvage*, and *J. Blanzat*, Tetrahedron *29*, 1629 (1973); *B. Dietrich, J. M. Lehn*, and *J. P. Sauvage*, *ibid. 29*, 1647 (1973); *J. M. Lehn* and *J. P. Sauvage*, Chem. Commun. *1971*, 440; *J. M. Lehn, J. P. Sauvage*, and *B. Dietrich*, J. Amer. Chem. Soc. *92*, 2916 (1970).
[3] *S. G. A. McLaughlin, G. Szabo, S. Ciani*, and *G. Eisenmann*, J. Membrane Biol. *9*, 1 (1972).
[4] The experimental set-up and the transport cell cf. ref. [5]. Two water phases (2 × 40 ml) (IN and OUT) are bridged by a chloroform membrane (8.5 ml) in which the carrier is dissolved (1.5 mmol l^{-1}, *i.e.* 12.7 µmol/8.5 ml). The area of the interface is about 2 cm^2. Initial alkali metal picrate concentrations were 10 mmol l^{-1} and 0.01 mmol l^{-1} in the IN and OUT water phases, respectively. All layers are stirred at 300 rpm and maintained at 20.0 ± 0.5 °C. The transport process was followed by monitoring the increase in picrate (UV absorption at 354 nm) and cation (atomic absorption) concentrations in the OUT phase. The membrane phase was also analyzed at the end of each experiment. Since the carriers are bases the set of experiments described here were performed using as water phases a iminodiethanol/HCl buffer at pH 10. The transport rates were determined from the slope of the tangent at each point after phase equilibration (about 1 h after addition of carrier).
[5] *K. Sollner* in *J. N. Sherwood, A. V. Chadwick, W. M. Muir*, and *F. L. Swinton*: Diffusion Processes. Gordon and Breach, London 1971, Vol. 2, p. 655.
[6] *R. Ashton* and *L. K. Steinrauf*, J. Mol. Biol. *49*, 547 (1970); *R. W. Roeske, S. Isaac, T. E. King*, and *L. K. Steinrauf*, Biochem. Biophys. Res. Commun. *57*, 554 (1974).
[7] *E. Grell, T. Funck*, and *F. Eggers*, Symposium on Molecular Mechanisms of Antibiotic Action on Protein Biosynthesis and Membranes. University of Granada, June 1971.
[8] *J. A. Jacquez*, Biochim. Biophys. Acta *79*, 318 (1964); *P. Läuger* and *G. Stark*, *ibid. 211*, 458 (1970); *M. Kirch* and *J. M. Lehn*, to be published.
[9] *B. C. Pressman* and *D. H. Haynes* in *D. C. Tosteson*: The Molecular Basis of Membrane Function. Prentice-Hall, Englewood Cliffs 1969, p. 211; *B. C. Pressman*, Ann. N. Y. Acad. Sci. *147*, 829 (1969).

Polyenes as Four-Stage Redox Systems[**]

By *Siegfried Hünig, Michael Horner*, and *Peter Schilling*[*]

Granted suitable structural prerequisites[1], stepwise transfer of two electrons often occurs (Wurster radical cations, semi-

[*] Prof. S. Hünig [+], Dipl.-Chem. M. Horner, and Dr. P. Schilling
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)
[+] To whom correspondence should be addressed.

[**] This work was supported by the Fonds der Chemischen Industrie, by Dechema Frankfurt and by BASF, Ludwigshafen.

quinone radical anions). However, very few four-stage redox systems are known in which the oxidized form OX_k of the two-stage cathodic redox system is identical with the reduced form RED_a of the two-stage anodic redox system (SEM denotes the radical ion):

$$RED_k^{2\ominus} \underset{+e}{\overset{-e}{\rightleftharpoons}} SEM_k^{\ominus} \underset{+e}{\overset{-e}{\rightleftharpoons}} OX_k = RED_a \underset{+e}{\overset{-e}{\rightleftharpoons}} SEM_a^{\oplus} \underset{+e}{\overset{-e}{\rightleftharpoons}} OX_a^{2\oplus}$$

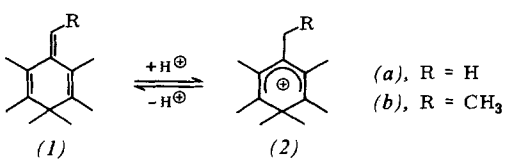
$$E_1^k \qquad E_2^k \qquad\qquad E_1^a \qquad E_2^a$$

$$K_{SEM}^k = \frac{[SEM_k^{\ominus}]^2}{[RED_k^{2\ominus}][OX_k]} \qquad K_{SEM}^a = \frac{[SEM_a^{\oplus}]^2}{[RED_a][OX_a^{2\oplus}]}$$

Characteristic representatives are polycyclic arenes such as anthracene[2] and perylene[3].

We now describe polyenes as four-stage redox systems. Of long-chain polyenes (*e.g.* β-carotene) it is known only that they can be reversibly reduced to radical anions ($SEM_k^{\ominus}$)[4a] or oxidized in one step to dications ($OX_a^{2\oplus}$)[4b]. However, oxidation of *e.g.* butadiene[5] and hexatriene[6] to radical cations ($SEM_a^{\oplus}$) occurs irreversibly.

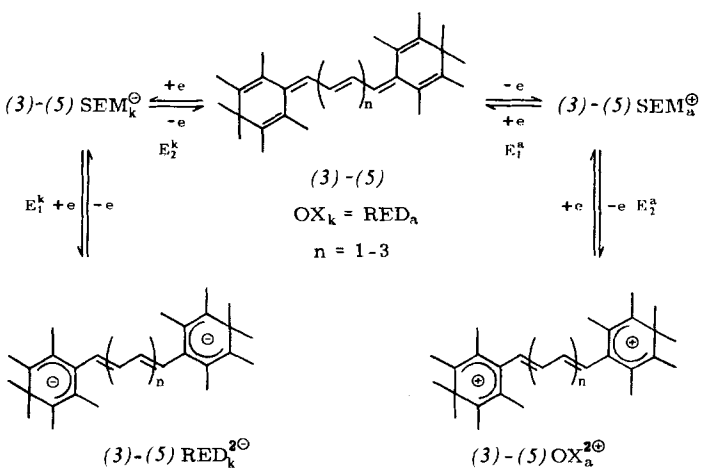
Because of the great stability of the pentadienyl cation *(2)*[7] which is formed on protonation of the crossed triene *(1)*[7], we synthesized the vinylogous polyenes *(3)*—*(5)*[8] which contain this system and studied their redox behavior[9].



(1) *(2)*

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

In dichloromethane from which the last traces of nucleophiles have been removed by suspended alumina[10], *(3)*—*(5)* behave reversibly at −60 °C both in the direct current polarogram and in the cyclic voltammogram[11], so that E_1^a and E_2^a can be determined. Thus we have here the first two-stage reversible oxidation of polyenes not involving aromatization during the transition into $OX_a^{2\oplus}$[12].



The reduction potentials of *(3)*—*(5)* appear with very negative values so that measurements must be performed in DMF/C_6H_6[4]. All three polyenes show reversible electron transfer for the step $OX_k/SEM_k^{\ominus}$ ($=E_2^k$) even at room temperature with half-lives for $SEM_k^{\ominus}$ of 10—20 s. However, even at −60 °C and with 20 V/s scan rate only for *(5)* could the stage $SEM_k^{\ominus}/RED_k^{2\ominus}$ ($=E_1^k$) be obtained reversibly, the half-life for $RED_k^{2\ominus}$ being 4 s (cf. Table 1). The polyene *(5)* can thus occur in five oxidation stages, which are connected by four reversible single-electron transfers. *(3)* and *(4)* differ therefrom only insofar as the lifetime of $RED_k^{2\ominus}$ is too short for observation of a reversible redox step.

Table 1. The potentials E_1^k, E_2^k, E_1^a, and E_2^a [V] of the polyenes *(3)*—*(5)* determined from direct current polarograms or cyclic voltammograms (200 mV/s) against Ag/AgCl/acetonitrile with $Bu_4N^{\oplus}BF_4^{\ominus}$ as supporting electrolyte at −60 °C; also the semiquinone formation constants K_{SEM}.

	E_1^k	E_2^k in DMF/benzene (2:1)	K_{SEM}^k	E_1^a	E_2^a in dichloromethane	K_{SEM}^a
(3)	−2.44 irr.	−1.95	—	+0.60	+0.68	8.1×10^1
(4)	−2.8 irr.	−1.83	—	+0.59	+0.68	1.4×10^2
(5)	−1.99	−1.67	4×10^7	+0.56 [a]	+0.60 [a]	4

[a] Index potentials according to *B. Elema*, Rec. Trav. Chim. Pays-Bas *54*, 76 (1935).

That the special structure of *(3)*—*(5)* is responsible for the unusual redox behavior is indicated by comparison with the "isolated end groups" *(1a)* and *(1b)*: the maxima in the cyclic voltammogram show irreversible oxidation [*(1a)*: +1.50 V; *(1b)*: +1.23 V] and irreversible reduction [*(1a)*: −2.80 V; *(1b)*: −2.93 V]. Further, these potentials are appreciably more positive than E_1^a or negative than E_2^k of *(3)*—*(5)*.

Whereas for the polycyclic arenes the potentials E_1^a and E_2^k lie symmetrically around the zero point potential[3], this is not so for the polyenes *(3)*—*(5)*. With a zero point potential of the working electrode of −0.22 V (against Ag/AgCl in CH_3CN) and $E_1^a = +0.60$ V determined for *(1)*, E_2^k should appear at −1.15 V, whereas the experimental value is −1.96 V.

This behavior may be due to the donor action of the methyl groups. According to MO calculations[13] they lower the HOMO in arenes and raise the LUMO, which is equivalent to a cathodic shift of the oxidation and reduction potential. The unexpectedly large difference between K_{SEM}^a and K_{SEM}^k of *(5)* could have the same reason. In arenes these values are equal[3, 14].

As has been shown for several vinylogous two-stage redox systems, there is a good linear relation between the Coulomb repulsion integral Jmm_{SEM} and $\log K_{SEM}$, with K_{SEM} becoming rapidly smaller with increasing chain length[15, 16]. According to Table 1 this is not so for K_{SEM}^a of *(3)*—*(5)*. The cause of this deviation can be seen in the twisting of the π-system by the methyl groups[15, 17]. This could affect the whole π-system and thus K_{SEM}^a would be smallest for the shortest polyene *(3)*.

Received: April 25, 1975 [Z 237 IE]
German version: Angew. Chem. *87*, 548 (1975)

CAS Registry numbers:
(3), 55712-11-3; *(4)*, 55712-12-4; *(5)*, 55712-13-5

[1] *E. Weitz*, Angew. Chem. *66*, 658 (1954); *S. Hünig*, Liebigs Ann. Chem. *676*, 32 (1964); *S. Hünig, H. Balli, H. Conrad, H. Friedrich, J. Gross, G. Kiesslich, G. Ruider, G. Sauer*, and *D. Scheutzow*, Pure Appl. Chem. *15*, 109 (1967).

[2] *O. Hammerich* and *V. D. Parker*, J. Amer. Chem. Soc. *96*, 4289 (1974); *B. S. Jensen* and *V. D. Parker*, J. C. S. Chem. Comm. *1974*, 367.

[3] *V. D. Parker*, J. Amer. Chem. Soc. *96*, 4289 (1974).

[4] a) *V. G. Mairanovskii, A. A. Engovatov*, and *G. J. Samokhvalov*, Zh. Org. Khim. *1970*, 6 (3), 632; b) *V. G. Mairanovskii, A. A. Engovatov, N. T. Ioffe*, and *G. J. Samokhalov* in *L. G. Feoktistov*: Novosti Elektrokhim. Org. Soedin., Tezisy Dokl. Vses. Soveshch. Elektrokhim. Org. Soedin. 8th, 1973. Zinatne, Riga 1973; Chem. Abstr. *82*, 36616n (1975); Elektrokhimiya *11*, 184 (1975).

[5] *K. K. Barnes* and *C. K. Mann*, J. Org. Chem. *32*, 1322 (1967).

[6] *A. Zweig, A. K. Hoffmann, D. L. Mariele*, and *A. H. Maurer*, Chem. Commun. *1967*, 106.

[7] *(2a): W. v. E. Doering, M. Saunders, H. G. Boyton, H. W. Earhart, E. F. Wadley, W. R. Edwards*, and *G. Laber*, Tetrahedron *4*, 178 (1958); *C. Jutz, W. Müller*, and *E. Müller*, Chem. Ber. *99*, 2479 (1966); *(2b): S. Hünig* and *P. Schilling, ibid.*, in press.

[8] *S. Hünig* and *P. Schilling*, Liebigs Ann. Chem., in press.
[9] *M. Horner* and *S. Hünig*, Liebigs Ann. Chem., in press.
[10] *O. Hammerich* and *V. D. Parker*, Electrochim. Acta *1973*, 537.
[11] The criteria are fully satisfied [cf. *R. S. Nicholson* and *I. Shain*, Anal. Chem. *36*, 706 (1964)].
[12] *S. Hünig, D. Scheutzow*, and *H. J. Friedrich*, Angew. Chem. *76*, 818 (1964); Angew. Chem. internat. Edit. *3*, 701 (1964).
[13] *G. J. Hoitink* and *J. van Schooten*, Rec. Trav. Chim. Pays-Bas *71*, 1089 (1952); *E. S. Pysh* and *N. C. Yang*, J. Amer. Chem. Soc. *85*, 2124 (1963).
[14] *P. Čarski, S. Hünig, D. Scheutzow*, and *R. Zahradník*, Tetrahedron *25*, 4781 (1969).
[15] *S. Hünig, D. Scheutzow, H. Schlaf*, and *H. Pütter*, Liebigs Ann. Chem. *1974*, 1436.
[16] *S. Hünig* and *H. C. Steinmetzer*, Tetrahedron Lett. *1971*, 643; Liebigs Ann. Chem., in press; *S. Hünig, F. Linhart*, and *D. Scheutzow*, *ibid.*, in press.
[17] *S. Hünig, J. Gross*, and *W. Schenk*, Liebigs Ann. Chem. *1973*, 324.

Building Units for Oligosaccharides. Synthesis of α-Glycosidically Linked 2-Amino Sugar Oligosaccharides

By *Hans Paulsen* and *Wolfgang Stenzel*[*]

The problem of direct selective synthesis of α-glycosidically linked 2-amino sugar oligosaccharides has not previously been solved. An indirect preparation that affords an α-glycoside preferentially is possible by addition to nitrosoglycals according to Lemieux's method[1, 2], but the difficulty of selective hydrogenation of the 2-ketoxime produced then remains to be solved.

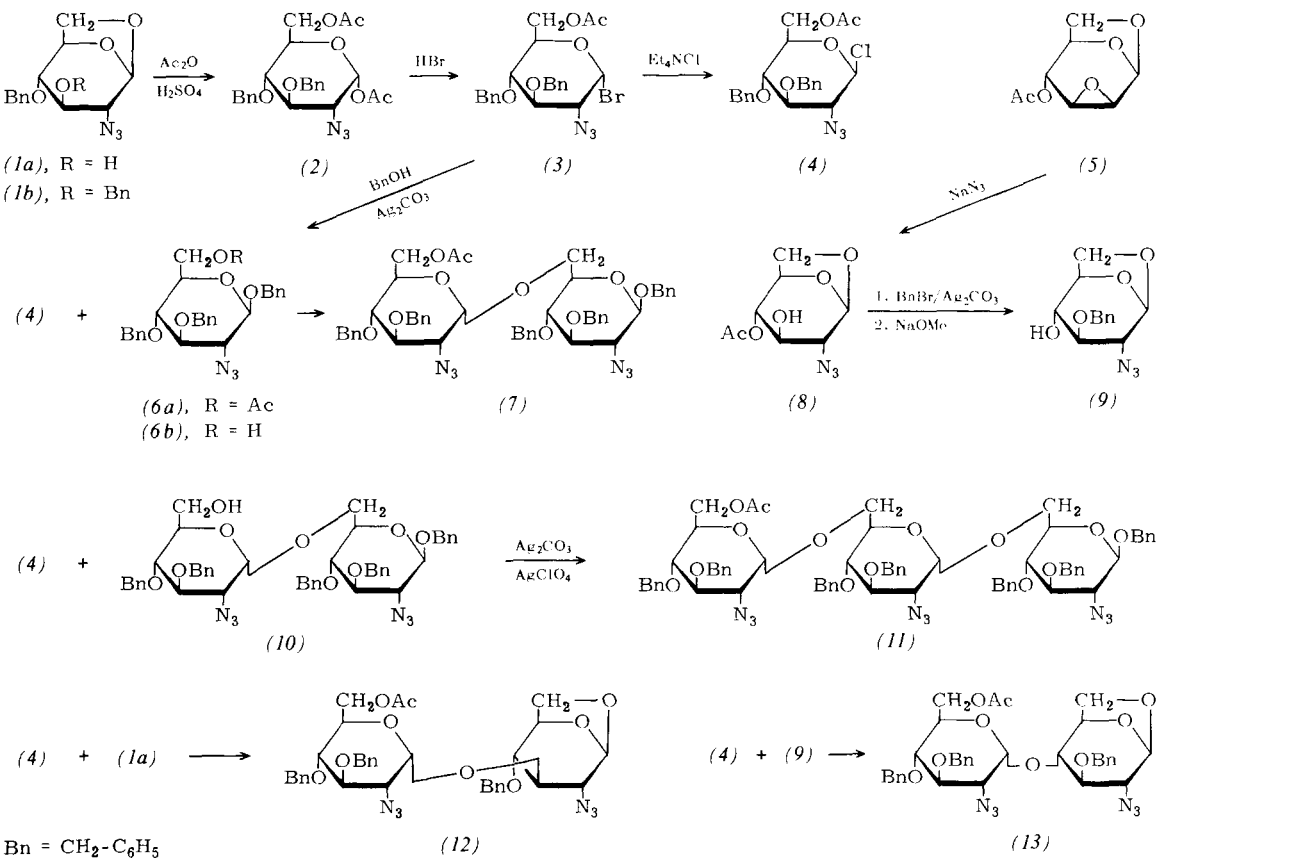
The azido group is an excellent "blocking group" for amino groups; it exerts no neighboring group effect. After having found a simple method of preparing 2-azido-2-deoxy-D-glucose[3] we were able to show that halogen derivatives of this compound can be used to accomplish glycoside syntheses with good yields and high selectivity.

The 2-azido sugar *(1a)* affords the 3,4-di-*O*-benzyl compound *(1b)* whose 1,6-anhydro ring can be opened by acetolysis, yielding the diacetate *(2)* (64%; m.p. 97 °C; $[\alpha]_D^{20} = +62°$). The α-bromide *(3)* (82%; m.p. 84 °C; $[\alpha]_D^{20} = +101°$) can be obtained by treatment of *(2)* with HBr in dichloromethane. Compound *(3)* can be used for selective synthesis of β-glycosides; for example, it reacts with benzyl alcohol in the presence of Ag_2CO_3 to give a 72% yield of a product that consists to the extent of 80% of the β-glucoside *(6a)* (m.p. 83 °C; $[\alpha]_D^{20} = -4°$).

The desired α-glycoside synthesis can be effected in the following way: The α-bromide *(3)* can be rearranged to the β-chloride by tetraethylammonium chloride[4] in acetonitrile. The rearrangement should be followed polarometrically and must be stopped at exactly the maximum negative rotation. For glycoside synthesis the extremely reactive β-chloride *(4)* (80%; a syrup) should be used directly since it anomerizes to the α-chloride on standing.

The C-6-unsubstituted compound *(6b)*, which is readily obtained from *(6a)*, reacts with *(4)* in dichloromethane in the presence of Ag_2CO_3, Drierite and catalytic amounts of $AgClO_4$[5, 6] in 5 min at −5 °C to give a 75% yield of a disaccharide containing 90% of the α-glycoside *(7)* which crystallizes well (m. p. 91 °C; $[\alpha]_D^{20} = +49°$). The linkage step can be continued without difficulty. If the disaccharide *(10)* obtained by partial deblocking of *(7)* is treated with *(4)* under the same conditions as before, a 71% yield of a trisaccharide is isolated, 90% of which was shown to be the α-glycoside *(11)* (m. p. 77—82 °C; $[\alpha]_D^{20} = +72°$).

Reaction of *(4)* with less reactive secondary hydroxyl groups can also be accomplished. The C-3-unsubstituted compound *(1a)*, with *(4)*, gives a 36% yield of a product containing 80% of the α-glycoside *(12)* (m.p. 110—111 °C; $[\alpha]_D^{20} = +90°$). A suitable C-4-unsubstituted reactant could be obtained from the 1,6-anhydro sugar *(5)*. The epoxide ring of *(5)* could be opened by means of NaN_3 to afford



[*] Prof. Dr. H. Paulsen and Dipl.-Chem. W. Stenzel
Institut für Organische Chemie und Biochemie der Universität
2 Hamburg 13, Papendamm 6 (Germany)

the azido sugar *(8)*. The 3-*O*-benzyl ether obtained by benzylation of *(8)* can be cleaved selectively to *(9)*, which reacts with the β-chloride *(4)* to give a 55% yield of a disaccharide mixture that contains 80% of the α-form *(13)*.

270-MHz ^{1}H-NMR spectra of all oligosaccharide derivatives prepared could be largely analyzed and provided definite proof of the α-linkage in each case. The azidoglycosides can readily be converted into aminoglycosides by hydrogenation using known techniques. The *O*-benzyl groups are also removed by hydrogenation under the usual conditions. The demonstration of three very important types of linkage shows the capability of the method which can clearly be extended in many ways.

Received: May 5, 1975 [Z 242 IE]
German version: Angew. Chem. 87, 547 (1975)

CAS Registry numbers:
(1a), 55682-47-8; *(1b)*, 55682-48-9; *(2)*, 55682-49-0; *(3)*, 55682-50-3; *(4)*, 55682-51-4; *(5)*, 55682-52-5; *(6a)*, 55682-53-6; *(6b)*, 55682-54-7; *(7)*, 55682-55-8; *(8)*, 55682-56-9; *(9)*, 55682-57-0; *(10)*, 55682-58-1; *(11)*, 55682-59-2; *(12)*, 55723-08-5; *(13)*, 55723-09-6

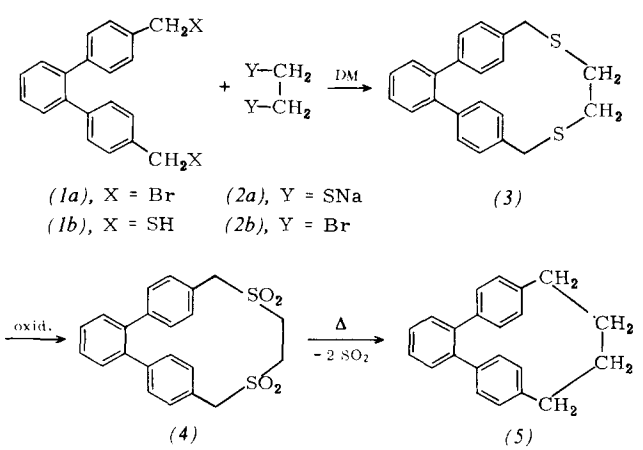
[1] *R. U. Lemieux, K. James*, and *T. L. Nagabushan*, Can. J. Chem. *51*, 48 (1973).
[2] Cf., however, *K. Migai* and *R. W. Jeanloz*, Carbohyd. Res. *21*, 45 (1972).
[3] *H. Paulsen, H. Koebernick, W. Stenzel*, and *P. Köll*, Tetrahedron Lett. *18*, 1493 (1975).
[4] *R. U. Lemieux* and *J. Havami*, Can. J. Chem. *43*, 2162 (1965).
[5] *B. Helferich, M. Müller*, and *S. Karbach*, Liebigs Ann. Chem. *1974*, 1514.
[6] *K. Igarashi, J. Irisawa*, and *T. Honma*, Carbohyd. Res. *39*, 341 (1975).

New Method for Synthesis of Many-membered Hydrocarbon Rings[**]

By *Fritz Vögtle* and *Joachim Grütze*[*]

We report here a new and simple method of synthesis, on a preparative scale, of medium- and many-membered cyclic hydrocarbons. The method originates from the ring contraction by thermolysis of cycles analogous to dibenzyl sulfone described by us earlier[1] and since found of proven value. Whereas previously only ethano bridges could be constructed between aromatic nuclei[2], the new method permits their connection by $-(CH_2)_n-$ bridges of various lengths. New carbocyclic ring systems of theoretical and practical interest thus become accessible rapidly and without great labor or expense.

The method was developed for the bridged *o*-terphenyl system: 2,5-Dithia[6](4,4″)orthoterphenylophane *(3)*[3] was obtained from 4,4″-bis(bromomethyl)-*o*-terphenyl *(1a)* and disodium 1,2-ethanedithiolate *(2a)* or alternatively from 4,4″-bis(mercaptomethyl)-*o*-terphenyl *(1b)* and 1,2-dibromoethane *(2b)* by the dilution method (DM) previously described by us in detail on several occasions[4]. This product *(3)* is oxidized to the disulfone *(4)* by H_2O_2 in glacial acetic acid/benzene in almost quantitative yield (for properties of the compounds see Table 1)[5].



(1a), X = Br *(2a)*, Y = SNa *(3)*
(1b), X = SH *(2b)*, Y = Br

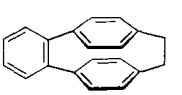
(4) *(5)*

Table 1. Compounds synthesized.

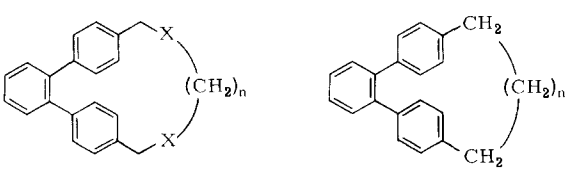
Cpd.	*n*	M.p. [°C]	^{1}H-NMR [a]
(1a)	—	116—117	4.45 (s)
(1b)	—	98—99	3.83 (d), $J = 6$ Hz
(3) ≡ *(7a)*	2	150—153	2.16—2.63 (m)
(4) ≡ *(8a)*	2	380 (dec.)	3.33 (s)
(5) ≡ *(9a)*	2	143—146	3.65 (s)
(7b)	3	132—134	3.73 (s)
(7c)	4	145—147	3.73 (s)
(7d)	5	139—140	3.73 (s)
(7e)	6	135—136	3.70 (s)
(8b)	3	295—297	4.36 (s)
(8c)	4	325—327	4.23 (s)
(8d)	5	262—264	4.21 (s)
(8e)	6	272—275	4.25 (s)
(9b)	3	205—207	2.28—2.93 (m)
(9c)	4	177—179	2.44—3.02 (m)
(9d)	5	84—87	2.40—2.77 (m)
(9e)	6	72—75	2.16—2.73 (m)

[a] Benzyl-H; δ-values [ppm], in $CDCl_3$.

Surprisingly, pyrolysis of the disulfone *(4)* (in a quartz tube at 500 °C/0.1 torr[6], length of the tube furnace 4 cm) does not lead to the [2.2]paracyclophane-analogous system *(6)*[7] with loss of SO_2 and ethylene, but instead the hydrocarbon [4](4,4″)orthoterphenylophane *(5)* is formed in 80–90% yield.



(6)



(7), X = S *(9)*
(8), X = SO_2

For planning of syntheses it is of value that the cyclic compounds *(9b)*—*(9e)* with longer bridges (Table 1) can also be obtained in good yield by this new method which involves two-fold extrusion of SO_2 without loss of the aliphatic $-(CH_2)_n-$ bridge after starting from the sulfone *(8)*. The mechanism is assumed to involve stepwise extrusion of SO_2[1] and radical recombination of the fragments[6]. Although, because of its rigidly bent molecular structure, the *o*-terphenyl system appears to favor this type of ring contraction, the method may well succeed in other cases under suitable conditions of temperature, pressure and residence time, leading to new oligocyclic medium- and many-membered hydrocarbons and heterocycles[8].

Received: May 5, 1975 [Z 243 IE]
German version: Angew. Chem. 87, 543 (1975)

CAS Registry numbers:
(1a), 55759-13-2; *(1b)*, 55759-14-3; *(2a)*, 23851-16-3; *(2b)*, 106-93-4; *(3)*, 55759-15-4; *(4)*, 55759-16-5;

[*] Prof. Dr. F. Vögtle and Dipl.-Chem. J. Grütze
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

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

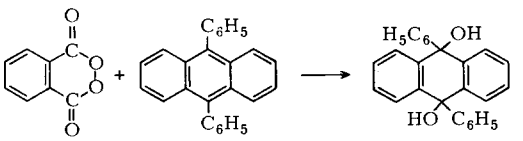
(5), 55759-17-6; (7b), 55759-18-7; (7c), 55759-19-8; (7d), 55759-20-1; (7e), 55759-21-2; (8b), 55759-22-3; (8c), 55759-23-4; (8d), 55759-24-5; (8e), 55759-25-6; (9b), 55759-26-7; (9c), 55759-27-8; (9d), 55759-28-9; (9e), 55759-29-0

[1] F. Vögtle, Angew. Chem. 81, 258 (1969); Angew. Chem. internat. Edit. 8, 274 (1969); Chem. Ber. 102, 3077 (1969).
[2] F. Vögtle and P. Neumann, Synthesis 1973, 85.
[3] For nomenclature cf. F. Vögtle and P. Neumann, Angew. Chem. 84, 75 (1972); Angew. Chem. internat. Edit. 11, 73 (1972).
[4] F. Vögtle, J. Grütze, R. Nätscher, W. Wieder, E. Weber, and R. Grün, Chem. Ber. 108, 1694 (1975), and references there cited.
[5] Correct elemental analyses and mass spectra were obtained from all the compounds.
[6] H. A. Staab and M. Haenel, Chem. Ber. 106, 2190 (1973).
[7] This compound is presently being synthesized.
[8] Here we have in mind, not only ortho-, meta- and para-cyclophanes, pyridinophanes, thiophenophanes etc. but also arenes that are bridged more than twice; e.g. the hexathia compound previously described by us [9] could be the starting point for synthesis of [4.4.4](1,3,5)cyclophane [10].
[9] R. G. Lichtenthaler and F. Vögtle, Chem. Ber. 106, 1319 (1973).
[10] Note added in proof: In the meantime the method has been successfully employed by us for the synthesis of ring compounds containing even longer bridges and bridges with oligoethylene glycol units, as in crown ether compounds.

Phthaloyl Peroxide as an Efficient Source of Singlet Oxygen

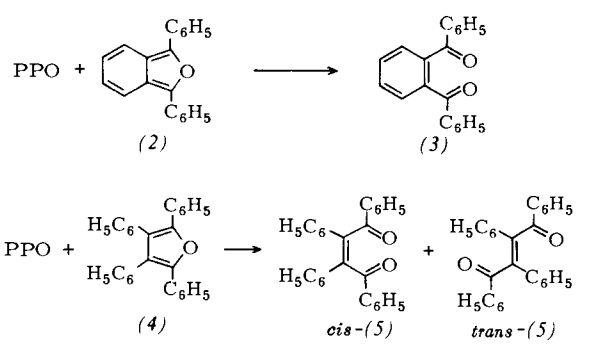
By *Karl-Dietrich Gundermann* and *Manfred Steinfatt*[*]

Investigation of the products formed in the chemiluminescence reaction of phthaloyl peroxide (PPO) with 9,10-diphenylanthracene (DPA)[1] revealed that, in addition to CO_2, phthalic acid, and numerous other oxygen-containing minor products, an approximately 30% yield of 9,10-diphenyl-9,10-dihydro-9,10-anthracenediol *(1)* is obtained[2]. This suggests that molecular oxygen is released by PPO under the conditions



PPO DPA *(1)*

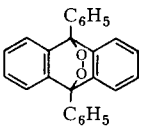
of the chemiluminescence reaction. That the species produced is excited singlet oxygen $^1O_2$ is shown by the reaction of PPO with 1,3-diphenylisobenzofuran *(2)* which affords the photooxidation product *o*-dibenzoylbenzene *(3)*[3] in 60% yield; reaction with tetraphenylcyclopentadienone *(4)* correspondingly furnishes *cis*- and *trans*-1,2,3,4-tetraphenyl-2-butene-1,4-dione (dibenzoylstilbene) *(5)*[4] in 34% yield. In the reactions, either weak or no chemiluminescence is observed—the chemiluminescence matching the fluorescence spectrum of *(2)* and *(4)*, respectively.



(2) *(3)*

(4) *cis-(5)* *trans-(5)*

The ratio chemiluminescence quantum yield/photooxidation depends upon the nature of the fluorophore present in the reaction with PPO: in contrast to *(2)* and *(4)*, diphenylanthracene, rubrene, and 9,10-bis(phenylethynyl)anthracene predominantly afford chemiluminescence; photooxidation products, in particular "endoperoxides" such as *(6)*, have not yet been detected.



(6)

The high yield of *(3)*, the photooxidation product of *(2)*, shows PPO to be a very efficient chemical generator of singlet oxygen[5]. The general applicability of this type of reaction is presently being studied.

o-Dibenzoylbenzene (3) from 1,3-diphenylisobenzofuran (2)

A solution of *(2)* (1.08 g) in benzene (50 ml) is shaken at room temperature with PPO (0.66 g). After the rapid disappearance of the yellowish fluorescence the reaction mixture is concentrated in vacuum and the residue induced to crystallize by addition of ethanol. Recrystallization from ethanol affords 0.68 g (59%) of *(3)*, m. p. 145—146 °C (ref. [3]: 145—146 °C).

cis- and trans-Dibenzoylstilbene (5) from tetraphenylcyclopentadienone (4)

A solution of *(4)* (1.54 g) in benzene (100 ml) is heated to 50—60 °C for about 10 min with PPO (1.32 g) until the reddish violet coloration of the solution has disappeared. The filtered solution is concentrated in vacuum and the residue rubbed with ethanol. The reaction yields 0.53 g (34%) of *(5)*, m. p. 213—214 °C, after separation m. p. 233 °C (ref. [4]: 213 °C (*cis*) and m. p. 232—233 °C (*trans*).

Received: May 6, 1975 [Z 245 IE]
German version: Angew. Chem. 87, 546 (1975)

CAS numbers:
(2), 5471-63-6; *(3)*, 1159-86-0; tetraphenylfuran *(4)*, 1056-77-5; *cis-(5)*, 6313-26-4; *trans-(5)*, 10496-80-7; PPO, 4733-52-2

[1] K.-D. Gundermann, M. Steinfatt, and H. Fiege, Angew. Chem. 83, 43 (1971); Angew. Chem. internat. Edit. 10, 67 (1971).
[2] M. Steinfatt, Dissertation, Technische Universität Clausthal 1975.
[3] C. Dufraisse and S. Ecary, C. R. Acad. Sci. 223, 735 (1946).
[4] H. H. Wasserman and J. R. Scheffer, J. Amer. Chem. Soc. 89, 3073 (1967).
[5] W. Adam, Chem.-Ztg. 99, 142 (1975).

Stable Pyrazolium Betaines by Addition of 1,1-Dialkylhydrazines to Acetylenecarboxylic Esters

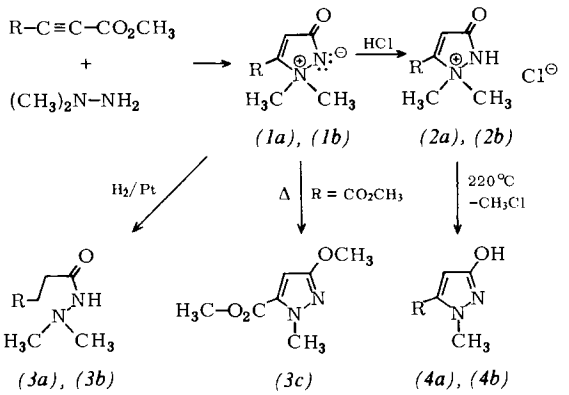
By *Wolfgang Sucrow*, *Marion Slopianka*, and *Vasilios Bardakos*[*]

While the addition of 1,1-dimethylhydrazine to α,β-unsaturated esters to give pyrazolinium betaines had already been

[*] Prof. Dr. K.-D. Gundermann and Dipl.-Chem. M. Steinfatt
Organisch-Chemisches Institut der Technischen Universität Clausthal
D-3392 Clausthal-Zellerfeld, Leibnizstrasse 6 (Germany)

[*] Prof. Dr. W. Sucrow and M. Slopianka
Institut für Organische Chemie der Technischen Universität
1 Berlin 12, Strasse des 17. Juni 115 (Germany)
Dr. V. Bardakos
Laboratory for Organic Chemistry of the National Polytechnicum Athens (Greece)
Exchange fellow of the Deutscher Akademischer Austauschdienst and the Gesellschaft von Freunden der Technischen Universität Berlin.

described about a decade ago[1], the analogous reaction with acetylenecarboxylic esters was not known. Three of the pyrazolium betaines expected to be formed by such a reaction were recently obtained by *Lockley* and *Lwowski*[2] by trapping aminoisocyanates with acetylenes, but the substitution pattern of this reaction is other than in the direct synthesis described here.

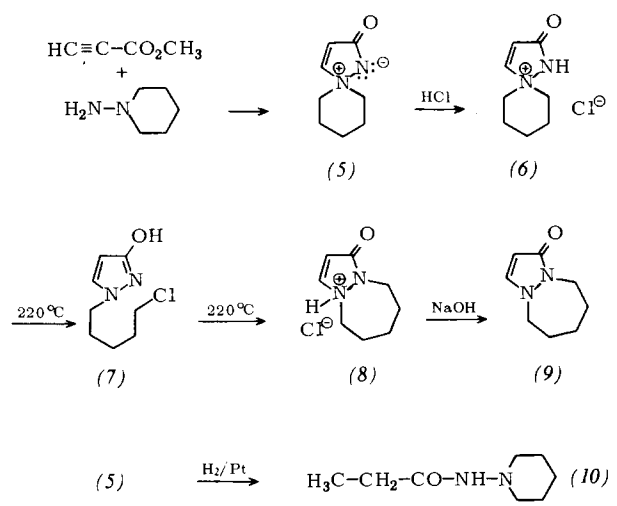


(1a), (1b) *(2a), (2b)* *(3a), (3b)* *(3c)* *(4a), (4b)*

(a), R = CO_2CH_3; *(b)*, R = H

Addition of 1,1-dimethylhydrazine to dimethyl acetylenedicarboxylate in aqueous ethanol at 0 °C affords a 40% yield of the betaine *(1a)*, whose unstable hydrochloride *(2a)* loses chloromethane to give the known methyl 3-hydroxy-1-methyl-5-pyrazolecarboxylate *(4a)*[3]. Thermolysis of *(1a)* leads *via* methyl-shift to the methyl ether *(3c)*, while hydrogenolysis, contrary to the observations of *Lockley* and *Lwowski*[2], mainly takes place at the $=C-\overset{\oplus}{N}$ bond and leads to (also independently synthesized) succinic acid derivative *(3a)*.

Addition of 1,1-dimethylhydrazine to methyl propiolate affords the betaine *(1b)*, whose stable hydrochloride *(2b)* is thermolyzed to the 3-hydroxy-1-methylpyrazole *(4b)*[3]. The direct thermolysis of *(1b)* is less clear-cut than that of *(1a)*; the hydrogenolysis of *(1b)* yields predominantly *N,N*-dimethylpropionohydrazide *(3b)*.



(5) *(6)* *(7)* *(8)* *(9)* *(10)*

The cleavage of pyrazolium chlorides of type *(2)* with elimination of alkyl halide can be observed especially clearly with the addition product *(5)* from 1-aminopiperidine and methyl propiolate. The hydrochloride *(6)* is thermally decomposed to the 1-(5-chloropentyl)-3-hydroxypyrazole *(7)*, which cyclizes on prolonged heating to the hydrochloride *(8)* from which the base *(9)* is liberated. Hydrogenolysis of *(5)* also gives mainly the substituted hydrazide of propionic acid *(10)*.

All compounds were verified by spectral data and correct elemental analyses.

Procedure

A solution of 1,1-dimethylhydrazine (1.20 g, 20 mmol) in methanol/water (20 ml) is added dropwise at 0 °C to a solution of methyl propiolate (1.68 g, 20 mmol). The mixture is stirred for 30 min at 0 °C and 30 min at room temperature and then evaporated under vacuum. Crystallization from methanol affords 0.87 g (39%) *(1b)*, m. p. 230 °C; IR (KBr): 1640, 1590 cm^{-1}; ^{1}H-NMR (CD_3OD): $\delta = 3.31$ (s, $N(CH_3)_2$); 6.32 (d, $\overset{\ominus}{O}C-CH=$); 7.94 (d, $\overset{\oplus}{N}CH=$, $J = 3.2$ Hz); mass spectrum (70 eV): *m/e* 112 (M^+, 100%), 97 (30%), 83 (52%), 42 (85%).

Received: April 23, 1975 [Z 246 IE]
German version: Angew. Chem. 87, 551 (1975)

CAS Registry numbers:
(1a), 55781-83-4; *(1b)*, 36555-26-7; *(2a)*, 55781-84-5; *(2b)*, 55781-85-6; *(3a)*, 28402-64-4; *(3b)*, 17883-59-9; *(3c)*, 55781-86-7; *(4a)*, 52867-42-2; *(4b)*, 52867-35-3; *(5)*, 55781-87-8; *(6)*, 55781-88-9; *(7)*, 55781-89-0; *(8)*, 55781-90-3; *(9)*, 55781-91-4; *(10)*, 55781-92-5; dimethyl acetylenedicarboxylate, 762-42-5; methyl propiolate, 922-67-8; 1,1-dimethylhydrazine, 57-14-7; 1-aminopiperidine, 2213-43-6

[1] *N. P. Zapevalova* and *T. A. Sokolova*, Izv. Akad. Nauk SSSR, Ser. Khim. *1965*, 1442; *N. P. Zapevalova*, *L. A. Ovsyannikova*, and *T. A. Sokolova*, *ibid. 1966*, 2200; Chem. Abstr. *63*, 16329 (1965) and *66*, 85394 (1967), respectively.

[2] *W. J. S. Lockley* and *W. Lwowski*, Tetrahedron Lett. *1974*, 4263.

[3] *W. Sucrow*, *C. Mentzel*, and *M. Slopianka*, Chem. Ber. *107*, 1318 (1974).

Applications of Field Desorption Mass Spectrometry in Inorganic Chemistry: Salts[**]

By *H.-R. Schulten* and *F. W. Röllgen*[*]

Field desorption mass spectrometry (FD-MS) serves mainly as an analytical method for the determination of molecular weight[1]. In this communication we report the application of FD-MS for the analysis of inorganic salts. As a rule salts cannot be investigated by the conventional methods of mass spectrometry because the compounds have to be evaporated before ionization and thereby undergo decomposition. In the case of FD this thermal stress on the molecule is largely avoided. Typical ionic products in the FD of salts are cat^+, $(M+cat)^+$ or general ions of the composition $(nM+cat)^+$ (salt cluster) where cat^+ signifies the cation and M the salt molecule (cation and anion). M^+ ions are seldom recorded (Table 1).

Table 1. Ions and salt clusters in the FD mass spectra of inorganic salts. Only the three most intense ions of the spectra are listed (except cat^+).

Salt	FD ions	Salt	FD ions
KF	$(KF)K^+$, $(KF)_2K^+$	$NaClO_3$	$(NaClO_3)Na^+$, $(NaClO_3)_2Na^+$, $(NaCl)Na^+$
KCl	$(KCl)K^+$, $(KCl)_2K^+$, $KCl^\ddagger$	$Na(CH_3CO_2)$	$[Na(CH_3CO_2)]Na^+$, $[Na(CH_3CO_2)]_2Na^+$
KBr	$(KBr)K^+$, Br^+	NaN_3	$(NaN_3)Na^+$
KI	$(KI)K^+$, $(KI)_2K^+$, I^+	AgCl	$AgCl^\ddagger$, $(AgCl)Ag^+$
NaCl	$(NaCl)Na^+$, $(NaCl)_2Na^+$, $NaCl^\ddagger$	$AgNO_3$	$(AgNO_3)Ag^+$, $(AgNO_3)_2Ag^+$
$NaNO_3$	$(NaNO_3)Na^+$, $(NaNO_3)_2Na^+$, $(NaNO_3)_3Na^+$	$CaCl_2$	$CaCl^+$, $Ca^\ddagger$, $CaCl_2^\ddagger$
Na_2SO_4	$(Na_2SO_4)Na^+$		

[*] Dr. H.-R. Schulten [+] and Prof. Dr. F. W. Röllgen
Institut für Physikalische Chemie der Universität
53 Bonn, Wegelerstrasse 12 (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Landesamt für Forschung und Wissenschaft des Landes Nordrhein-Westfalen and the Fonds der Chemischen Industrie.

There are essentially two causes for the gentleness of ionization in FD:

1. the thermal activation required for desorption of a molecular ion is lower than for evaporation of a neutral molecule[1].

2. a characteristic "salt effect" is observed[2, 3], *i.e.* cat^+ and $(nM+cat)^+$ already desorb at field strengths which do not suffice for the ionization of molecules that are not salts and have a comparable ionization potential. Moreover it is possible to compensate for a lowering of emitter temperature by increasing the field strength. In the FD of LiCl the Li^+ ions desorb at 1×10^7 V/cm and *ca.* 200 °C or at about 3×10^7 V/cm and temperatures < 100 °C.

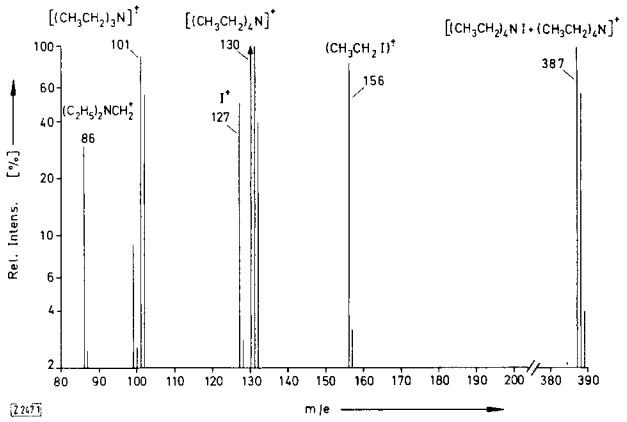


Fig. 1. Field desorption mass spectrum of tetraethylammonium iodide recorded with a modified CEC21-110B mass spectrometer with photographic detection. The sample material was deposited from aqueous solution onto the high-temperature activated 10 µm tungsten wire emitter. For further experimental data see ref. [1].

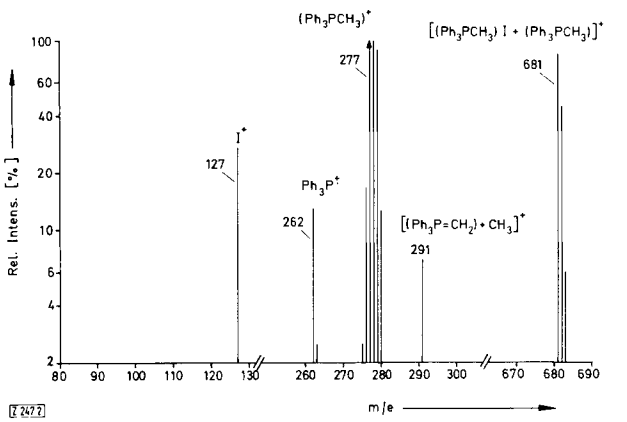


Fig. 2. Field desorption spectrum of methyltriphenylphosphonium iodide (for conditions see Fig. 1).

Figures 1 and 2 show the FD mass spectra of tetraethylammonium iodide and methyltriphenylphosphonium iodide, respectively. In addition to the characteristic cat^+ and $(M+cat)^+$ signals[4] the spectra also contain ions which can be formulated as fragments of the cation, *e.g.* $(C_2H_5)_3N^+$ and Ph_3P^+, and provide evidence for the presence of onium salts. So far the detection of inorganic salt clusters has met with success in the pyrolysis of biopolymers[5] and in the chemical analysis of the inorganic components of aerosols[6]. Field desorption mass spectrometry opens up new possibilities for the determination of the molecular weight and structure of nonvolatile inorganic compounds and considerably increases the scope of mass spectrometric investigations.

Received: May 6, 1975 [Z 247 IE]
German version: Angew. Chem. 87, 544 (1975)

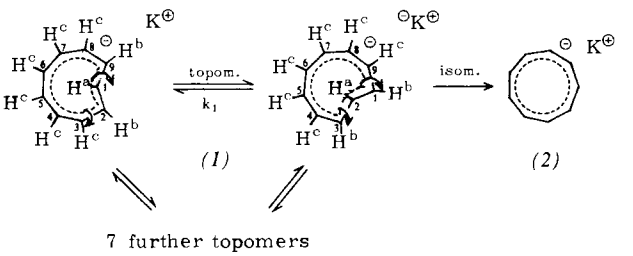
CAS Registry numbers:
$[(CH_3CH_2)_4N]^{\oplus}I^{\ominus}$, 68-05-3; $(Ph_3PCH_3)^{\oplus}I^{\ominus}$, 2065-66-9

[1] *H. D. Beckey* and *H.-R. Schulten*, Angew. Chem. *87*, 425 (1975); Angew. Chem. internat. Edit. *14*, 403 (1975).
[2] *H.-R. Schulten* and *F. W. Röllgen*, Org. Mass Spectrom. *10*, 649 (1975).
[3] *F. W. Röllgen* and *H.-R. Schulten*, Org. Mass Spectrom. *10*, 660 (1975).
[4] *D. A. Brent, D. J. Rouse, M. C. Sammons*, and *M. M. Bursey*, Tetrahedron Lett. *1973*, 4127; *G. W. Wood, J. M. McIntosh*, and *Pui-Yan Lau*, J. Org. Chem. *40*, 636 (1975).
[5] *H.-R. Schulten, H. D. Beckey, A. J. M. Boerboom*, and *H. L. C. Meuzelaar*, Anal. Chem. *45*, 2358 (1973).
[6] *H.-R. Schulten* and *U. Schurath*, Atmos. Environ., in press.

Topomerization of the *cis,cis,cis,trans*-[9]Annulene Anion[**]

By *Gernot Boche, Andreas Bieberbach*, and *Heinrich Weber*[*]

The conformational mobility of the annulenes is always greater than that of the π isoelectronic annulene ions[1]. Quantitative determination of the conformational mobility of the annulene ions is especially important since this is the only method by which information can be gained about the stability of these species. We have therefore investigated the thermal behavior of the diatropic *cis,cis,cis,trans*-[9]annulene anion *(1)*[5] ^{1}H-NMR spectroscopically with regard to its conformational mobility.



The potassium salt of *(1)* shows the following ^{1}H-NMR signals in dimethyl sulfoxide (DMSO) at 38 °C: the inner H^a, as a sharp triplet at $\delta = -3.52$, the two H^b, as a doublet of doublets at $\delta = 7.27$, and the six H^c, as a broad band centered at $\delta = 6.7$.

On warming the DMSO-solution of *(1)* to 90 °C the signals of the triplet broaden, and on further heating they coalesce at 135 ± 4 °C. Similar reversible changes occur especially in the case of the H^b signals.

Although coalescence of all signals is not observable (the anion *(1)* reacts irreversibly above 150 °C), we interpret the temperature dependence of its ^{1}H-NMR spectrum to indicate a rotation of the *trans* bond about the neighboring bonds. Continuation of this process will involve the participation of all ring positions and leads to a dynamic equilibrium of nine topomers. From a line shape analysis of the triplet[6] the rate constants k_1 of topomerization between 89 and 120 °C were determined (Table 1).

The saturation transfer method[7] provided the k_1 values at 61 and 62 °C (Table 1).

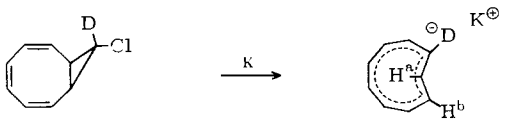
Proof of the topomerization of *(1)* was afforded by the reaction of *syn*-9-deuterio-*anti*-9-chloro-*cis*-bicyclo[6.1.0]-nona-2,4,6-triene *(3)* with potassium in tetrahydrofuran (THF) (6 h at −30 °C).

[*] Priv.-Doz. Dr. G. Boche, Dipl.-Chem. A. Bieberbach, and Dipl.-Chem. H. Weber
Institut für Organische Chemie der Universität
8 München 2, Karlstr. 23 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and BASF, Ludwigshafen (Germany).

Table 1. Rate constants k_1 for the topomerization of the anion *(1)* in the form of its potassium salt.

Method	T [°C]	Solvent	k_1 [s^{-1}]
Equilibration	27	THF	4.5×10^{-4}
after D-labeling	33	THF	1.4×10^{-3}
Saturation	61	DMSO	1.1×10^{-1}
transfer	62	DMSO	1.7×10^{-1}
Line-shape	89	DMSO	1
analysis	99.5	DMSO	4
	108	DMSO	7
	115	DMSO	11
	120	DMSO	20



(3)

Conrotatory ring opening leads to formation of a monodeuterio-*cis,cis,cis,trans*-[9]annulene anion in which deuterium is found predominantly at an H^b position. The ^{1}H-NMR signal at $\delta = -3.52$ showed mainly a doublet broadened by D—H coupling along with a small superimposed triplet. Warming to 30 °C (3 h) led to a triplet:doublet ratio = 3:1, the value expected for complete scrambling of the deuterium over all ring positions.

Solution of the complex kinetics for equilibration of the nine deuterated isomers of *(1)*[8] provided further information. The rate constant k_1 for a single isomerization step (equivalent to the topomerization rate constant, k_1, for the undeuterated species) could be determined (Table 1) from the time-dependence of the deuterium equilibration. This was accessible experimentally *via* measurement of the change in the triplet-doublet ratio at 27 and 33 °C.

The Eyring plot of the rate constants k_1, measured by three methods over a temperature range of 93 °C, showed a straight line. This finding provides good evidence that the measurements between 61 and 120 °C also involved the topomerization directly demonstrated at 27 and 33 °C. The activation entropy, near zero ($\Delta S^{\neq} = 6 \pm 8$ e.u.), is in accord with the intramolecular character of the topomerization. The activation enthalpy is $\Delta H^{\neq} = 23.6 \pm 1.5$ kcal/mol. Hence the rotation of the *trans* bond in the *cis,cis,cis,trans*-[9]annulene anion requires a considerably higher activation energy than the corresponding process in the uncharged larger annulenes and in the π-isoelectronic *cis,cis,cis,cis,trans*-[10]annulene[9].

This fact can be best explained in terms of the energetically unfavorable localization of charge required in intramolecular reactions of *(1)* (and other charged annulenes). A comparison of the topomerization and isomerization of *(1)* to the thermodynamically more stable all-*cis*-[9]annulene anion *(2)*[10] confirms this interpretation. Thus, preliminary measurements show that isomerization of *(1)* to *(2)* at 65 °C is $\geq 10^6$ times slower than the topomerization. The transition state of the isomerization necessitates a much more pronounced charge localization than that of the topomerization[11].

Received: April 30, 1975 [Z 250 IE]
German version: Angew. Chem. 87, 550 (1975)

CAS Registry numbers:
(3), 55820-91-2; C_9H_8DK, 55954-94-4; C_9H_9K, 55740-60-8

[1] Cf., *e.g.*, the rotation of *trans* bonds in the [18]annulene requires an activation enthalpy of $\Delta H^{\neq} = 16.1$ kcal/mol [2], while the [17]annulene anion [3] and the [16]annulene dianion do not show any line broadening in the ^{1}H-NMR spectrum, even on warming to 140 °C [4].

[2] *J. F. M. Oth*, Pure Appl. Chem. *25*, 573 (1971); *F. Sondheimer*, Accounts Chem. Res. *5*, 81 (1972).

[3] *G. Schröder, G. Plinke, D. M. Smith*, and *J. F. M. Oth*, Angew. Chem. *85*, 350 (1973); Angew. Chem. internat. Edit. *12*, 325 (1973); *G. Schröder*, private communication.

[4] *J. F. M. Oth, G. Anthoine*, and *J. M. Gilles*, Tetrahedron Lett. *1968*, 6265.

[5] *G. Boche, D. Martens*, and *W. Danzer*, Angew. Chem. *81*, 1003 (1969); Angew. Chem. internat. Edit. *8*, 984 (1969).

[6] We thank Prof. *G. Binsch*, Universität München, for valuable information and the Program DNMR II.

[7] *S. Forsén* and *R. Hoffmann*, J. Chem. Phys. *39*, 2892 (1963); *F. A. L. Anet* and *A. J. R. Bourn*, J. Amer. Chem. Soc. *89*, 760 (1967).

[8] *A. A. Frost* and *R. G. Pearson*: Kinetik und Mechanismen homogener chemischer Reaktionen. Verlag Chemie, Weinheim 1964, pp. 161 ff.; we thank Prof. *L. Bieberbach* for help with a few mathematical problems.

[9] *S. Masamune, K. Hojo, K. Hojo, G. Bigam*, and *D. L. Rabenstein*, J. Amer. Chem. Soc. *93*, 4966 (1971).

[10] *T. J. Katz* and *P. J. Garratt*, J. Amer. Chem. Soc. *85*, 2852 (1963); *E. A. Lalancette* and *R. E. Benson*, *ibid.* *85*, 2853 (1963).

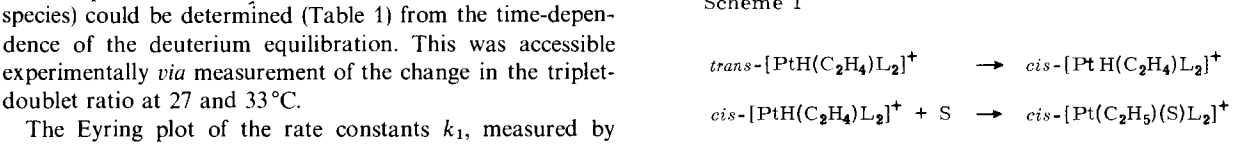
[11] *G. Boche* and *A. Bieberbach*, unpublished results.

Insertion of Ethylene into a Platinum(II)-Hydrido-Complex Containing a Bidentate Ligand Spanning *trans*-Positions[**]

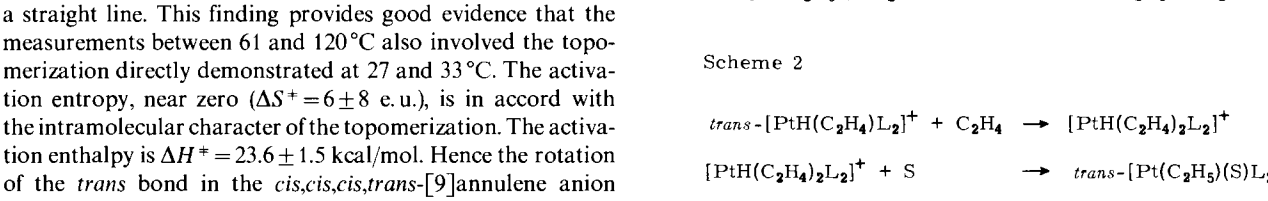
By *G. Bracher, P. S. Pregosin*, and *L. M. Venanzi*[*]

The insertion of ethylene into Pt—H bonds has been discussed in a number of recent papers[1]. The two mechanisms which have been put forward for reactions of this type are summarized below:

Scheme 1



Scheme 2



(L = tertiary phosphane; S = solvent)

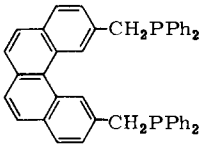
As pointed out[1] the kinetic data reported are compatible with either scheme.

We report here the occurrence of ethylene insertion into a complex which cannot react by Scheme 1.

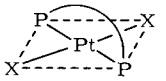
It has recently been shown[2] that 2,11-bis(diphenylphosphinomethyl)benzo[*c*]phenanthrene *(1)* forms square planar complexes of type *(2)* in which the bidentate ligand spans *trans*-positions. As ligand *(1)* cannot form mononuclear complexes of the type *cis*-$[PtX_2(1)]$ because of severe overlap of the phenyl groups[2], we have prepared acetone solutions of *trans*-$[PtH(acetone)(1)][BF_4]$ *(3)* and studied their reactions with ethylene.

[*] Prof. Dr. L. M. Venanzi, Dr. P. S. Pregosin, and G. Bracher
Laboratorium für Anorganische Chemie der Eidgenössischen Technischen Hochschule
Universitätstrasse 6, CH-8006 Zürich (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung.



(1)



(2)

trans-[PtHCl(*1*)] (*4*), prepared by addition of ligand (*1*) to a benzene solution of *trans*-[PtHCl(Ph_3P)$_2$][3], was suspended in acetone and treated with one equivalent of Ag[BF_4]. After filtering off the precipitated AgCl, the solution, containing complex (*3*), was treated with ethylene (*ca.* 1.2 atm) for 12 h.

The organometallic species present in the resulting solution was characterized as done for the corresponding complexes with monodentate phosphanes[1], *i.e.*, either by addition of chloride and isolation of *trans*-[Pt(C_2H_5)Cl(*1*)] (*5*) or by bubbling carbon monoxide through the solution and isolating *trans*-[Pt(C_2H_5)(CO)(*1*)][BF_4] (*6*). Complexes (*4*) to (*6*) gave satisfactory elemental analyses. The ^{1}H- and ^{31}P-NMR- and IR spectra of complexes (*3*) to (*6*) are in agreement with their respective formulations. Thus, our experiments show that ethylene insertion occurs under relatively mild conditions even in complex (*3*).

The implications of our results as to whether Scheme 1 or Scheme 2 provides a better description of the olefin insertion reaction in complexes *trans*-[PtH(acetone)(R_3P)$_2$]$^+$ (*7*) are not clear. On the one hand they seem to provide evidence in favor of Scheme 2. On the other, it could be argued that the significant differences in rates of ethylene insertion between (*3*) and (*7*)[1] indicate that Scheme 1 does indeed correspond to the lower energy pathway and that Scheme 2 becomes operative only when the *cis*-intermediates required by Scheme 1 cannot be formed[4].

The significance of our experiments, however, rests in the demonstration that ethylene insertion occurs even when the hydrido and olefin ligands cannot adopt mutually *cis*-orientations in a square-planar complex.

Received: May 13, 1975 [Z 256 IE]
German version: Angew. Chem. *87*, 547 (1975)

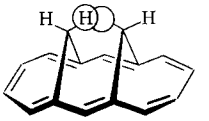
CAS Registry numbers:
(*3*), 55758-62-8; (*4*), 55758-63-9; (*5*), 55758-64-0;
(*6*), 55758-66-2; C_2H_4, 74-85-1; *trans*-[PtHCl(PPh_3)$_2$], 16841-99-9

[1] *H. C. Clark, C. Jablonski, J. Halpern, A. Mantovani,* and *T. A. Weil,* Inorg. Chem. *13*, 1541 (1974); *H. C. Clark* and *C. R. Jablonski, ibid. 13*, 2213 (1974).
[2] *N. J. DeStefano, D. K. Johnson,* and *L. M. Venanzi,* Angew. Chem. *86*, 133 (1974); Angew. Chem. internat. Edit. *13*, 133 (1974).
[3] *J. C. Bailar* and *H. Itatani,* Inorg. Chem. *4*, 1618 (1965).
[4] It is doubtful whether direct comparison of rates of ethylene insertion in (*3*) and (*7*) is really meaningful as activation energies for reactions of complexes of type (*2*) are expected to be higher than for those of the *trans*-[$PtX_2(R_3P)_2$] type.

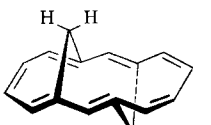
syn-1,6:8,13-Bismethano[14]annulene[1]

By *Emanuel Vogel, Johannes Sombroek,* and *Wolfgang Wagemann*[*]

The synthesis of *syn*-1,6:8,13-bismethano[14]annulene (*1*) has been the object of intense effort in this laboratory since our recognition that anthracene is formally convertible into bridged [14]annulenes exhibiting *syn-anti* configurational isomerism by insertion of a CH_2, O, or NH insulator into the bonds common to two rings (bridging principle)[2].

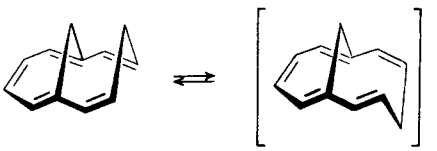


(1)
arene



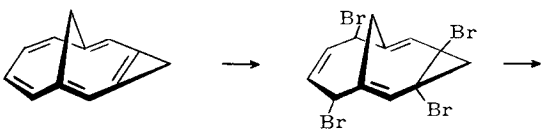
(2)
olefin

An approximately planar arrangement of the peripheral annulene ring of (*1*) can be achieved only at the expense of a certain degree of steric compression of the two inner bridge hydrogen atoms. The effective radii of these hydrogen atoms should thus determine whether (*1*) possesses a delocalized or a fluxional π-electron system, *i.e.*, whether the hydrocarbon (*1*) is an arene or an olefin.

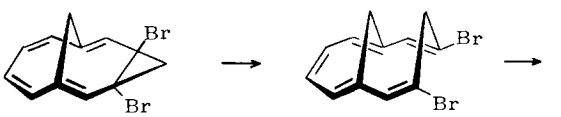


(3) (4)

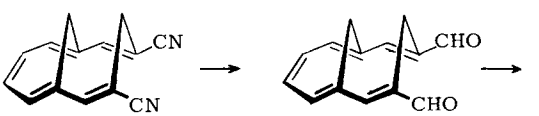
All attempts to prepare (*1*) by conventional methods from 1,4,5,8,9,10-hexahydroanthracene have so far failed. A new synthetic concept based on (a) the observation that the conformational equilibrium between *syn*- and *anti*-bicyclo[5.4.1]dodeca-2,5,7,9,11-pentaene [(*3*) and (*4*), respectively] lies practically entirely on the side of the *syn* conformer (*3*)[3], and (b) the course of bromination of the recently discovered cyclopropa-arene 1*H*-3,8-methanocyclopropa[10]annulene (*5*)[4] provided the desired breakthrough.



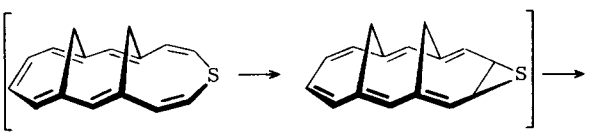
(5) (6)



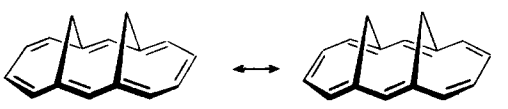
(7) (8)



(9) (10)



(11) (12)



(1)

[*] Prof. Dr. E. Vogel, Dr. J. Sombroek, and Dipl.-Chem. W. Wagemann
Institut für Organische Chemie der Universität
5 Köln 41, Greinstrasse 4 (Germany)

The readily accessible compound *(5)* reacts with 2 moles of bromine in carbon tetrachloride at 0 °C to form tetrabromide *(6)* [m.p. 155—157 °C (dec.); yield 18%] of as yet unknown stereochemistry as sole crystalline product[5]. On treatment of *(6)* with potassium iodide in acetone at room temperature, the doubly allylic bromine atoms are selectively eliminated to form the thermolabile compound *(7)* [m.p. 84—86 °C; yield 90%]. When *(7)* is heated in boiling benzene (2 h) the cyclopropane ring undergoes thermally allowed disrotatory ring opening (10π electrocyclic process)[6] to give *(8)* [m.p. 131—132 °C; yield 95%] which, like the subsequent products *(9)* and *(10)*, may be assigned the *syn* conformation.

Reaction of *(8)* with copper(I) cyanide in boiling dimethylformamide leads to the dinitrile *(9)* [m.p. 224—225 °C (dec.); yield 80%], which on reduction with diisobutylaluminum hydride in benzene furnishes the stable dialdehyde *(10)* [m.p. 215—216 °C (dec.); yield 80%; ^{1}H-NMR (CD_2Cl_2): $\tau = 0.63$ (s, 2H), 2.70—3.22 (m, 6H), 5.08 (d, $J = 16.5$ Hz, 1H), 5.82 (d, $J = 12.5$ Hz, 1H), 6.67 (d, $J = 16.5$ Hz, 1H), 9.36 (d, $J = 12.5$ Hz, 1H); UV (dioxane): $\lambda_{max} = 288$ ($\varepsilon = 59300$), 396 nm (4550)].

The method of choice for transforming *(10)* in the direction of *(1)* proved to be Wittig reaction with thiodimethylenedi(triphenylphosphonium bromide)[7] and lithium methoxide in dimethylformamide (4 h, room temperature). We thus obtained *(11)* which was already accompanied by *(1)*. In order to complete sulfur elimination from *(11)* the mixture of *(11)* and *(1)* was then heated for two hours with triphenylphosphane in benzene. As suggested by the recently demonstrated fragmentation of benzene episulfide to benzene and sulfur[8], the arene episulfide *(12)*, which owes its formation to an allowed disrotatory process with 14 π electrons[6], appears only as a short-lived intermediate[9]. The desired *(1)* was obtained as a stable yellowish orange compound of m.p. 116 °C (needles from methanol); yield 6% (based on *(10)*).

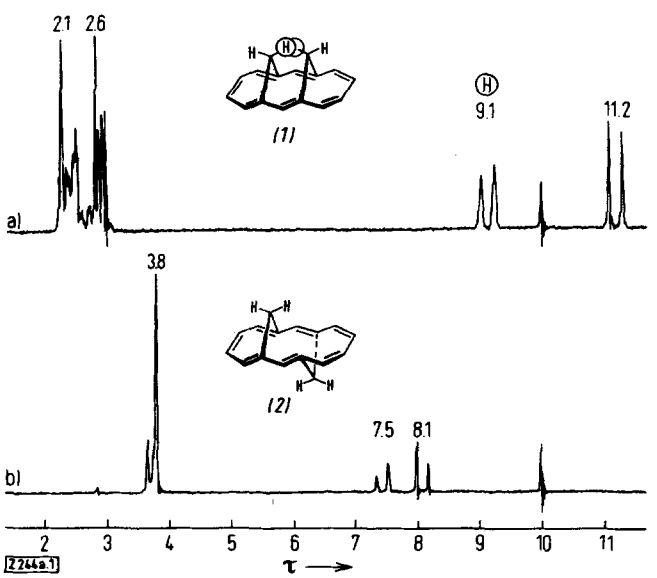


Fig. 1. 60 MHz ^{1}H-NMR spectra of a) *syn*-1,6:8,13-bismethano[14]annulene *(1)* and b) *anti*-1,6:8,13-bismethano[14]annulene *(2)* (each in $CDCl_3$ with TMS as internal standard).

The spectra unequivocally indicate the hydrocarbon *(1)* to be an arene. The ^{1}H-NMR spectrum (Fig. 1a) is in almost complete agreement with that of the aromatic 1,6:8,13-propanediylidene[14]annulene *(13)*[10] [*(1)*, CH_2 in place of inner bridge hydrogen atoms], with regard to both the chemical shifts of the annulene protons (including the relevant coupling constants) and the outer bridge protons. Concerning the signals of the inner bridge protons, their occurrence at relatively low field is very striking. It appears that the compression deduced for these protons from molecular models, which would suggest some degree of deshielding, is thus manifested. However, the downfield shift of the inner bridge protons is presumably only partly explained by a deshielding "proximity effect"[11], for it is conceivable that the shielding effect of the diamagnetic ring current at the site of the inner bridge protons is lower than at that of the outer ones. In accord with the NMR findings, the UV spectrum [(in cyclohexane): $\lambda_{max} = 303$ ($\varepsilon = 146600$), 320 (28000, sh), 361 (7560), 469 (208, sh), 473 (232), 479 (247), 487 (244), 493 (240), 498 nm (184, sh)] is in excellent agreement with that of *(13)*. Without wishing to anticipate the result of an X-ray structure analysis[5] it is thus already permissible to conclude that the annulene ring of *(1)* has approximately the same conformation as that of *(13)*[12].

The properties of *(1)* differ fundamentally from those of the *anti* isomer *(2)* (cf. Fig. 1b)[2]. As confirmed by X-ray structure analysis[13], *(2)* contains a puckered annulene ring in which the torsional angles of the 2 p_z orbitals of neighboring C atoms reach values up to 70°. As a result of this sterically unfavorable situation, delocalization of the 14 π electron system is no longer possible in *(2)*; hence *(2)* is a cyclopolyolefin with fluxional π bonds.

The studies on *(1)* and *(2)* provide the most impressive demonstration yet available that the molecular geometry is of crucial importance for the occurrence of aromaticity in cyclically conjugated ring systems with $(4n+2)\pi$ electrons—in accord with the steric criterion of the Hückel rule.

Received: May 5, 1975 [Z 244a IE]
German version: Angew. Chem. *87*, 591 (1975)

CAS Registry numbers:
(1), 55821-04-0; *(2)*, 7068-22-6; *(5)*, 53883-19-5; *(6)*, 55759-35-8; *(7)*, 55759-36-9; *(8)*, 55759-37-0; *(9)*, 55759-38-1; *(10)*, 55759-39-2; *(11)*, 55759-40-5; *(12)*, 55759-41-6; *(13)*, 55759-42-7; *(14)*, 55759-43-8

[1] Based on a plenary lecture delivered at the South West Regional Symposium in Organic Chemistry, The Perkin Division of the Chemical Society, Cardiff (Wales), March 1975.
[2] *E. Vogel*, Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 215 (1968); *E. Vogel, U. Haberland*, and *H. Günther*, Angew. Chem. *82*, 510 (1970); Angew. Chem. internat. Edit. *9*, 513 (1970).
[3] *E. Vogel, U. H. Brinker, K. Nachtkamp, J. Wassen*, and *K. Müllen*, Angew. Chem. *85*, 760 (1973), footnote 12; Angew. Chem. internat. Edit. *12*, 758 (1973).
[4] *E. Vogel* and *J. Sombroek*, Tetrahedron Lett. *1974*, 1627.
[5] X-Ray structure analyses of *(6)* and *(1)* are currently being performed by Prof. *M. Simonetta* (University of Milan).
[6] *R. B. Woodward* and *R. Hoffmann*: The Conservation of Orbital Symmetry. Verlag Chemie, Weinheim 1970, pp. 38ff.
[7] *K. Dimroth, H. Follmann*, and *G. Pohl*, Chem. Ber. *99*, 642 (1966).
[8] *E. Vogel, E. Schmidbauer*, and *H.-J. Altenbach*, Angew. Chem. *86*, 818 (1974); Angew. Chem. internat. Edit. *13*, 736 (1974).
[9] Elimination of sulfur from episulfides has recently proved to be a valuable preparative method on several occasions; see the syntheses of vitamin B_{12} [*A. Eschenmoser*, Quart. Rev. Chem. Soc. *24*, 366 (1970)], corroles [*M. J. Broadhurst, R. Grigg*, and *A. W. Johnson*, J. C. S. Perkin I *1972*, 1124], cycloalkylidenecycloalkanes (*D. H. R. Barton, E. H. Smith*, and *B. J. Willis*, Chem. Commun. *1970*, 1226) and *cis*-1,4-dihydro-1,4-naphthalenediol [*A. M. Jeffrey, H. J. C. Yeh*, and *D. M. Jerina*, J. Org. Chem. *39*, 1405 (1974)].
[10] *E. Vogel, A. Vogel, H.-K. Kübbeler*, and *W. Sturm*, Angew. Chem. *82*, 512 (1970); Angew. Chem. internat. Edit. *9*, 514 (1970).
[11] For examples, see *P. T. Lansbury*, Accounts Chem. Res. *2*, 210 (1969); *J. Heller, A. Yogev*, and *A. S. Dreiding*, Helv. Chim. Acta *55*, 1003 (1972), and references cited therein.
[12] *A. Gavezzotti, A. Mugnoli, M. Raimondi*, and *M. Simonetta*, J. C. S. Perkin II *1972*, 425.
[13] *C. M. Gramaccioli, A. S. Mimun, A. Mugnoli*, and *M. Simonetta*, J. Amer. Chem. Soc. *95*, 3149 (1973).

2-Hydroxy-4,10-methano[11]annulenone—A 10π Analog of α-Tropolone[1]

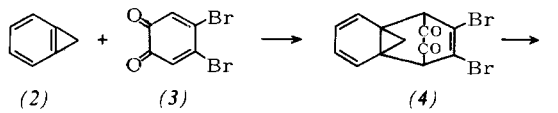
By *Emanuel Vogel, Joachim Ippen,* and *Veit Buch*[*]

The 1,6-methano[11]annulenylium ion[2]—an aromatic 10π analog of the tropylium ion—represents the parent of numerous bridged [11]annulenones and hydroxy[11]annulenones (5 and 36 possible isomers, respectively). As expected, the members of this annulenone family synthesized to date[3] closely resemble tropone and the tropolones, respectively, in their physical and chemical properties so that they can be justifiably termed 10π troponoid compounds[4].

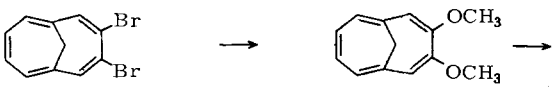
(1)

Among the hydroxy[11]annulenone derivatives of the 10π ion, 2-hydroxy-4,10-methano[11]annulenone *(1)* is doubtless the most interesting since it is the only isomer to comply with the structural requirements for an intramolecular "degenerate prototropic shift" and should therefore resemble α-tropolone particularly closely. The synthesis of *(1)* has now been accomplished by exploiting the versatile chemistry of cyclopropabenzene[5].

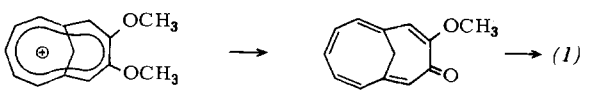
Cyclopropabenzene *(2)*, which we recognized as a dienophile some time ago[6], adds to 4,5-dibromo-*o*-benzoquinone *(3)* in acetonitrile with heating to form *(4)* containing a dicarbonyl bridge *trans* to the three-membered ring; orange crystals of m. p. 178—179 °C (yield 65 %). If *(4)* is irradiated in benzene with a Hg high pressure lamp (Hanau, 1000 watt) in an argon atmosphere with cooling, the principal reaction is decarbonylation to form *(5)* which can be readily isolated by chromatography on silica gel (dichloromethane/hexane); yellow crystals, m. p. 84—85 °C (yield 65%).



(2) *(3)* *(4)*



(5) *(6)*



(7) *(8)*

In analogy with a procedure reported by *Bacon et al.*[7] for transforming aromatic bromides into the corresponding methoxy compounds, we heated *(5)* with sodium methoxide and Cu I in collidin and worked up the products by chromatography (silica gel; dichloromethane); we obtained the yellow compound *(6)*, m. p. 133—134 °C (yield 64 %). Expecting to obtain *(8)* as one of the final products, we subjected *(6)* to $(CuCl)_2$-catalyzed reaction with diazomethane in dichloromethane, allowed the crude homologization product to react with triphenylmethyl hexafluorophosphate at 0 °C, and subsequently hydrolyzed the resulting carbenium ion mixture [*(7)* plus isomers] with 5 % potassium hydroxide. On chromatography (alumina, Woelm neutral; dichloromethane) of the oily mixture obtained in this way we isolated a yellowish orange fraction which yielded *(8)* on preparative thin-layer chromatography (silica gel; ether/hexane): *(8)*, m. p. 103—104 °C (yield 5 %). Heating of *(8)* in 2 N caustic soda leads to a red solution of the Na salt of *(1)* which on acidification to pH 4—5 furnishes the desired 2-hydroxy-4,10-methano[11]annulenone *(1)*; yellowish orange leaflets (from diisopropyl ether/acetic ester) having m. p. 126—127 °C (yield 54 %).

The spectra and chemical properties of *(1)* confirm its structure and the close similarity in behavior to α-tropolone.

The ^{1}H-NMR spectrum ($CDCl_3$/acetone), which exhibits no temperature dependence (at least down to −80 °C), contains a poorly resolved multiplet at τ = 2.5—3.2 (vinylic H), an AB system at τ = 9.05 and 9.57 with J = 11 Hz (bridge H), and a singlet at τ = 2.18 (OH). This spectrum fails to reveal the effective C_{2h} molecular symmetry required by a fast (NMR time scale) prototropism since the multiplet of the vinylic protons proved to be too complex for analysis. As was anticipated from experience gained with α-tropolone[8], the symmetry relationships of *(1)* could be readily established with the aid of ^{13}C-NMR spectroscopy. The ^{13}C-NMR spectrum of *(1)* at room temperature displayed only seven signals, thus indicating C_{2h} symmetry for the compound and hence the occurrence of fast prototropism. The activation energy of the prototropism is apparently very low since the simplicity of the spectrum is also retained at −80 °C. The UV spectrum [λ_{max} (ethanol) = 308 (ε = 31 100), 385 (6000), 445 nm (4400, sh)] is informative because it demonstrates the close structural similarity of *(1)* to the recently synthesized 3,9-methano[11]annulenone [*(1)*, H in place of OH][9]. In the IR spectrum (KBr) characteristic bands appear at 3295 (OH), 1585, 1565, and 1535 cm^{-1} (C=O and C=C).

Compound *(1)* is protonated by CF_3COOH to the 3,4-dihydroxy-1,6-methano[11]annulenylium ion [*(7)*, H in place of CH_3]. In the ^{1}H-NMR spectrum this is manifested in the marked downfield and upfield shift, respectively, of the vinylic (τ = 0.9—1.8) and bridge proton signals (τ = 10.3 and 11.4). In accord with the generation of this ion, *(1)* is found to give a UV spectrum in ethanolic perchloric acid which closely resembles that of 1,6-methano[11]annulenylium ion. The ability of *(1)* to form salts with alkali hydroxides is already apparent from its synthesis; a Cu complex obtained with copper(II) acetate in water/chloroform has yet to be characterized. According to the pK_a value of 8.1 determined by potentiometric titration the acidity of *(1)* is not quite as high as that of α-tropolone (pK_a = 7.0). However, the acidity of *(1)* permits its methylation by ethereal diazomethane without a catalyst to form *(8)*.

The analogy between *(1)* and α-tropolone (and between their methyl ethers) does not appear to extend as far as ring contraction in the presence of strong bases. Whereas the methyl ether of α-tropolone rearranges to methyl benzoate on heating with sodium methoxide in methanol, attempts to transform *(8)* into the theoretically interesting 1,5-methano[10]annulene-3-carboxylic ester[10] by heating with bases have so far been unsuccessful.

Received: May 5, 1975 [Z 244b IE]
German version: Angew. Chem. 87, 592 (1975)

CAS Registry numbers:
(1), 55759-49-4; *(2)*, 4646-69-9; *(3)*, 55759-50-7; *(4)*, 55759-51-8; *(5)*, 55759-52-9; *(6)*, 55759-53-0; *(8)*, 55759-54-1

[*] Prof. Dr. E. Vogel, Dipl.-Chem. J. Ippen, and Dipl.-Chem. V. Buch
Institut für Organische Chemie der Universität
5 Köln 41, Greinstrasse 4 (Germany)

[1] *T. Nozoe, S. Seto, Y. Kitahara, M. Kunori,* and *Y. Nakayama,* Proc. Jap. Acad. *26* (7), 38 (1950); *J. W. Cook, A. R. M. Gibb, R. A. Raphael,*

and *A. R. Sommerville*, Chem. Ind. (London) *1950*, 427; *W. v. E. Doering* and *L. H. Knox*, J. Amer. Chem. Soc. *72*, 2305 (1950).
[2] *W. Grimme, H. Hoffmann*, and *E. Vogel*, Angew. Chem. *77*, 348 (1965); Angew. Chem. internat. Edit. *4*, 354 (1965); *E. Vogel, R. Feldmann*, and *H. Düwel*, Tetrahedron Lett. *1970*, 1941.
[3] *W. Grimme, J. Reisdorff, W. Jünemann*, and *E. Vogel*, J. Amer. Chem. Soc. *92*, 6335 (1970); *E. Vogel*, XXIIIrd Internat. Congr. of Pure and Appl. Chem. *1*, 275 (1971); *J. Reisdorff* and *E. Vogel*, Angew. Chem. *84*, 208 (1972); Angew. Chem. internat. Edit. *11*, 218 (1972).
[4] *T. Nozoe* in *D. Ginsburg*: Non-benzenoid Aromatic Compounds. Interscience, New York 1959, pp. 339ff.
[5] *E. Vogel, W. Grimme*, and *S. Korte*, Tetrahedron Lett. *1965*, 3625; *W. E. Billups, A. J. Blakeney*, and *W. Y. Chow*, Chem. Commun. *1971*, 1461; *W. E. Billups, W. Y. Chow*, and *C. V. Smith*, J. Amer. Chem. Soc. *96*, 1979 (1974); *B. Halton*, Chem. Rev. *73*, 113 (1973).
[6] *E. Vogel*, Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 215 (1968).
[7] *R. G. R. Bacon* and *S. C. Rennison*, J. Chem. Soc. *C 1969*, 312.
[8] *L. Weiler*, Can. J. Chem. *50*, 1975 (1972).
[9] 3,9- and 2,8-Methano[11]annulenone: *E. Vogel et al.*, to be published.
[10] In the still hypothetical 1,5-methano[10]annulene, the torsional angles of the $2p_z$ orbitals on adjacent carbon atoms are calculated by the "molecular mechanics method" to reach values of up to 54° so that a 10π electron system with alternating single and double bonds can be predicted for this hydrocarbon: *N. L. Allinger* and *J. T. Sprague*, J. Amer. Chem. Soc. *95*, 3893 (1973).

Insertion of an Ethoxycarbonylmethylene Moiety into a Ni—N Bond of *meso*-Tetraphenylporphinatonickel(II)

By *H. J. Callot, Th. Tschamber, B. Chevrier*, and *R. Weiss*[*]

The reaction of the nickel(II) complex *(1)* with base first yielded the aziridine *(2)* (up to *ca.* 50%, stereochemistry undetermined)[1]. However, for longer reaction periods, *(2)* disappeared with the simultaneous formation of a new complex *(3)* (65%).

Complex *(3)* showed the visible spectrum expected of a porphyrin: 419 nm (ε = 138000) and 547 (9500) in CH_2Cl_2. The substituents on the extra carbon were strongly shielded: (H: δ = −3.38; CH_3: −0.31; CH_2: 2.25), as was observed for *N*-substituted porphyrins such as base *(4)*[1], and the corresponding Zn complex. The non-pyrrolic carbon atom attached to the nitrogen atom was found to be strongly shielded in compound *(3)* (δ = 25.7 ppm) as compared to *(4)* (43.5 ppm).

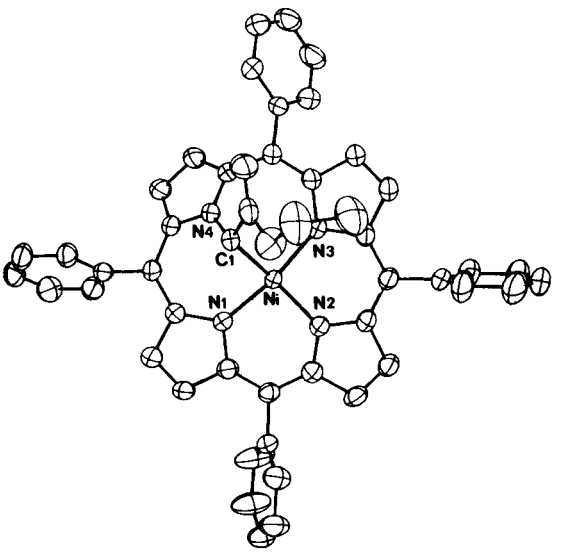
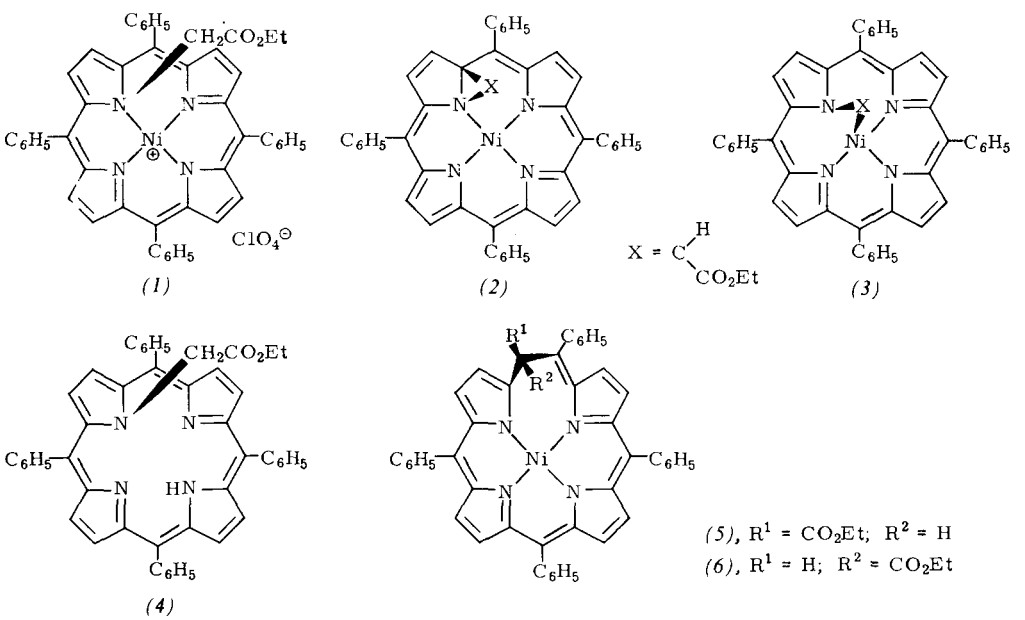


Fig. 1. Crystal structure of complex *(3)*.

The crystal structure[2, 3] of *(3)* is shown in Figure 1. The nickel atom is tetra-coordinated with the C1 extra carbon atom and with three nitrogen atoms of the pyrrole bases. The three Ni—N bond lengths are equal to 1.916 ± 0.010 Å. The Ni—C1 bond length of 1.905(4) Å is close to the predicted single bond length of 1.92 Å, based on the accepted covalent radii of Ni^{II} (1.15 Å) and a tetrahedrally hybridized carbon atom (0.77 Å). The Ni—C1—N4 bond angle is reduced to 102.9(2)°. Important distortion occurs in the macrocyclic ligand where (N4) pyrrole nucleus makes dihedral angles of 39.4 and 43.6° with (N1) and (N3) pyrrole planes, respectively.

Related products were earlier isolated by *Johnson et al.*[4] and may possess a similar structure, although no X-ray structure determination has yet been reported.



[*] Dr. H. J. Callot [+] and Dr. Th. Tschamber
Laboratoire de Chimie organique biologique associé au C.N.R.S.
Université Louis Pasteur, Institut de Chimie
1 rue Blaise Pascal, F-67008 Strasbourg (France)
Dr. B. Chevrier and Prof. R. Weiss
Laboratoire de Cristallochimie associé au C.N.R.S.
Université Louis Pasteur, Institut de Chimie
Strasbourg (France)
[+] Author to whom correspondence should be addressed.

The formation of compound *(3)* from salt *(1)* could be explained by a slow protonation and ring opening of the kinetically favored aziridine *(2)* followed by base catalyzed ring closure to nickel and loss of Ni—N bond. We demonstrated that *(2)*, in CH_2Cl_2/CH_3NO_2 (1:1) solution, was quantitatively transformed into *(3)* (15 minutes, 25 °C), confirming the required acid-base catalysis.

The complex *(3)* was stable in inert solvents ($T < 100$ °C) but was quantitatively demetalated by acids into base *(4)*, as its corresponding salt (CF_3COOH < 5 min; AcOH: 24 h). Reaction with ethanolic KOH gave tetraphenylporphinatonickel in 100% yield. When heated in solution (0.5% in xylene, 18 h under argon), compound *(3)* rearranged to the known homoporphinatonickel derivatives *(5)* and *(6)* (89%; ratio 46:54, as well as 10% tetraphenylporphinatonickel). This reaction may occur *via* aziridine *(2)*, which was already known to yield *(6)* on heating at 80 °C in solution[1]. The higher temperature (140 °C) required to transform *(3)* into *(5)* and *(6)* explained the occurrence of both products, whose interconversion by ring inversion is rapid above 110 °C.—Reactions of the type described here could warrant attention for understanding the substrate binding in porphyrin and corrin coenzymes.

N-Ethoxycarbonylmethylene-meso-tetraphenylporphinatonickel(II) (3)

Triethylamine (35 ml) and Na_2SO_4 (3 g) were added to a stirred solution of *(1)* (735 mg) in CH_2Cl_2 (40 ml). After 3 days' stirring at 25 °C the solution was filtered, the solvent evaporated and the residue chromatographed on silica gel. Toluene eluted the product which was crystallized from CH_2Cl_2/CH_3OH. Crystals suitable for the X-ray studies were obtained from $CHCl_3/CH_3OH$. All physica data for *(3)* are compatible with the structure (IR, visible absorption, MS, ^{13}C- and ^1H-NMR, elemental analysis).

Received: April 29, 1975 [Z 253]
German version: Angew. Chem. 87, 545 (1975)

CAS Registry numbers:
(1), 55758-68-4; *(2)*, 55758-69-5; *(3)*, 55822-50-9; *(5)*, 55820-92-3; *(6)*, 55820-93-4

[1] *H. J. Callot* and *Th. Tschamber*, Tetrahedron Lett. *1974*, 3155, 3159; Bull. Soc. chim. Fr. *1973*, 3192.

[2] The asymmetric unit cell contains one molecule of complex and one $CHCl_3$ molecule present as uncomplexed solvent of crystallization.

[3] Crystal data: P_1; $a = 13.677(6)$, $b = 14.212(8)$, $c = 11.958(5)$ Å; $\alpha = 98.85(8)$, $\beta = 99.21(8)$, $\gamma = 113.73(7)°$; $Z = 2$; $d_{calc.} = 1.43$ g cm^{-3}; 5493 independent reflections with $I > 3\sigma(I)$; $R = 0.061$.

[4] *P. Batten, A. Hamilton, A. W. Johnson, G. Shelton*, and *D. Ward*, J. C. S. Chem. Comm. *1974*, 550.

Formation of O^- Centers by Homolytic Decomposition of OH^- Groups on Magnesium Oxide[**]

By *Friedemann Freund, N. Scheikh-ol-Eslami*, and *Horst Gentsch*[*]

One of the few examples of a chemical reaction that still proceeds at a measureable rate at 77 K is the H/D exchange reaction in H_2-D_2 gas mixtures on thermally[1] or UV[2] activated, fine-grained MgO. The catalytic activity can be attributed to a paramagnetic center, V_I, which according to *Derouane et al.*[3] consists of three O^- ions on a metastable (111) face of the MgO crystallites. No detailed theory has so far been put forward for the formation of this center; all that was hitherto known is that the MgO must be extraordinarily pure, *i.e.* free from transition-metal impurities, and superficially hydroxylated or present in the form of hydroxycarbonate or hydroxide prior to thermal activation.

It has already been indicated[4] that "isolated" residual OH^- groups must remain behind after dehydration of a hydroxylated oxide surface, which preferentially proceeds by proton transfer in accordance with Scheme (1).

$$OH^- + OH^- \rightleftharpoons O^{2-} + H_2O\uparrow \quad (1)$$

Stochastic model calculations indicated *ca.* 10% of such residual OH^- groups[4], for which a finite dissociation probability according to Scheme (2) was put forward.

$$OH^- \rightarrow O^- + \tfrac{1}{2}H_2\uparrow \quad (2)$$

That is, simultaneous formation of paramagnetic O^- ions and liberation of hydrogen ought to take place in the homolytic decomposition. Earlier attempts[5] to detect the evolution of hydrogen by mass spectroscopy remained inconclusive[6] on account of the starting substance having been insufficiently pure, for transition metal cations can also lead to a liberation of hydrogen in accordance with Scheme (3),

$$M^{n+} + H_2O \rightleftharpoons M^{(n+1)} + OH^- + \tfrac{1}{2}H_2\uparrow \quad (3)$$

or react further with the O^- ions in accordance with Scheme (4)[7].

$$M^{n+} + O^- \rightarrow M^{(n+1)} + O^{2-} \quad (4)$$

We have now succeeded in confirming beyond doubt the liberation of D_2 from deuteroxylated MgO by means of mass spectroscopy.

High-grade purity MgO (Materials Research Corp. Orangeburg, N.J., batch no. 3066) was annealed for 2 h at 1000 °C in an argon-purged fused silica tube which was fused to a Duran glass grease-free ultrahigh vacuum apparatus, outgassed at 450 °C, fitted with two Hg diffusion pumps in tandem. The sample tube was separated from the UHV system by means of a sapphire-sealed Varian valve. The sample was either superficially deuteroxylated with D_2O (Merck Uvasol 99.75%) at 80 °C ($p_{D_2O} = 20$ torr, 16 h) or completely converted into $Mg(OD)_2$ at 80 °C ($p_{D_2O} = 350$ torr, 16 h). After prolonged drying (several hours) at 150—200 °C/10^{-8} torr the samples were heated stepwise at increments of 25—50 °C up to *ca.* 1000 °C.

The gasses evolved during each of the isothermally held periods (each of 7 min duration) were analyzed with an Omegatron mass spectrometer. The Omegatron tube including inlet capillary and feedthroughs was made of noble metal, predominantly Pt10Ir[8]. A ThO_2 coated iridium wire was used as relatively "inert" hot cathode of only 0.5 mm^2 surface area. The gas was fed through a capillary into the measuring tube and then pumped away *via* a wide tube so as to keep the residence time in the hot cathode region short.

Evaluation of the mass spectra showed that hydrogen is formed in the temperature range 300—350 °C and oxygen between 600—850 °C. It could be concluded from the very low intensity of the mass peaks for D^+ and O_2^+ that hydrogen is released from the sample preferentially in molecular form, the oxygen however in atomic form.

Two arguments support the assumption[9] that the hydrogen molecules are generated by simultaneous dissociation of two

[*] Prof. Dr. F. Freund and Dipl.-Min. N. Scheikh-ol-Eslami
Mineralogisch-Petrographisches Institut der Universität
5 Köln 1, Zülpicher Strasse 49 (Germany)
Prof. Dr. H. Gentsch
Institut für Physikalische Chemie und Elektrochemie der Technischen Universität
3 Hannover, Callinstrasse 46 (Germany)

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

OH^- groups adjacent to a cation vacancy [V''_{Mg}] in the MgO lattice:

$$OH^-[V''_{Mg}]OH^- \rightarrow O^-[V''_{Mg}]O^- + H_2 \quad (5)$$

1. Reaction (5) appears to be reversible under increased H_2 pressure[10]; 2. An *ab initio* LCAO calculation for a linear lattice complex Mg—O—H[V''_{Mg}]H—O—Mg yielded an energetic minimum at an H—H distance of *ca.* 0.8 Å in the cation vacancy[11].

The evolution of atomic oxygen observed in the range 600—850 °C can be attributed to the decomposition of O^- ions, probably according to

$$2O^- \rightarrow O^{2-} + O\uparrow \quad (6)$$

and/or to transformation of the V_I centers into V_I^+ centers, as is supported by ESR measurements for these temperatures[3].

Received: January 10, 1975;
revised: March 3, 1975 [Z 213 IE]
German version: Angew. Chem. 87, 593 (1975)

CAS Registry numbers:
MgO, 1309-48-4

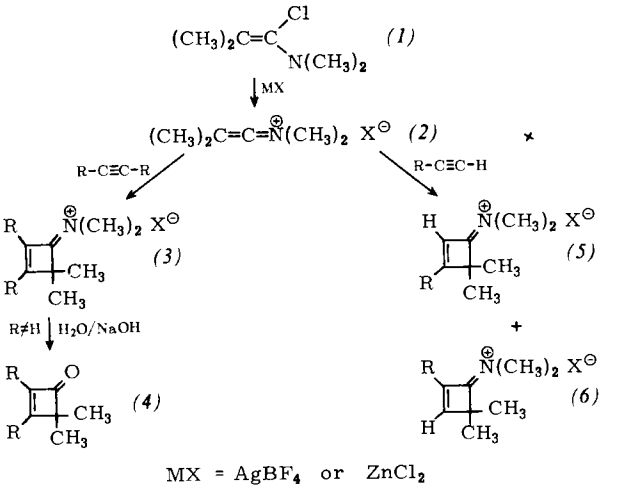
[1] *M. Boudart, A. Delbouille, E. G. Derouane, V. Indovina,* and *A. B. Walters,* J. Am. Chem. Soc. *94*, 6622 (1972).
[2] *J. H. Lunsford* and *T. W. Leland,* J. Phys. Chem. *66*, 2591 (1962).
[3] *E. G. Derouane, V. Indovina, A. B. Walters,* and *M. Boudart* in *F. S. Stone, M. W. Roberts,* and *J. S. Anderson:* Reactivity of Solids. Proc. 7th Symp. React. Solids, Bristol 1972. Chapman and Hall, London 1972, p. 703.
[4] *F. Freund,* Angew. Chem. *77*, 431 (1965); Angew. Chem. internat. Edit. *4*, 445 (1965); J. Am. Ceram. Soc. *50*, 494 (1967).
[5] *F. Freund* and *H. Gentsch,* Ber. Dtsch. Keram. Ges. *44*, 51 (1967).
[6] *K. J. D. Mackenzie,* J. Inorg. Nucl. Chem. *32*, 3731 (1970).
[7] *E. G. Derouane* and *V. Indovina,* Bull. Soc. Chim. Belg. *82*, 645 (1973).
[8] *H. Gentsch, W. Grossmann, N. Guillen, M. Köpp,* and *H. Rinne,* Vak. Tech. *23*, 230 (1974).
[9] *F. Freund,* discussion remark in [3], p. 712.
[10] *W. Gieseke, H. Nägerl,* and *F. Freund,* J. Phys. Chem. *78*, 758 (1974).
[11] *E. G. Derouane, J. G. Fripiat,* and *J. M. André,* Chem. Phys. Lett. *28*, 445 (1974).

Cyclobutenylideneammonium Salts from the Cycloadditions of Keteniminium Salts to Acetylenes[**]

By *C. Hoornaert, A. M. Hesbain-Frisque,* and *L. Ghosez*[*]

α-Chloroenamines *(1)* are versatile synthetic intermediates[1, 2] which can react either as enamines derived from carboxylic acid chlorides or as alkylideneammonium (keteniminium) salts. The utility of keteniminium salts *(2)* for building four-membered rings[2] is now illustrated by the facile [2+2]cycloadditions of tetramethylketeniminium tetrafluoroborate or trichlorozincate *(2)* (X = BF_4 or $ZnCl_3$ resp.), our model reagents, to acetylenes.

The salts *(2)* were prepared by reaction of *N,N*-dimethyl-1-chloro-2-methylpropenylamine *(1)* with $AgBF_4$ or $ZnCl_2$ as described previously[2]. Reaction of *(2)* with diphenylacetylene, 3-hexyne or 2-butyne in CH_2Cl_2 gave cycloadducts[3] *(3a)*, *(3b)* and *(3c)* respectively, in excellent yields (Table 1).



These first representatives[4] of cyclobutenylideneammonium salts could be hydrolyzed in high yields with 1 N NaOH to the cyclobutenones *(4a)*, *(4b)* and *(4c)*. The exceptional reactivity of *(2)* in [2+2] cycloadditions is further demonstrated by an unprecedented addition to acetylene itself at atmospheric pressure to give cycloadduct *(3d)* in 77—80 % yield. Hydrolysis of *(3d)* with 1 N NaOH did not form the corresponding cyclobutenone but led to opening of the four-membered ring[5].

Information regarding the regiochemistry of the cycloaddition could be obtained from the reactions of *(2)* with propyne and 3,3-dimethyl-1-butyne. Both alkynes reacted with *(2)* in CH_2Cl_2 to give mixtures of two regioisomers (Table 1) as shown by the presence of two different signals for the vinylic proton in each reaction mixture. The regioisomers *(5a)* and *(5b)* were assigned[6] the signals at higher field (δ = 6.40 and 6.53, respectively) whereas the isomers *(6a)* and *(6b)* were assigned the signals at lower field (δ = 7.76 and 7.86, respectively). The isomer ratios based on NMR integration were *(5a)*:*(6a)* = 3:1 and *(5b)*:*(6b)* = 1:1. These results are surprising in view of the regiospecificity of similar cycloadditions of ketenes[7].

Table 1. Preparation and hydrolysis of cyclobutenylideneammonium salts *(3)*, *(5)* and *(6)*.

Compound	R	Lewis Acid	T [°C]	Yield [%] [a]	Hydrolysis Product	Hydrolysis Yield [%]
(3a)	C_6H_5	$AgBF_4$	20	82 [b]	*(4a)*	90 [a]
(3b)	C_2H_5	$AgBF_4$	20	80 [c]	*(4b)*	80 [a]
(3b)	C_2H_5	$ZnCl_2$	40	100 [d]	*(4b)*	95 [a]
(3c)	CH_3	$ZnCl_2$	40	56 [e]	*(4c)*	100 [g]
(3d)	H	$AgBF_4$	20	77 [f]	[h]	
(3d)	H	$ZnCl_2$	40	80 [d]		
(5a)	CH_3	$AgBF_4$	20	80 [c]	[h]	
(6a)	CH_3	$AgBF_4$	20		[h]	
(5b)	$(H_3C)_3C$	$AgBF_4$	20	70 [b]	[h]	
(6b)	$(H_3C)_3C$	$AgBF_4$	20		[h]	

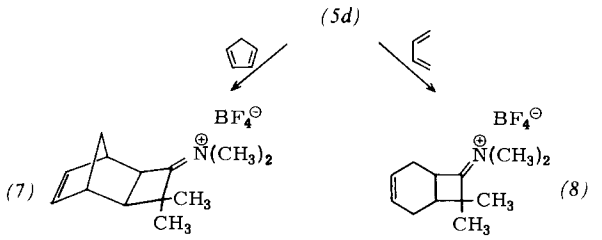
[a] Yields are based on *(1)*.
[b] Recrystallized from chloroform/ether.
[c] Pure material after washing the crude product with ether.
[d] Determined by NMR on the crude material.
[e] As perchlorate obtained by treatment of the crude mixture with a saturated solution of $KClO_4$.
[f] Recrystallized from CH_2Cl_2/ether.
[g] Based on *(3c)* recrystallized as perchlorate.
[h] Hydrolysis with NaOH resulted in opening of the four-membered ring.

The present results open a new route to unsaturated four-membered rings which could lead to a number of interesting synthetic developments. For example they could be useful

[*] C. Hoornaert, Lic. Sc., Dr. A. M. Hesbain-Frisque and Prof. Dr. L. Ghosez
Laboratoire de Chimie Organique de Synthèse
Université de Louvain, Place Louis Pasteur, 1
B-1348 Louvain-la-Neuve (Belgium)

[**] This work was supported by the Fonds de la Recherche Fondamentale Collective and the Institut pour l'Encouragement de la Recherche dans l'Industrie et l'Agriculture (Fellowship to C. H.).

synthons for the design of more elaborate molecules containing a four-membered ring. Thus *(3d)* is a reactive dienophile which cycloadds to cyclopentadiene at 20 °C or to butadiene at 80 °C to give high yields (84 % and 86 %, respectively) of adducts[3] *(7)* and *(8)*. These adducts were smoothly hydrolyzed with 0.1 N NaOH to the known[8] cyclobutanones.



N,N-dimethyl-4,4-dimethylcyclobutenylideneammonium tetrafluoroborate (3d)

Under a flow of acetylene, 0.87 g of *(2)* was added slowly to a slurry of 1.27 g of $AgBF_4$ in 20 ml of dry CH_2Cl_2 at −60 °C. The mixture was warmed to room temperature and the acetylene flow maintained for 3 h. After filtration of AgCl (0.94 g) and evaporation of the solvent, *(3d)* was recrystallized from CH_2Cl_2/ether; yield 1.07 g (77 %).

Received: May 26, 1975 [Z 252 IE]
German version: Angew. Chem. *87*, 552 (1975)

[1] *L. Ghosez*, Angew. Chem. *84*, 901 (1972); Angew. Chem. internat. Edit. *11*, 852 (1972); *L. Ghosez, B. Haveaux*, and *H. G. Viehe*, Angew. Chem. *81*, 468 (1969); Angew. Chem. internat. Edit. *8*, 454 (1969); *J. Marchand-Brynaert* and *L. Ghosez*, J. Amer. Chem. Soc. *94*, 2869 (1972); *J. Toye* and *L. Ghosez*, ibid. *97*, 2276 (1975).

[2] *J. Marchand-Brynaert* and *L. Ghosez*, J. Amer. Chem. Soc. *94*, 2870 (1970); *A. Sidani, J. Marchand-Brynaert*, and *L. Ghosez*, Angew. Chem. *86*, 272 (1974); Angew. Chem. internat. Edit. *13*, 267 (1974); *M. De Poortere, J. Marchand-Brynaert*, and *L. Ghosez*, Angew. Chem. *86*, 272 (1974); Angew. Chem. internat. Edit. *13*, 267 (1974); Tetrahedron Lett. *1974*, 377.

[3] All new compounds exhibit the expected spectroscopic data.

[4] A cyclobutenylideneammonium salt has been postulated as an intermediate in the rearrangement of a cyclopropenylmethyl cation, *R. Breslow* and *T. Eicher*, private communication cited in *M. P. Cava* and *M. J. Mitchell*: Cyclobutadiene and Related Compounds. Academic Press, New York 1967, p. 41.

[5] See also: *S. L. Manatt, M. Vogel, D. Knutson*, and *J. D. Roberts*, J. Amer. Chem. Soc. *86*, 2645 (1964); *E. Vogel* and *K. Hasse*, Liebigs Ann. Chem. *615*, 22 (1958).

[6] *J. B. Sieja*, J. Amer. Chem. Soc. *93*, 2481 (1971).

[7] *M. D. Gheorghiu, C. Draghici, L. Stanescu*, and *M. Avram*, Tetrahedron Lett. *1973*, 9; *N. S. Isaacs* and *P. Stanbury*, J. Chem. Soc. Perkin II *1973*, 166; *D. C. England* and *C. G. Krespan*, J. Amer. Chem. Soc. *87*, 4019 (1965); J. Org. Chem. *35*, 3308 (1970).

[8] *J. Marchand-Brynaert*, Dissertation, UCL (1973); *T. R. Kelly* and *R. W. McNutt*, Tetrahedron Lett. *1975*, 285.

$[(n\text{-}C_4H_9)_4N]_2Mo_5Cl_{13}$—A Compound with the Cluster Group $[Mo_5Cl_8^i]$[**]

By *Klaus Jödden, Hans Georg von Schnering*, and *Harald Schäfer*[*]

In connection with kinetic studies on the formation of $[M_6]$-groups from monomeric units, carried out for example on $[Mo_6Cl_8^i]Cl_4^a$[1], a previously unknown complex of the type $[Mo_5Cl_8^i]Cl_5^{(2-)}$ has been found. The synthesis of $[Mo_5]$-, $[Mo_6]$-, and $[W_6]$-compounds was accomplished at relatively low temperatures in homogeneous chloroaluminate melts at definite $AlCl_3$ activity and suitable redox level using starting materials such as K_3MoCl_6 or "monomeric" $MoCl_2$[2] and $K_3W_2Cl_9$ or WCl_6. Depending upon the reaction conditions preferential formation of either $[Mo_5]$- or $[Mo_6]$-groups takes place.

The synthesis of the complex cluster groups $Mo_5Cl_{13}^{2-}$, was carried out in melts with 63 mol-% $AlCl_3$ + 32 mol-% KCl + 5 mol-% $BiCl_3$ as solvent. The redox potential can be adjusted by addition of bismuth (250 mg-atoms Bi/kg solvent), which forms dark solutions containing low valency bismuth halides in $BiCl_3$-containing melts[3]. K_3MoCl_6 can be used as starting material (120 mmol/kg solvent, 306 °C, reaction time 1–2 h) for building the cluster. From a preparative point of view, however, it is found expedient to use the so-called "monomeric" $MoCl_2$[2] as starting material; this can be prepared easily and rapidly just prior to its use in the actual synthesis.

Reaction of $Mo(CO)_6$ (2.40 g) in liquid chlorine (−60 °C) first leads to formation of the carbonyl chloride $Mo(CO)_4Cl_2$[4], which on decomposition in a vacuum affords the required starting material $MoCl_2$. Afterwards the solvent mixture $AlCl_3$ + KCl + $BiCl_3$ (17 g) and Bi (880 mg) is introduced into the reaction vessel; after melting the contents of the vessel the actual reaction sets in and is allowed to proceed for 5 hours at 306 °C (benzophenone bath). The very dark homogeneous melt solution then contains the complex anions $Mo_6Cl_{14}^{2-}$ and $Mo_5Cl_{13}^{2-}$. After extraction of the melt with semi-concentrated hydrochloric acid, $MoCl_{14}^{2-}$ is separated off, partly in crystalline needles as $(H_3O)_2Mo_6Cl_{14}\cdot 6H_2O$, the rest with 8-hydroxyquinoline as $(\text{oxine H})_2Mo_6Cl_{14}$. The $Mo_5Cl_{13}^{2-}$ remaining in solution is precipitated with tetrabutylammonium chloride. The dry crude product can be recrystallized by dissolution in dichloromethane and subsequent treatment with petroleum ether. A very dark, finely crystalline substance of composition $Mo_5Cl_{13}C_{32}H_{72}N_2$[5] is obtained; yield 500—600 mg (19—23 % based on $Mo(CO)_6$).

$(n\text{-}Bu_4N)_2Mo_5Cl_{13}$ is stable in air, and depending on the degree of order, is more or less soluble in alcohol and sparingly soluble in dichloromethane and acetone at room temperature. Dilute solutions are yellowish-brown. On slow crystallization the substance is obtained as black shiny crystals.

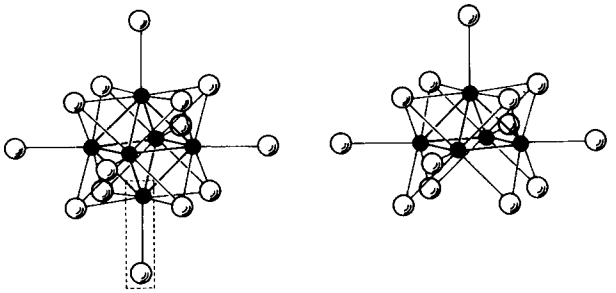
The complex salt crystallizes tetragonally in the space group P4/n (No. 85) with $a = 13.481(7)$, $c = 14.725(7)$ Å; $Z = 2$ ($d_x = 1.769$, $d_{exp} = 1.77\ g\cdot cm^{-3}$). The atoms occupy the following positions $[x;y;z]$: Mo(1) in 2(c) with [1/4; 1/4; 0.3699(2)], Mo(2) in 8(g) with [0.3814(1); 0.2214(1); 0.2435(1)], Cl(1) in 8(g) with [0.4036(3); 0.3485(3); 0.3638(3)], Cl(2) in 8(g) with [0.4009(3); 0.3475(3); 0.1271(3)], Cl(3) in 2(c) with [1/4; 1/4; 0.5338(6)], Cl(4) in 8(g) with [0.5581(3); 0.1833(3); 0.2443(3)]. The Bu_4N cations surround the positions 2(a) and 2(b). In the structural determination with diffractometer data (MoK_α, 2613 reflections *hkl*, $R = 0.061$) great difficulties were met with on account of the pronounced I4/m pseudosymmetry.

The structure of $(n\text{-}Bu_4N)_2Mo_5Cl_{13}$ is built up from isolated $Mo_5Cl_{13}^{2-}$ units, in which the Mo atoms form a square pyramid surrounded by eight Cl^i atoms in the form of a cube (Fig. 1). Each Mo atom is bound to four Cl^i and a terminal Cl^a, *i.e.* the structure of the cluster corresponds completely to a $([Mo_6Cl_8^i]Cl_6^a)^{2-}$ cluster formally lacking an (Mo—Cl^a) unit. The Mo—Mo bond lengths of 2.602(3) and 2.563(3) Å are somewhat shorter than those in $[Mo_6]$-clusters (2.61 Å). This corresponds qualitatively to an increase in the bonding electrons per M—M bond. The Mo—Cl^i distances are between 2.434 and 2.473 Å, the Mo—Cl^a distances are 2.418 and 2.440 Å.

[*] Dipl.-Chem. K. Jödden, Prof. Dr. H. G. von Schnering, and Prof. Dr. H. Schäfer [+]
Anorganisch-chemisches Institut der Universität
44 Münster, Gievenbecker Weg 9 (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *K. Peters* for the four-circle diffractometer measurements.



$|[Mo_6Cl_8^i]Cl_6^a|^{2-}$ $|[Mo_5Cl_8^i]Cl_5^a|^{2-}$

2254.1

Fig. 1. Anionic chloromolybdenum complexes with $[M_6]$- and $[M_5]$-clusters.

The formal oxidation number of the Mo atoms is 2.20, *i.e.* the Mo_5 groups have 19 electrons for Mo—Mo bonds and the compound is paramagnetic.

The structure, and our other findings, indicate that the complex $[Mo_5Cl_8^i]^{3+}$ is an intermediary in the build-up of $[Mo_6Cl_8^i]^{4+}$ groups.

Received: May 5, 1975 [Z 254 IE]
German version: Angew. Chem. 87, 594 (1975)

CAS Registry numbers:
$[(n\text{-}C_4H_9)_4N]_2Mo_5Cl_{13}$, 55913-48-9

[1] *H. Schäfer, H. G. v. Schnering, J. Tillack, F. Kuhnen, H. Wöhrle*, and *H. Baumann*, Z. Anorg. Allg. Chem. *353*, 281 (1967).
[2] *G. Holste* and *H. Schäfer*, J. Less Common Met. *20*, 164 (1970).
[3] *R. M. Friedman* and *J. D. Corbett*, Inorg. Chem. *12*, 1134 (1973); literature cited therein.
[4] *R. Colton* and *J. B. Tomkins*, Aust. J. Chem. *19*, 1143 (1966).
[5] Analysis: Mo 33.3% (calc. 33.69), Cl 31.8% (32.34), C 27.96% (26.95), N 1.95% (1.965), H 5.02% (5.09). C/H/N analysis by Bernhardt, 5251 Elbach über Engelskirchen (Germany).

Simple Synthesis of $[C_5H_5Fe(CO)dppe]^+$ and its Photochemical Conversion into the Dinitrogen Complex $[\{C_5H_5Fe(dppe)\}_2N_2]^{2+}$[1]

By *Dieter Sellmann* and *Ernst Kleinschmidt*[*]

Synthesis of the cationic complex $[C_5H_5Fe(CO)dppe]^+$ *(1)* [dppe = $(C_6H_5)_2PCH_2CH_2P(C_6H_5)_2$ *(2)*] has hitherto been possible only by circuitous routes[2].

We have found that *(1)* can also be obtained more simply:

$$C_5H_5Fe(CO)_2Cl + (2) \xrightarrow[-CO]{20\,^\circ C} [C_5H_5Fe(CO)dppe]Cl \quad (1a)$$
(3)

$$[C_5H_5Fe(CO)dppe]Cl \xrightarrow[+NH_4PF_6]{CH_3OH} [C_5H_5Fe(CO)dppe]PF_6 \quad (1b)$$

Solid *(3)*[3] is mixed with *(2)*, and a small amount of tetrahydrofuran is added thereto; within 2—3 s yellow *(1a)* is formed with vigorous evolution of CO. After dissolution of *(1)* in methanol, precipitation with NH_4PF_6 and recrystallization from CH_2Cl_2 an almost quantitative yield of analytically pure *(1b)* is obtained.

From this product we were able to obtain the dppe-stabilized Fe—N_2 complex *(4)*[4, 5].

$$2\ (1b) \xrightarrow[\text{acetone}/N_2]{h\nu/-30\,^\circ C} [\{C_5H_5Fe(dppe)\}_2N_2](PF_6)_2 + 2\ CO$$
(4)

[*] Priv.-Doz. Dr. D. Sellmann and Dipl.-Chem. E. Kleinschmidt
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

In this reaction besides *(4)* also the acetone complex $[C_5H_5Fe(dppe)acetone]PF_6$ *(5)* is formed. Since *(4)* is almost insoluble, but *(5)* readily soluble in THF, the two complexes can be separated by extraction with THF. Under N_2 the THF solutions of *(5)* also afford *(4)*, which leads to a total yield of 75% of *(4)*.—The simple synthesis of the starting material and the high yields of *(1b)* and *(4)* make *(4)* a readily accessible N_2 complex.

After washing twice with THF/ether, *(4)* is obtained as an analytically pure, orange solid. Its IR spectrum contains no bands for the N_2 ligand but in the Raman spectrum there is a very strong ν_{N_2} band at 2040 cm^{-1}, so that the cation of *(4)* probably contains a centrosymmetric FeNNFe group. In the ^{1}H-NMR spectrum ([D_6]acetone, −78 °C) there is, besides the multiplets for the dppe protons at $\tau = 2.2$, 7.47 and 7.68 a sharp peak at $\tau = 5.50$ for the C_5H_5 protons; in comparison with the C_5H_5 peak of *(1b)* at $\tau = 4.94$ the C_5H_5 peak of *(4)* is shifted by more than 0.5 ppm to high field. The replacement of CO by N_2 thus clearly increases the electron density at the central metal.

At room temperature *(4)* reacts with acetone to yield *(5)*. Removal of nitrogen from the equilibrium and evaporation of the solvent yields *(5)* as black crystals. *(5)* reacts with

$$(4) + 2\ \text{acetone} \rightleftharpoons 2\ [C_5H_5Fe(dppe)acetone]PF_6 + N_2 \quad (5)$$

N_2H_4 or NH_3 in THF to give the pure red complexes $[C_5H_5Fe(dppe)L]PF_6 \cdot THF$ (L = N_2H_4 or NH_3]. With CO or $NaBH_4$ *(4)* affords the compounds *(1b)* and $[C_5H_5Fe(dppe)H]$ respectively, the last of which is isolated as yellow crystals [τ_{Fe-H} 25.6; ν_{Fe-H} 1860 cm^{-1} (KBr)].

Received: May 20, 1975 [Z 259 IE]
German version: Angew. Chem. 87, 595 (1975)

CAS Registry numbers:
$C_5H_5Fe(CO)_2Cl$, 12107-04-9; $[C_5H_5Fe(CO)dppe]PF_6$, 55904-75-1;
$[\{C_5H_5Fe(dppe)\}_2N_2](PF_6)_2$, 55853-18-4;
$[C_5H_5Fe(dppe)acetone]PF_6$, 55853-20-8;
$[C_5H_5Fe(dppe)N_2H_4]PF_6$, 55853-22-0;
$[C_5H_5Fe(dppe)NH_3]PF_6$, 55853-24-2; $[C_5H_5Fe(dppe)H]$, 51509-20-7

[1] Reactions of Complex-bound Ligands, Part 16. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 15: *D. Sellmann, A. Brandl*, and *R. Endell*, J. Organometal. Chem., in the press.
[2] *M. L. H. Green* and *R. N. Whiteley*, J. Chem. Soc. *A 1971*, 1943; *M. L. Brown, J. L. Cramer, J. A. Ferguson, T. J. Meyer*, and *N. Winterton* J. Am. Chem. Soc. *94*, 8707 (1972); *R. J. Haines* and *A. L. Du Preez*, Inorg. Chem. *11*, 330 (1972).
[3] *(3)* was prepared according to *B. D. Dombek* and *R. J. Angelici*, Inorg. Chim. Acta 7, 345 (1973) by aerial oxidation of $[C_5H_5Fe(CO)_2]_2$ and treatment with NaCl.
[4] For the process see *D. Sellmann* and *G. Maisel*, Z. Naturforsch. *27b*, 465, 718 (1972).
[5] $[\{C_5H_5Fe(dmpe)\}_2N_2](BF_4)_2 \cdot H_2O$, which is analogous to *(4)* and contains the much more nucleophilic ligand ethylenebis(dimethylphosphane), was obtained by a different method before: *W. E. Silverthorn*, Chem. Commun. *1971*, 1310.

Stabilization of Unknown Phosphanes: Secondary Amino- and Alkoxyphosphanes as Complex Ligands[**]

By *Gottfried Huttner* and *Hans-Dieter Müller*[*]

Secondary phosphanes RP(H)X, which contain both a P—H bond and a P—X bond (X = NHR, NR_2, OR, Cl), are not known to exist in the free state. They decompose *via* α-elimina-

[*] Doz. Dr. G. Huttner and Dipl.-Chem. H. D. Müller
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

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

tion to phosphinidenes {R—P} and their secondary products. In investigations on the complex stabilization of phosphinidenes we have now succeeded for the first time in stabilizing such phosphanes as complex ligands.

Reaction of cyclopentadienyldicarbonylmanganese(phenylphosphane) $C_5H_5(CO)_2MnP(C_6H_5)H_2$ *(1)* with *N,N*-dichlorocyclohexylamine, $C_6H_{11}NCl_2$ *(2)*, in tetrahydrofuran (THF) yields a brownish-red product from which a mixture of $C_5H_5(CO)_2MnP(C_6H_5)Cl_2$ *(3)* and $C_5H_5(CO)_2MnP(C_6H_5)(H)Cl$ *(4)* can be separated as a yellow solid by sublimation.

Pure *(4)* could not be prepared since this complex decomposes with disproportionation into *(1)* and *(3)* even at −30 °C during attempted chromatographic purification. However, $C_5H_5(CO)_2MnP(C_6H_5)(H)NHC_6H_{11}$ *(5)* can be obtained as a very stable derivative of *(4)* if cyclohexylamine is added to the mixture at the begining of the reaction. *(5)* is stable towards air even at room temperature; α-elimination of $C_6H_{11}NH_2$ is not observed even under more drastic conditions.

(1) reacts with *N*-chlorodibutylamine, $(n\text{-}C_4H_9)_2NCl$, without addition of amine to give $C_5H_5(CO)MnP(C_6H_5)(H)N(C_4H_9)_2$ *(6)*, which is isolated as a yellow oil. *(6)* is also stable towards air at 20 °C.

Reaction of *(1)* with I_2 in THF leads to formation of the complex $C_5H_5(CO)_2MnP(C_6H_5)(H)O—(CH_2)_3CH_2I$ *(7)* whose ω-iodobutoxy substituent is formed by ether-cleavage of THF with the HI formed in the reaction. This complex is also stable at room temperature; the α-elimination of ω-iodobutanol to be expected for the free phosphane ligand is not observed.

Since the reaction of phenylphosphanes with oxidizing agents such as haloamines or iodine leads to cyclooligophosphanes $(C_6H_5P)_n$[1] *via* phenylphosphinidene, $\{C_6H_5P\}$ we assume that the reactions described here proceed *via* intermediary complexed phenylphosphinidenes[2, 3]:

$$(1) \xrightarrow[-2\,H]{\text{oxidation}} \{C_5H_5(CO)_2MnPC_6H_5\} \xrightarrow{HCl(HI)} C_5H_5(CO)_2MnP(C_6H_5)(H)Hal \xrightarrow[-HCl(HI)]{+HX} C_5H_5(CO)_2MnP(C_6H_5)(H)X$$

X = NHR, NR_2, OR

Experimental:

All experiments were carried out in an inert atmosphere (N_2). Preparation of *(3)*—*(5)*: *(2)* (0.9 ml, 6.4 mmol) is added at −60 °C with vigorous stirring to a solution of *(1)* (2.0 g, 7.0 mmol) and $C_6H_{11}NH_2$ (1.2 ml, 9.7 mmol) in THF (50 ml). The red solution that is formed is allowed to warm to 10 °C within 1 h; precipitated $C_6H_{11}NH_3Cl$ is removed by filtration over silica gel and the solvent removed by evaporation. On double chromatographic separation at −30 °C (silica gel Merck, particle size 0.063—0.200 mm, 3% H_2O; column: length 20 cm, diameter 2 cm) a yellow-brown zone of *(5)* can be eluted with toluene/*n*-pentane (2:1) and after removal of solvent obtained in analytically pure form (m. p. 42 °C (dec.)); ^{31}P-NMR (C_6D_6, external standard conc. H_3PO_4, δ [ppm]): 37.7 (P); mol. wt. 383 (MS); yield 290 mg (11%).—In an analogous way, without addition of cyclohexylamine, initial red coloration is followed by formation of a yellow reaction solution from which a mixture of *(3)* and *(4)* can be separated by sublimation (80 °C/10^{-2} torr) after removal of solvent.

Preparation of *(6)*: $(n\text{-}C_4H_9)_2NCl$ (1.2 ml, 7.4 mmol) is added with stirring at −60 °C to a solution of *(1)* (2.1 g, 7.4 mmol) in THF (50 ml). Work-up of the reaction solution as in the preparation of *(5)* affords an orange-colored zone (fronts of *(1)* and unidentified by-products eluted with toluene/pentane 1:3, zone of *(6)* with toluene/pentane 1:1), from which *(6)* is obtained as yellow oil after removal of solvent in analytically pure form. ^{31}P-NMR (C_6D_6 ext. conc. H_3PO_4, δ [ppm]): 65.2 (P); mol. wt. 413 (MS); yield: 420 mg (14%).

Preparation of *(7)*: A solution of *(1)* (1.2 g, 4.2 mmol) in THF (50 ml) is treated at −60 °C with a solution of I_2 (1.3 g, 10 mmol) in THF (400 ml). The reaction mixture is allowed to warm to room temperature within 2 hours and then subjected to the same procedure as in the preparation of *(5)*. After elution of the fronts with toluene/pentane (1:3) further passage of toluene affords a broad orange-yellow zone of *(1)* along with other products which were not further investigated. Double chromatography and drying at 20 °C/10^{-2} torr gave analytically pure *(7)* as a yellow-brown oil. ^{31}P-NMR (C_6D_6, ext. conc. H_3PO_4, δ [ppm]): 181; mol. wt. 484 (MS); yield: 260 mg (13%).

Received: May 5, 1975 [Z 255a IE]
German version: Angew. Chem. 87, 596 (1975)

CAS Registry numbers:
(1), 36311-99-6; *(2)*, 26307-01-7; *(3)*, 12276-83-4; *(4)*, 55758-58-2; *(5)*, 55758-59-3; *(6)*, 55822-48-5; *(7)*, 55758-60-6; cyclohexylamine, 108-91-8; *N*-chlorodibutylamine, 999-33-7

[1] *G. M. Kosolapoff* and *L. Maier*: Organic Phosphorous Compounds, Vol. I. Wiley-Interscience, New York 1972.

[2] $[C_5H_5(CO)_2Mn]_2PC_6H_5$ is detectable in the fragmentation of $[C_5H_5(CO)_2Mn]_3P_3(C_6H_5)_3$; this indicates that phenylphosphinidene can occur as complex ligand. Cf. *G. Huttner, H. D. Müller, A. Frank*, and *H. Lorenz*, Angew. Chem. *87*, 597 (1975); Angew. Chem. internat. Edit. *14*, 572 (1975).

[3] Reaction of *(1)* with *(2)* and isopropylamine yields a mixture of *(5)* and $C_5H_5(CO)_2MnP(C_6H_5)(H)NHC_3H_7$ under conditions which exclude transamination of *(5)*. We assume that both compounds are formed from the common precursor *(4)*.

Preparation of the Trinuclear Triphenylcyclotriphosphane Complex $(C_6H_5)_3P_3[Mn(CO)_2C_5H_5]_3$ by Demetalation of $C_5H_5(CO)_2MnP(C_6H_5)Li_2$[**]

By *Gottfried Huttner, Hans-Dieter Müller, Albin Frank*, and *Hans Lorenz*[*]

Demetalation of pentacarbonylchromium(phenyldilithioarsane), $(CO)_5CrAs(C_6H_5)Li_2$ with *N,N*-dihaloamines leads to the arsinidene complex $C_6H_5As[Cr(CO)_5]_2$[1]. Unexpectedly, demetalation of $C_5H_5(CO)_2MnP(C_6H_5)Li_2$[2] gave the trinuclear compound *(2)* instead of the analogous phosphinidene complex $C_6H_5P[Mn(CO)_2C_5H_5]_2$ *(1)*.

$$C_5H_5(CO)_2MnP(C_6H_5)Li_2 \xrightarrow[THF]{C_6H_{11}NCl_2} [C_5H_5(CO)_2MnPC_6H_5]_3 \quad (2)$$

After chromatographic purification and crystallization from toluene/pentane *(2)* is obtained as a red, finely crystalline solid. *(2)* is also stable towards air at 20 °C; when heated under nitrogen in a sealed tube it does not decompose below 140 °C. The IR spectrum of *(2)* shows, in addition to the characteristic bands for C_6H_5- and η^5-C_5H_5 groups, two strong absorptions of equal intensity at 1934 and 1880 cm^{-1},

[*] Doz. Dr. G. Huttner, Dipl.-Chem. H. D. Müller, A. Frank, and Dr. H. Lorenz
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

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

which are indicative of the presence of $Mn(CO)_2$ groups. In the ^{1}H-NMR spectrum two multiplets for the phenyl protons ($\delta = 6.8$, 7.6 ppm internal TMS) are accompanied by two signals (intensity ratio 1:2) for the protons of the cyclopentadienyl rings ($\delta = 3.80$ and 3.96 ppm). Although the osmometric molecular weight determination and elemental analysis identify *(2)* as a trinuclear complex with $M_r = 852$, no corresponding peak for such a compound is observed in the mass spectrum. The heaviest ion is observed at *m/e* 460 and can be plausibly assigned only to the molecular ion of the dinuclear phosphinidene complex *(1)*. This is also supported by the observed fragmentation pattern.

X-ray structure analysis[3] showed that *(2)* contains the triphenylcyclotriphosphane ligand $(PC_6H_5)_3$ *(3)*, whose synthesis and ligand properties have already been investigated by *Baudler*[4] (Fig. 1).

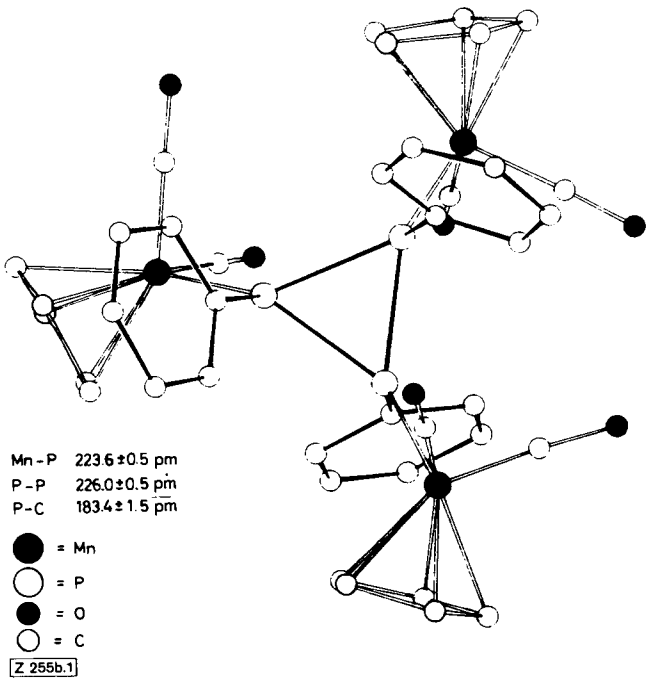


Fig. 1. Structure of triphenylcyclotriphosphanetris(cyclopentadienyldicarbonylmanganese) $(C_6H_5P)_3[Mn(CO)_2C_5H_5]_3$ *(2)*.

Two $C_5H_5(CO)_2Mn$ groups lie above and one below the three-membered phosphorus ring. The Mn—P bond lengths (223.6 ± 0.5 pm) are considerably shorter than the sum of the covalent radii of Mn and P (248 pm[5]); hence *(3)* is characterized as a good back-bonding ligand.

(2) presents a sterically greatly hindered system in which none of the substituents (C_6H_5 or $C_5H_5(CO)_2Mn$) of the three membered phosphorus ring can be freely rotatable; their orientation in the crystal lattice corresponds to the arrangement with least possible steric hindrance, yet interfering interactions still occur. The formation of the highly strained three-membered ring, which is very surprising at first sight, could be due to the possible formation of an intermediary mononuclear phosphinidene complex $C_5H_5(CO)_2MnPC_6H_5$[6] whose stabilization in the three-membered ring arrangement permits orientation of the bulky substituents of neighboring phosphorus atoms at a maximum distance from one another.

Experimental:

All work was carried out in an inert atmosphere (N_2). A 1 M solution of *n*-C_4H_9Li in *n*-pentane (16 ml) is added rapidly from a pipette to a solution of $C_5H_5(CO)_2MnP(C_6H_5)H_2$ (2.3 g, 8.0 mmol) in THF (50 ml) at -70 °C; the solution of $C_5H_5(CO)_2MnP(C_6H_5)Li_2$[2] thus obtained is immediately treated with $C_6H_{11}NCl_2$ (1.9 ml, 13.5 mmol). After stirring at -70 °C (0.5 h) and at room temperature (1.5 h) the brownish-red reaction mixture is filtered over silica gel (solvent diethyl ether) and the solvent removed by evaporation at 10^{-2} torr/20 °C. The sticky residue is then chromatographed on silica gel (column length 80 cm, diam. 2 cm; Merck, particle size 0.063—0.200 mm, 3% H_2O) at -30 °C. Unchanged $C_5H_5(CO)_2MnP(C_6H_5)H_2$ is separated by elution with toluene/pentane (1:1). With pure toluene a dark red zone is formed with brown fronts and tailings. After removal of solvent at 20 °C this zone is re-chromatographed: with toluene/pentane 1:1 (conditions as above) an intense red front develops; the main red zone of *(2)* is eluted with toluene. After removal of solvent and crystallization from toluene/pentane (1:20), *(2)* is obtained as a bright-red, analytically pure fine crystalline powder; mol. wt. 871 (osmom. in C_6H_6, calc. 852), yield 300 mg (14%).

Received: May 5, 1975 [Z 255b IE]
German version: Angew. Chem. *87*, 597 (1975)

CAS Registry numbers:
$C_5H_5(CO)_2MnP(C_6H_5)Li_2$, 55758-70-8; $C_6H_{11}NCl_2$, 26307-01-7, $[C_5H_5(CO)_2MnPC_6H_5]_3$, 5578-71-9

[1] *G. Huttner* and *H.-G. Schmid*, Angew. Chem. *87*, 454 (1975); Angew. Chem. internat. Edit. *14*, 433 (1975).
[2] *G. Huttner* and *H. D. Müller*, Z. Naturforsch. *30b*, 235 (1975).
[3] 2300 Diffractometer data (Syntex-$P2_1$); $R_1 = 7.4\%$ (Syntex-XTL).
[4] *M. Baudler* and *M. Bock*, Z. Anorg. Allg. Chem. *395*, 37 (1973); Angew. Chem. *86*, 124 (1974); Angew. Chem. internat. Edit. *13*, 147 (1974).
[5] *M. R. Churchill* in *J. D. Dunitz* and *J. A. Ibers*: Perspectives in Structural Chemistry, Vol. III. Wiley, New York 1970.
[6] The intermediacy of $C_5H_5(CO)_2MnPC_6H_5$ is also indicated in other investigations: *G. Huttner* and *H. D. Müller*, Angew. Chem. *87*, 596 (1975); Angew. Chem. internat. Edit. *14*, 571 (1975).

Crystalline Compound with Isolated $W_3S_9^{2-}$ Ion: A Thio Analog of Transition Metal Isopolyanions

By *E. Königer-Ahlborn* and *Achim Müller*[*]

Although numerous studies have been performed on isopolyanions of Group V A and VI A elements and evidence accrued that isolated polymeric anions occur in solutions of many oxometalates and also in the solid state[1–3], their thio analogs have hitherto remained unknown[4]. The main reason is to be found in the ready decomposition of thioanions such as WS_4^{2-}, MoS_4^{2-}, and VS_4^{3-} to form metal sulfides when their aqueous solutions are acidified[4], and in the lower proton affinity of thioanions compared to oxoanions (protonation of the anion is assumed as the initial step of polyanion formation) which necessitates higher H^+ concentrations for polythioanion formation.

We have now succeeded in isolating $[(C_6H_5)_4P]_2W_3S_9$ *(1)* and $[(C_6H_5)_4As]_2W_3S_9$ *(2)* as dark red triclinic crystals and in characterizing them by elemental analysis, vibrational spectrum, ultraviolet-visible spectrum, and molecular weight determination.

The thiotritungstates *(1)* and *(2)* are insoluble in methanol or ether but dissolve readily in methylene chloride, acetonitrile, and nitromethane. Their color is very similar to that of $(NH_4)_2MoS_4$[5]. The darkening in color relative to the WS_4^{2-} ion (yellow) is explained by a splitting or broadening of the first charge transfer band $t_1 \rightarrow 2e$ ($^1A_1 \rightarrow {}^1T_2$) of WS_4^{2-}[5].

Compound *(1)* forms triclinic crystals of space group P1 with $Z = 1$ ($a = 13.306$, $b = 9.076$, $c = 10.532$ Å; $\alpha = 96.12$,

[*] Prof. Dr. A. Müller and Dipl.-Chem. E. Königer-Ahlborn
Institut für Chemie der Universität
46 Dortmund 50, Postfach 500500 (Germany)

$\beta = 86.98, \gamma = 94.88°$; $d_{exp} = 1.98, d_{X\text{-}ray} = 2.00\,g\,cm^{-3}$). Preliminary results of an X-ray structure analysis[6] performed on single crystals show that the two terminal tungsten atoms W-1 and W-3 are tetrahedrally coordinated while the central W-2 is in a strongly distorted square pyrimidal environment. The WS_n polyhedra are edge linked (see Fig. 1[6]).

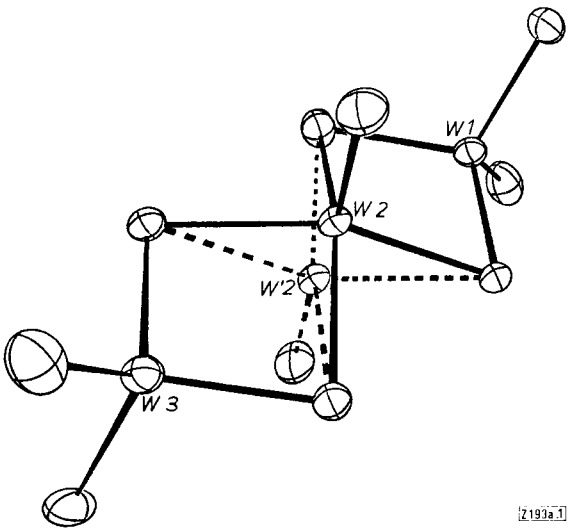


Fig. 1. Structure of the anion $W_3S_9^{2-}$. (The statistical distribution of W-2 is symbolized with broken lines; see Fig. 1 in Ref. [6].)

The WS stretching vibrations are unambiguously compatible with the proposed structure of the anion. The IR solid state spectra of *(1)* and *(2)* show bands at 525 [ν(W(2)=S)], 490, 485 [ν(W(1,3)=S)], 465 and 435 cm^{-1} [ν_{as}(W—S—W)] (concerning the frequency of ν(WS) vibrations see ref. [7]).

Procedure:

a) 40 % HF (40 ml) is added to a vigorously stirred solution of $(NH_4)_2WS_4$ (1.2 g) in H_2O (360 ml). After addition of a solution of $[(C_6H_5)_4P]Cl$ (0.4 g) in H_2O (50 ml) there results a reddish brown precipitate of *(1)* which is filtered off, washed with alcohol and ether, and recrystallized from nitromethane. M. W. in CH_2Cl_2: 1452 (calc. 1519).

b) Alternatively, *(1)* is formed on heating (250 °C, 0.5 h) of a thoroughly stirred mixture of $(NH_4)_2WS_4$ and $[(C_6H_5)_4P]Cl$ (molar ratio 3:2) under N_2. The reaction product is recrystallized as above.

c) Compound *(2)* can be obtained in analogous manner from $[(C_6H_5)_4As]Cl$. M.W. in CH_2Cl_2: 1624 (calc. 1602).

Received: January 27, 1975
revised: July 18, 1975 [Z 193a IE]
German version: Angew. Chem. 87, 598 (1975)

CAS Registry numbers:
(1), 54844-39-2; *(2)*, 54823-22-2; $(NH_4)_2WS_4$, 13862-78-7

[1] *D. L. Kepert*, Progr. Inorg. Chem. *4*, 199 (1962); *O. Glemser, H. Holznagel, W. Höltje*, and *E. Schwarzmann*, Z. Naturforsch. *20b*, 725 (1965).
[2] *P. Souchay:* Polyanions and Polycations. Gauthier-Villars, Paris 1963.
[3] *F. A. Cotton* and *G. Wilkinson:* Advanced Inorganic Chemistry. Wiley-Interscience, New York 1972; Anorganische Chemie. Verlag Chemie, Weinheim 1974.
[4] *E. Diemann* and *A. Müller*, Coord. Chem. Rev. *10*, 79 (1973).
[5] *A. Müller, E. Diemann*, and *C. K. Jørgensen*, Struct. Bonding *14*, 23 (1973).
[6] We are grateful to Dr. *Preut*, Dortmund, for his assistance. The crystal structure determination is very complicated because of the statistical distribution of W-2 over two different lattice sites. When accurate results become available we shall report the structure of *(1)* jointly with Dr. *Preut*.
[7] *K. H. Schmidt* and *A. Müller*, Coord. Chem. Rev. *14*, 115 (1974).

Chloromolybdate(VI): A Halomolybdate Having Tetrahedral Coordination

By *E. Königer-Ahlborn* and *Achim Müller*[*]

While halochromates of type CrO_3X^- (X = F, Cl, Br) having isolated tetrahedral anions have been known for some time and are readily accessible by reaction in solution[1, 2], the corresponding molybdates and tungstates are not formed in analogous manner since the central atoms prefer the coordination number 6, as for example in the compounds containing the anions $[MO_2F_3]_n^{n-}$ (fluorine bridging)[3], $MO_2X_4^{2-}$[4], and $MO_3F_3^{3-}$[5] (M = Mo, W; X = F, Cl).

Our studies on halovanadates(V) showed that the size of the cation exerts a decisive influence on the coordination number of the anion. Thus isolated $VO_2F_2^-$ units are present in $[(C_6H_5)_4P]VO_2F_2$ prepared in solution[6], whereas the corresponding alkali metal salts exhibit oxygen and fluorine bridges[7]. We have now succeeded in the first preparation of a halomolybdate, the analog of chlorochromate, having tetrahedral coordination by a simple and novel method, and in its unequivocal characterization by vibrational spectra and X-ray studies. If tetraphenylphosphonium or tetraphenylarsonium chloride is sintered with stoichiometric amounts of MoO_3 at 250—280 °C in an H_2O-free atmosphere of N_2 for 1 h (process repeated several times with thorough mixing of product between each repetition and with rigorous exclusion of moisture) there results $[(C_6H_5)_4P]MoO_3Cl$ *(1)* or $[(C_6H_5)_4As]MoO_3Cl$ *(2)*. The MoO_3Cl^- ion is isoelectronic with TcO_3Cl. Compounds *(1)* and *(2)* are expectedly prone to hydrolysis and colorless. While the electronic spectrum of the anion could not be measured (the longest wave band corresponding to a $^1A_1 \rightarrow {}^1E$ ($a_2 \rightarrow e$) transition should lie at 40000 cm^{-1}[8]) because the cations absorb at relatively long wavelengths, all the characteristic modes of the anion, which can be classified according to $\Gamma(C_{3v}) = 3A_1 + 3E$, were observed (cf. Table 1). The frequencies are in approximate agreement with those of TcO_3Cl.

Table 1. Fundamental modes of MoO_3Cl^- [b] in cm^{-1} (the frequencies of CrO_3Cl^- and TcO_3Cl are given for the sake of comparison).

	CrO_3Cl^- [a]	MoO_3Cl^-	TcO_3Cl [a]
$\nu_1(A_1) = \nu(MCl)$	438	402	445
$\nu_2(A_1) = \nu_s(MO)$	907	934	950
$\nu_3(A_1) = \delta_s(MO_3)$	295	278	299
$\nu_4(E) = \nu_{as}(MO)$	954	894	932
$\nu_5(E) = \rho(MO_3)$	209	181	197
$\nu_6(E) = \delta_{as}(MO_3)$	365	326	340

[a] Cf. ref. [9].
[b] From IR and Raman solid state spectra.

We have recently reported on the assignment of $\nu_2(A_1)$ and $\nu_3(A_1)$ and the problem of distinguishing between them[9]. The valence force constants calculated by the L matrix method[10] amount to $f_{MoO} = 6.67$, $f_{MoCl} = 2.40$ mdyn/Å and are thus expectedly somewhat smaller than in neutral TcO_3Cl[9].

Powder diagrams (Cu-K_α radiation) show that *(1)* and *(2)* are isostructural with the corresponding salts of the ions MnO_4^-[11], $FeCl_4^-$[12], and CrO_3X^-[13]. The systematic extinctions (*hkl* only with $h+k+l=2n$) reveal a pseudotetragonal structure (a complete crystal structure determination is available for $[(C_6H_5)_4As]FeCl_4$[12]; space group $S_4^2 - I\bar{4}$). The lattice dimensions [*(1)*, $a_0 = 12.48$, $c_0 = 7.36$ Å; *(2)*, $a_0 = 12.66$,

[*] Prof. Dr. A. Müller and Dipl.-Chem. E. Königer-Ahlborn
Institut für Chemie der Universität
46 Dortmund 50, Postfach 500500 (Germany)

$c_0 = 7.23$ Å] are comparable with those of the compounds cited.

Received: January 27, 1975 [Z 193b IE]
German version: Angew. Chem. 87, 599 (1975)

CAS Registry numbers:
(1), 54823-26-6; (2), 54823-27-7; MoO_3, 1313-27-5; $[(C_6H_5)_4P]Cl$, 2001-45-8; $[(C_6H_5)_4As]Cl$, 507-28-8

[1] G. Brauer: Handbuch der präparativen anorganischen Chemie. F. Enke-Verlag, Stuttgart 1960.
[2] E. Ahlborn, E. Diemann, and A. Müller, Z. Naturforsch. 27b, 1108 (1972).
[3] R. Mattes, G. Müller, and H. J. Becher, Z. Anorg. Allg. Chem. 389, 177 (1972).
[4] Y. A. Buslaev and R. L. Davidovitch, Russ. J. Inorg. Chem. 10, 1014 (1965); W. P. Griffith and T. D. Wickins, J. Chem. Soc. A 1967, 675.
[5] G. Pausewang and W. Rüdorff, Z. Anorg. Allg. Chem. 364, 69 (1969).
[6] E. Ahlborn, E. Diemann, and A. Müller, J. C. S. Chem. Comm. 1972, 378.
[7] R. Mattes and H. Rieskamp, Z. Anorg. Allg. Chem. 399, 205 (1973).
[8] A. Müller, E. Diemann, and C. K. Jørgensen, Struct. Bonding 14, 23 (1973).
[9] A. Müller, K. H. Schmidt, E. Ahlborn, and C. J. L. Lock, Spectrochim. Acta 29A, 1773 (1973); see also K. H. Schmidt and A. Müller, Coord. Chem. Rev. 14, 114 (1974).
[10] A. Müller, Z. Phys. Chem. (Leipzig) 238, 116 (1968).
[11] E. J. Baran, Z. Anorg. Allg. Chem. 382, 80 (1971).
[12] B. Zaslov and R. E. Rundle, J. Phys. Chem. 61, 490 (1957).
[13] E. Diemann, E. Ahlborn, and A. Müller, Z. Anorg. Allg. Chem. 390, 217 (1972).

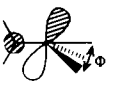
Sudden Polarization in the Zwitterionic Z_1 Excited States of Organic Intermediates. Photochemical Implications

By *Vlasta Bonačić-Koutecký, Peter Bruckmann, Philippe Hiberty, Jaroslav Koutecký, Claude Leforestier,* and *Lionel Salem*[*]

In 1971, in a relatively unnoticed paper[1], *Wulfman* and *Kumei* pointed out that the two lowest excited singlet states of 90°-twisted olefins should show a remarkably large polarizability. These states are the zwitterionic[2] Z_1 *(1)* and Z_2 *(2)* excited states of the twisted olefin diradical; the (−) and (+) signs refer to out-of-phase and in-phase resonance interactions respectively. Since numerous bitopic photochemical reactions, in which two radical sites are created in the primary photochemical step, are expected to involve the lowest such excited state, Z_1[3], it appears important to study the extent of charge separation which can be created in Z_1 by chemical perturbations.

Z_1 Z_2

Let us first consider the effect of a slight *distortion of the molecule* at one end of the CC bond on the charge separation in Z_1. In a 90°-twisted ethylene molecule one CH_2 group is slowly pyramidalized:



The distortion is carried out in such a manner as to preserve a plane of symmetry (plane of the paper) for the molecule. Under these conditions the odd orbitals belong to different symmetry representations (heterosymmetric diradical)[12]. The ground singlet is a purely covalent diradical state ^1D, while the two excited singlets Z_1 and Z_2 are purely ionic. The energies and charge distributions of these three singlet states can be calculated by the Nesbet restricted open-shell SCF technique, augmented by configuration interaction between the three lowest singlet state configurations[4].

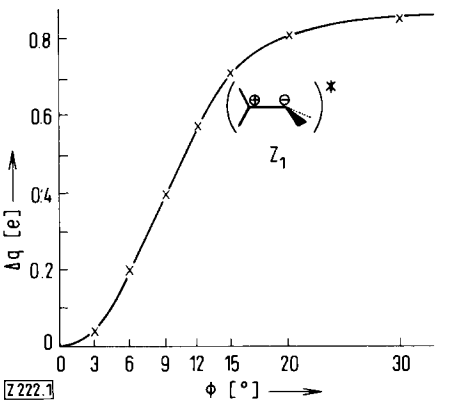
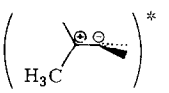


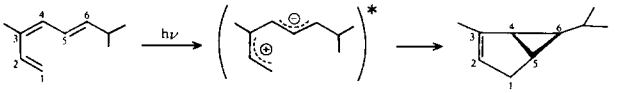
Fig. 1. Charge separation Δq in Z_1 excited singlet state of 90°-twisted ethylene as a function of the pyramidalization angle ϕ. The number Δq has been corrected for the intrinsic charge separation in the ground state (which never exceeds 0.04 e).

Figure 1 shows the charge separation Δq between the two carbon atoms in the Z_1 excited state, as a function of pyramidalization angle ϕ, calculated with an extended basis set (4-31G) of Gaussian orbitals[5]. The curve has an interesting sigmoid shape. Remarkably, the charge separation reaches 0.72 e for a pyramidalization of only 15°. It then increases slowly towards a limit of 0.87 e for a full sp^3 carbon atom ($\phi = 55°$). Throughout the pyramidalization process the energy of Z_1 remains constant, within 4 kcal/mol. This is confirmed by a 271-configuration interaction calculation, constructed on a limited basis set (STO-3G) of Gaussian orbitals[5], which shows the energy to decrease by only 8 kcal/mol in the full pyramidalization process.

The large polarization of the CC bond can also be obtained by simple *chemical substitution.* Thus, a similar calculation for 90°-twisted propene molecule, with the same symmetry plane, yields a large charge separation ($\Delta q = 0.84$ e) without any pyramidalization.

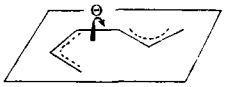


As a first application of these results, let us consider the photocyclization of 1,3,5-hexatrienes to bicyclo[3.1.0]hexenes[6]. Formally, a typical such reaction can be written[3]:



We have performed a similar open-shell, calculation of the charge distribution in the Z_1 state of *s-cis,s-trans* diallyl (1,3,5-hexatriene) as a function of twist angle θ. (The starting planar conformation *(3)* corresponds to $\theta = 0°$.)

[*] Dr. P. Bruckmann (Deutsche Forschungsgemeinschaft Scholarship), Dr. P. Hiberty, Mr. C. Leforestier and Prof. L. Salem [+]
Laboratoire de Chimie Théorique (E. R. A. N° 549)
Université de Paris-Sud, 91405 Orsay (France)
Dr. V. Bonačić-Koutecký and Prof. J. Koutecký (Exchange Professorship, Université de Paris-Sud)
Institut für Physikalische Chemie und Quantenchemie der Freien Universität
1 Berlin 33, Thielallee 63–67 (Germany)
[+] Author to whom correspondence should be addressed.

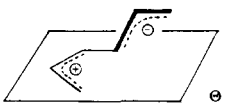


(3)

For almost all values of θ in the range 0°, 180°, the charge distribution in Z_1 is found to be equally divided between the two allyl moieties. This corresponds to out-of-phase resonance between two equally weighted ionic structures (see *(1)*):

(4)

However there is a narrow range of θ values ($89° \leqslant \theta \leqslant 91°$), corresponding to a nearly perpendicular conformation, for which a large charge separation occurs:



(5)

Θ = 90°, Δq = 0.86e

Figure 2 shows the charge separation between the allyl groups as a function of θ, calculated with a minimal (STO-3G) basis set of Gaussian orbitals[5]. A sharp, bell-shaped curve, is obtained. The explanation of this sudden polarization of the molecule is as follows. At all θ values, the dissymmetry between *cis*-linked allyl moiety and *trans*-linked allyl moiety would suffice to polarize the molecule were it not for the significant overlap between the two non-bonding allylic orbitals. This overlap—which vanished in the previous examples—is very small here only near $\theta = 90°$. At other angles the overlap is large enough to allow the charge to transfer back and forth between the two allyl groups.

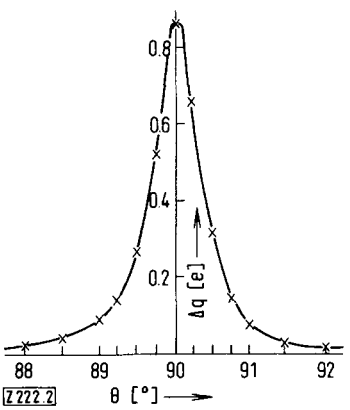


Fig. 2. Charge separation Δq in Z_1 excited state of *s-cis,s-trans*-diallyl (1,3,5-hexatriene) as a function of twist angle θ. The curve is not symmetric about 90°.

We can now interpret the intimate mechanism of the cyclization step of the photochemical reaction. First, the hexatriene is excited to the Z_1 state in its coplanar geometry *(3)*. Next, as the central C^3—C^4 bond lengthens, the two allyl moieties become free to rotate relative to each other. As the molecule passes through the $\theta = 90°$ region, *charge suddenly flows into the trans-allylic portion of the molecule*[7]. The $C^4C^5C^6$ allyl anion, extremely rich in electrons, then immediately closes to a cyclopropane ring[8].

We can draw three general conclusions from our study of the excited zwitterionic singlet states of organic diradical intermediates:

1. A slight dissymmetry between the two odd-electron sites can cause a large separation of charge if the overlap between these sites is sufficiently small. *Both* the dissymmetry *and* a sufficiently small overlap are prerequisites for sudden polarization (for instance, $\Delta q = 0$ at all angles in *s-trans,s-trans*-diallyl).

2. Under no circumstances should one rely on ordinary chemical intuition to estimate the extent of charge separation in excited Z_1 states. The general tendency will be to vastly underestimate the zwitterionic character of slightly dissymmetric molecules[9].

3. This novel effect can discriminate sharply between the different conformations available to excited reactant species. Although the excited zwitterion is short-lived, it can play a crucial role in determining the outcome of the reaction.

Finally, we have already pointed out that the charge-separated Z_1 state should be highly stabilized in polar solvents[10].

Received: March 25, 1975 [Z 222 IE]
German version: Angew. Chem. *87*, 599 (1975)

[1] *C. E. Wulfman* and *S. Kumei*, Science *172*, 1061 (1971).
[2] *L. Salem* and *C. Rowland*, Angew. Chem. *84*, 86 (1972); Angew. Chem. internat. Edit. *11*, 92 (1972); *L. Salem*, Pure Appl. Chem. *33*, 317 (1973). The ionic nature of the $^1A_1$ and $^1B_2$ states of twisted ethylene was first pointed out by *R. S. Mulliken*, Phys. Rev. *43*, 279 (1933).
[3] *W. G. Dauben, L. Salem*, and *N. J. Turro*, Acc. Chem. Res. *8*, 41 (1975).
[4] For a description of this technique see *L. Salem, C. Leforestier, G. Segal*, and *R. Wetmore*, J. Am. Chem. Soc. *97*, 479 (1975).
[5] The program is Gaussian 70 (*W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton*, and *J. A. Pople*, Program No. 236 QCPE, Univ. of Indiana, Bloomington, Indiana).
[6] *W. G. Dauben, M. S. Kellog, J. I. Seeman, N. D. Vietmeyer*, and *P. H. Wendschuh*, Pure Appl. Chem. *33*, 197 (1973) and references cited therein. We thank Professor *Dauben* for introducing us to this reaction.
[7] The reason why the negative charge prefers the *trans*-linked allyl to the *cis*-linked allyl is not clear, though it may be due to the 4π-electron analogy with stable *trans*-butadiene.
[8] The fact that the allyl anion closes in a *conrotatory* manner is not in contradiction with the *excited* nature of the molecule, since the electronic excitation is essentially localized in the C^3C^4 bond.
[9] In certain cases (diallyl) the energy difference between Z_2 and Z_1 is so small that the Z_2 state, with opposite polarization to Z_1, will be partially populated, thereby decreasing the overall polarization on a macroscopic level (*E. Scrocco* and *J. P. Malrieu*, personal communication).
[10] *L. Salem* and *W. D. Stohrer*, J. C. S. Chem. Comm. *1975*, 140. We thank Dr. *Stohrer* for an interesting discussion.

Reviews

Abstracts of selected progress reports and review articles

Metrizamide, a new density gradient medium, is described in an article by *D. Rickwood* and *D. G. Birnie*. The experimental difficulties encountered with the media employed so far, mainly CsCl, sucrose, and Ficoll, can be overcome by the use of metrizamide (2-[3-acetamido-5-(*N*-methylacetamido)-2,4,6-triiodobenzamido]-2-deoxy-D-glucose). The substance is not ionic and is stable under sterile conditions; its solubility is satisfactory for the generation of sufficiently dense yet low viscosity solutions. One disadvantage is the UV absorption, which interferes with the photometric determination of proteins and nucleic acids. Since metrizamide, unlike media such as CsCl, neither dehydrates nor interacts appreciably with biological macromolecules lower buoyant densities than hitherto are found and even subcellular particles, viruses and whole cells can be separated from one another by isopycnic centrifugation. [Metrizamide, a New Density Gradient Medium. FEBS Lett. *50*, 102—110 (1975); 42 references]

[Rd 786 IE—R]

Covalent modifications of nuclear proteins during aging are discussed in an article by *C. C. Liew* and *A. G. Gornall*. Of these processes, which are held responsible for the age-related deterioration of regulation of gene expression at the transcriptional and translational levels, acetylation and phosphorylation were studied in detail. Even unfractionated nuclear proteins can be acetylated to a greater extent in older animals than in younger ones; phosphorylation proceeds equally intensively in both cases. Differences between old and young animals became clearer after prior electrophoretic separation of the proteins. Two fractions of acid proteins from the cell nuclei of old animals were particularly active acyl group acceptors. [Covalent Modification of Nuclear Proteins during Aging. Fed. Proc. *34*, 186—187 (1975); 14 references]

[Rd 788 IE—R]

The hormonal regulation of phosphoenol pyruvate carboxykinase during development is discussed in an article by *R. W. Hanson, L. Reshef,* and *J. Ballard*. This liver enzyme, which plays a key role in gluconeogenesis, first appears at birth in rats. This is probably due to an increased cAMP level in the liver, which in turn appears to be related to the increase in glucagon concentration. Insulin, whose concentration is known to decrease strongly at birth, inhibits the synthesis of carboxykinase. [Hormonal Regulation of Hepatic P-Enolpyruvate Carboxykinase (GTP) during Development. Fed. Proc. *34*, 166—171 (1975); 32 references]

[Rd 789 IE—R]

Perinatal enzyme capacity for degradation of drugs and other xenobiotics is discussed in an article by *J. R. Gillette* and *B. Stripp*. The enzyme systems responsible for degradation, *i. e.* the cytochrome P-450 enzymes, are not present in laboratory animal fetuses, but develop within 3–8 weeks after birth. In human fetuses, however, they already appear in the first half of pregnancy and finally reach a third of the activity of the enzymes of adults. This difference between various species is also reflected in the development of the endoplasmic reticulum of the liver. Despite their earlier development in humans these enzymes hardly inhibit accumulation of xenobiotics in the fetus; they could, however, play a role in drug-caused intoxications through formation of reactive metabolites. [Pre- and Postnatal Enzyme Capacity for Drug Metabolite Production. Fed. Proc. *34*, 172—178 (1975); 80 references]

[Rd 790 IE—R]

Age-related changes in glucocorticoid binding by rat splenic leukocytes is the subject of an article by *G. S. Roth*. Isolated cells are more suitable than tissue samples for such experiments, since otherwise extracellular effects falsify the picture. Leukocytes from senescent animals have far fewer binding sites than those from mature adult ones. Parallel with the reduced cortisone binding capacity there is also a decrease in the inhibition of uridine incorporation in leukocytes. The age-related decrease in binding sites can thus be considered responsible, at least in part, for the altered response of splenic leukocytes to glucocorticoids. [Age-Related Changes in Glucocorticoid Binding by Rat Splenic Leukocytes: Possible Cause of Altered Adaptive Responsiveness. Fed. Proc. *34*, 183—185 (1975); 9 references]

[Rd 791 IE—R]

Fenton's reagent ($H_2O_2+Fe^{2+}$), an effective oxidizing agent for organic compounds (RH) which was discovered some 80 years ago, is reviewed in an article by *C. Walling*. The key steps in Fenton's reagent oxidations are

$$H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + HO^- + HO$$
$$HO + RH \rightarrow H_2O + R$$

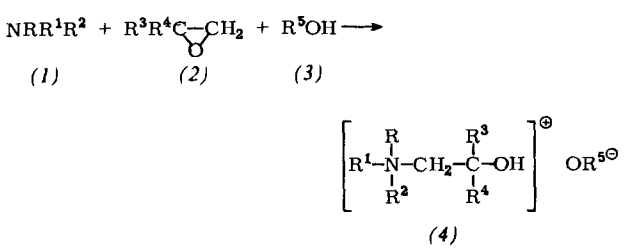
The radical R· can react further in three different ways: it can dimerize, be reduced by Fe^{2+}, or oxidized by Fe^{3+}. [Fenton's Reagent Revisited. Accounts Chem. Res. *8*, 125—131 (1975); 37 references]

[Rd 797 IE—L]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Quaternary hydroxyalkylammonium alkoxides and phenoxides *(4)* are formed by treatment of tertiary amines *(1)* with an alkylene oxide *(2)* and an alcohol or phenol *(3)* in the absence of a solvent. The compounds *(4)* can be used in



(1) *(2)* *(3)* *(4)*

R, R^1, R^2 = alkyl hydroxyalkyl, (subst.) cycloalkyl, aryl, or aralkyl; R^3, R^4 = H, alkyl, aryl, or aralkyl; R^5 = alkyl (C_1 or C_2), aryl, or aralkyl (C_6—C_{10})

many ways as basic catalysts, *inter alia* for the preparation of polyurethane or polyurethane-polyisocyanurate foams or

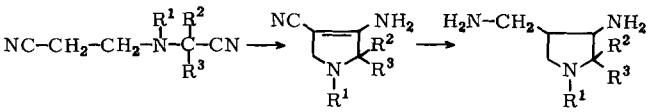
for the hydroxyalkylation of polyols. [DOS 2420774; Air Products and Chemicals, Inc., Allentown (USA)]

[PR 275 IE—D]

***N,N,N',N'*-Tetramethyl-2,2'-oxydiethylamine** (bis[2-(*N,N*-dimethylamino)ethyl] ether is a very effective catalyst for reactions of organic isocyanates. It is particularly suitable in combination with organic tin compounds such as tin(II) octanoate for catalysis of the preparation of polyurethane foams. [DOS 1795762; Union Carbide Corp., New York (USA)]

[PR 276 IE—D]

3-Amino-4-(aminomethyl)pyrrolidines *(3)* **suitable as hardening agents for epoxide resins,** are formed on catalytic hydrogenation of 3-amino-4-cyano-3-pyrrolines *(2)* under pressure in the presence of ammonia. The compounds *(2)* can be obtained in good yield by Thorpe-Ziegler cyclization of the dinitriles



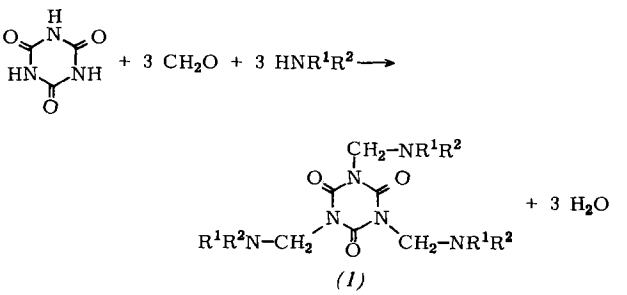
(1) *(2)* *(3)*

R^1 = (subst.) hydrocarbon group; R^2 = H (subst.) hydrocarbon group; R^3 = H, alkyl group (C_1—C_6), or R^2R^3 = pentamethylene group

(1) which are accessible by condensation of cyanohydrins with monocyanoethylated amines. [DOS 2435167; Ciba Geigy AG, Basel (Switzerland)]

[PR 277 IE—D]

Polyols suitable for the preparation of flame-resistant polyurethanes are obtained by the addition of alkylene oxides to the



(1)

R^1 = an aliphatic group containing at least one alcoholic OH group; R^2 = H, alkyl, or an aliphatic group containing at least one alcoholic OH group

liquid (hydroxyalkylaminomethyl)isocyanurate *(1)* obtained by condensation of isocyanic acid, formaldehyde, and amino alcohols. [DOS 2166652; Naphthachimie S.A., Paris (France)]

[PR 278 IE—D]

BOOK REVIEWS

Ullmanns Encyklopädie der technischen Chemie (Ullmann's Encyclopedia of Industrial Chemistry). Edited by *E. Bartholomé, E. Biekert, H. Hellmann*, and *H. Ley* (deceased). Vol. 4: Verfahrensentwicklung und Planung von Anlagen. Dokumentation (Process Development and Plant Design. Documentation). Verlag Chemie, GmbH, Weinheim 1974, 4th Edit., XVI, 728 pp., 600 figs., 90 tables, subscription price DM 345.—, final price *ca.* DM 385.—.

This volume of the general part of the new Ullmann[*] is the last of the four volumes dealing with the whole sector of chemical process technology and reaction engineering. Two further volumes will complete the general part, dealing with physical and physicochemical methods of analysis and with the techniques of measurement, protection of the environment, and protection at work.

The subjects of the present volume are process development and plant design, including the methods used for these fields of work; in addition, it contains a section on documentation and the combined index to volumes 1—4 in German and English. In detail, it consists of the following contributions:

Process Development (69 pp.), Planning and Construction of Chemical Plant (89 pp.), Network Technology (13 pp.), General Methods of Control (96 pp.), Plant Control (44 pp.), Digital Computers (programing languages 22 pp., construction and methods of operation 26 pp.), Process Computers (48 pp.), Analog Computers (42 pp.), Mathematical Models (127 pp.), Regression Analysis (13 pp.), Optimization (26 pp.), Documentation (16 pp.). The chemist, and particularly the industrial chemist engaged in research and production, will find special interest in the contributions on process development and mathematical models, of which the latter treats the construction of models in general and also methods of calculation for specific general operations (*e.g.* rectification) and reactor types (*e.g.* cooled tube reactors). The section on process development is short compared with other sections, and the reviewer at any rate would have liked this chapter to have been more detailed. The section on documentation is also worth reading by every chemist, particularly as chemical documentation, *i.e.* the documentation of chemical compounds and reactions, is most emphasized; the special problems of documenting industrial processes are only lightly touched upon.

As in the case of the previous volumes, recognized specialists have been commissioned as authors. Correlation of the individual contributions is naturally far from easy, and overlapping cannot be avoided: in some cases it is indeed an advantage, so as to provide a comprehensive picture of one theme, and this is shown in the present volume by the series of problems raised by cost estimation, as treated from the point of view of the development chemist (in the section on process development) and of the development engineer (in the section on plant design); in any case, both here and elsewhere, more frequent cross-references in the text would have been welcome; there is no such cross-reference in the second of the sections just mentioned.

The overall verdict must be that the book represents an excellent production by the press, editors, and authors, no less than the previous volumes.

Ulfert Onken [NB 277 IE]

[*] Cf. Angew. Chem. internat. Edit. *14*, 268 (1975).

Kunststoff-Handbuch (Plastics Handbook). Vol. 9. Polymethacrylate (Polymethacrylates). Edited by *R. Vieweg* and *F. Esser*. Carl Hanser Verlag, München. 1975. 1st Edit., XX, 954 pp., 855 figs., 110 tables, bound, DM 395.—.

The methacrylic ester volume is the last in this series of handbooks arranged according to the material concerned. In correspondence with the importance of these esters—one of the major plastics—the book has become very large; and in view of their use in many fields of industry, in particular their excellent properties when used outdoors, a major part of the book is devoted to acrylic glasses.

Like the preceding volumes, this one is divided into preparation, properties, and uses. After a section on the polymerization of methacrylate resins the mechanical, optical, electrical, thermal, and chemical properties of acrylic glasses are treated in separate sections. To these are added chapters on the manufacture and use of polymethacrylates, which provide information as detailed as it is comprehensive concerning these plastics. Numerous diagrams and tables are used to display the foundations from which the suitability of polymethacrylates for various applications can be derived. The sections on the use of acrylic glasses in building, for illumination, in electrical appliances, in the household, in medicine, and in dentistry made particularly interesting reading.

Since none who work with plastics, be they engineers, builders, or electricians, can get through without polymethacrylates, the publication of this book will be particularly welcome to them, but chemists and physicists will also find uses for it, even if the heaviest stress is laid on applications. Recognition is due both to the editors and to the publishers for this excellent volume, even if those interested had to wait for it for a long time. While in a new edition further economic data on this important class of plastics would be desirable, this recommendation does not detract from this magnificent volume.

Otto Horn [NB 279 IE]

Transfer and Storage of Energy by Molecules. Vol. 4: The Solid State. Edited by *G. M. Burnett, A. E. North*, and *J. N. Sherwood*. John Wiley & Sons, London 1974. 1st Edit., XXIII, 612 pp., numerous figs., bound, £ 16.00.

The present volume comprises ten contributions from solid state physics. The article "Excitons and Electronic Spectra in Molecular Crystals" *(G. Fischer)* contains a very precise theory of the optical properties of Frenkel excitons in pure and mixed crystals; it provides the basis for understanding the influence of crystals on the electronic spectra of molecules; the actual transport properties (diffusion, sensitization of emission) are mentioned only briefly. "Electronic Excitations in Semiconductors" by *D. Pugh* is an article describing the energy bands and excitons in semiconductors and the methods for their calculation; special attention is paid to reflectivity, high exciton states, and absorption edges. In the third contribution, "Activation Energies for Electronic Conduction in Crystalline Solids", *G. G. Roberts* reviews the physical basis for activation energies of electrical conduction in molecular crystals.

The article "Electronic Conduction in Amorphous Solids" by *W. L. McCubbin* is purely theoretical. *G. S. Pawley* treats "Phonons in Molecular Crystals" only very cursorily, while "Phonon Processes in Amorphous Solids" by *P. Dean* is very detailed, yet with few experimental examples. In addition, *R. T. Bailey* reports on "Raman and Infrared Studies of Molecular Movements in Organic Crystals" and *A. M. North* and *R. A. Pethrich* discuss, very briefly, "Acoustic Investigations of Liquid Crystals and Molecular Solids." The last two articles are on "Nuclear Spin Energy Exchange in Solids" *(G. P. Jones)* and "Magnetic Excitations" *(C. G. Windsor)*. This is a good introduction into the field of magnons.

The chapter headings indicate the wealth and variety of the material. Necessarily, the individual articles are only a compromise between an introduction to the field and a review of the state of research. Topical research is considered especially in the first and the last articles (excitons and magnons). The readers of this book will be mostly research workers in the field of solid state physics or solid state chemistry who want to find a point of entry into the subjects treated.

There is a permanent shortage of review articles of this type, and in that sense the book is certainly valuable. Those working in the solid state field will find the book valuable, but the expectations raised by the title are not fully satisfied by the contents.

H. C. Wolf [NB 281 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Separation and Purification Methods, Vol. 3. Edited by *E. S. Perry, C. J. van Oss*, and *E. Grushka*. Marcel Dekker, Inc., New York 1975. XII, 463 pp., bound, $ 29.50.

Organophosphorus Chemistry, Vol. 6. Senior Reporter: *S. Trippett*. The Chemical Society, London 1975. XI, 271 pp., bound, £ 11.00.—A volume of the series "Specialist Periodical Reports".

Molecular Spectroscopy. By *I. N. Levine*. John Wiley & Sons, London 1975. X, 491 pp., bound, £ 10.50.

Sorption and Filtration Methods for Gas and Water Purification. Edited by *M. Bonnevie-Svendsen*. Nato Advanced Study Institute Series, Series E: Applied Sciences, Vol. 13. Noordhoff, Leyden 1975. IX, 547 pp., bound, Dfl. 117.00.

International Review of Science. Biochemistry Series One. Vol. 12: Physiological and Pharmacological Biochemistry. Consultant Editors: *H. L. Kornberg* and *D. C. Phillips*. Volume Editor: *H. K. F. Blaschko*. Butterworths, London/University Park Press, Baltimore 1975. 276 pp., bound, £ 8.95.

Chemische Evolution und der Ursprung lebender Systeme. By *K. Dose* and *H. Rauchfuss*. From the series "Bücher der Zeitschrift Naturwissenschaftliche Rundschau". Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart 1975. XI, 217 pp., bound, DM 56.—.

Immunchemie. By *M. W. Steward*. From the pocket-book series "Führer zur modernen Biologie". Gustav Fischer Verlag, Stuttgart 1975. VIII, 86 pp., stitched, DM 9.80.

Polymer Chemistry. An Introduction. By *M. P. Stevens*. Addison-Wesley Publishing Company, Reading, Mass. 1975. XV, 458 pp., bound, $ 25.00/stitched, $ 17.50.

Infrared and Raman Spectroscopy of Lunar and Terrestrical Minerals. Edited by *C. Karr, Jr.* Academic Press, New York 1975. XII, 375 pp., bound, $ 38.50.

Dielectric Phenomena and the Double Layer in Disperse Systems and Polyelectrolytes. By *S. S. Dukhin* and *V. N. Shilov*.

John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1975. VII, 192 pp., bound, £ 9.00.

Metal Carbonyl Spectra. By *P. S. Braterman.* From the series "Organometallic Chemistry". Edited by *P. M. Maitlis* and *F. G. A. Stone.* Academic Press, New York 1975. VIII, 286 pp., bound, $ 22.25.

Solid Phase Synthesis. Edited by *E. C. Blossey* and *D. C. Neckers.* Vol. 2 of the series "Benchmark Papers in Organic Chemistry". Edited by *C. A. VanderWerf.* Halsted Press, a division of John Wiley & Sons, New York 1975. XVIII, 360 pp., bound, £ 13.00.

Boron Hydride Chemistry. Edited by *E. L. Muetterties.* Academic Press, New York 1975. XII, 532 pp., bound, $ 49.50.

Chemische Farbreaktionen von Pilzen. By *A. Meixner.* J. Cramer, Vaduz 1975. 286 pp., stitched, DM 29.50.

Isotopes in Organic Chemistry. Edited by *E. Buncel* and *C. C. Lee.* Vol. 1: Isotopes in Molecular Rearrangements. Elsevier Scientific Publishing Company, Amsterdam 1975. XI, 301 pp., bound, Dfl. 100.00.

Biopharmaceutics and Pharmacokinetics. By *R. E. Notari* in collaboration with *J. L. deYoung* and *R. C. Anderson.* Marcel Dekker, New York 1975. 2nd edit., X, 285 pp., bound, $ 13.75.

Struktur, Stoff, Reaktion. By *H. R. Christen.* Allgemeine und Anorganische Chemie, Sekundarstufe I, Lehrerband. 1. Lieferung: Methodik und Didaktik—Liste der Versuche. Diesterweg Salle, Frankfurt/Verlag Sauerländer, Aarau 1975. IV, 138 pp., loose-leaf collection in ring file, DM 17.80.

Dünnschicht-Chromatographie. Experimente für den Naturwissenschaftlichen Unterricht. By *W. Christen.* G-I-T Verlag E. Giebeler, Darmstadt 1975. 100 pp., ring file DIN A 4, DM 30.—.

Diffusional Mass Transfer. By *A. H. P. Skelland.* John Wiley & Sons, New York 1974. xv, 510 pp., bound £ 13.25.

Applied Spectroscopy Reviews, Vol. 7. Edited by *E. G. Brame, Jr.* Marcel Dekker, Inc., New York 1974. xv, 381 pp., bound $ 25.50.

Introductory Organic Chemistry. By *J. T. Gerig.* Academic Press, New York 1974. xvii, 404 pp., bound $ 9.95.

Massenspektrometrie von Kondensationskeimen in der Gasphase. By *H. Knof.* From the series "Reprotext—Spezielle naturwissenschaftliche und technische Texte in Direktreproduktion". Physik-Verlag, Weinheim 1974. 186 pp., stitched DM 39.—.

Probleme und Problemlösungen. Contributions from the journal "Chemie in unserer Zeit". Verlag Chemie, Weinheim 1974. 114 pp., bound DM 27.50.

Chemistry for Changing Times. By *J. W. Hill.* Burgess Publishing Company, Minneapolis 1972. xiii, 272 pp., stitched $ 5.95. Teacher's Guide/ iv, 72 pp., stitched, gratis.

Chemical Problems for Changing Times. By *L. M. Zaborski* and *J. W. Hill.* Burgess Publishing Company, Minneapolis 1973. v, 87 pp., stitched $ 2.95. Teacher's Guide: 32 pp., stitched, gratis.

Chemical Investigations for Changing Times. By *L. W. Scott, L. M. Zaborowski, J. W. Hill,* and *P. Muto.* Burgess Publishing Company, Minneapolis 1972. ix, 173 pp., stitched $ 4.50. Teacher's Guide: x, 22 pp., stitched, gratis.

Structure and Bonding, Vol. 17: Metal Bonding in Proteins. Edited by *J. D. Dunitz, P. Hemmerich, J. A. Ibers, C. K. Jørgensen, J. B. Neilands, D. Reinen,* and *R. J. P. Williams.* Springer-Verlag, Berlin 1973. iii, 268 pp., bound DM 72.—.

Variational Methods Applied to Problems of Diffusion and Reaction. By *W. Strieder* and *R. Aris,* Vol. 24 of "Springer Tracts in Natural Philosophy". Edited by *B. D. Coleman.* Springer-Verlag, Berlin 1973. ix, 109 pp., bound DM 36.—.

Careers in Industrial Research and Development. By *J. H. Saunders.* Marcel Dekker, Inc., New York 1974. xi, 254 pp., stitched $ 11.75.

Chemical Principles. By *R. E. Dickerson, H. B. Gray,* and *G. P. Haight, Jr.,* W. A. Benjamin, London 1974. 2nd Edit. xxii, 872 pp., bound $ 12.00.

Programmed Reviews of Chemical Principles. By *J. D. Lassila, G. M. Barrow, M. E. Kenney, R. L. Litle,* and *W. E. Thompson.* W. A. Benjamin, London 1974. 2nd Edit. viii, 743 pp., stitched $ 5.75.

Organometallic Reaction Mechanism of the Nontransition Elements. By *D. S. Matteson.* From the series "Organometallic Chemistry". Edited by *P. M. Maitlis, F. G. A. Stone,* and *R. West.* Academic Press, New York 1974. xii, 353 pp., bound $ 24.00.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 14036. Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and 24/28 Oval Road, London NW1, England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim. Pappelallee 3. P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE
CHEMIE
International Edition in English

Volume 14 · Number 9
September 1975
Pages 581–654

Heterocyclic Systems Having Eight π-Electrons. Synthesis, Properties, and Significance[1]

By Richard R. Schmidt[*]

The terms "aromatic" and "antiaromatic" have attracted widespread interest in recent years. After all the discussion about the meaning of words, one fact remains: the energy content of planar systems displaying cyclic electron delocalization depends upon the number of, and the orbital interactions between, the participating electrons. The concept underlying this progress report is that the electronic destabilization of systems having eight π-electrons should be especially pronounced in the case of six-membered rings for steric and electronic reasons. Such systems are found primarily in anionic, but also in neutral, heterocycles containing hetero ring members which possess electron pairs capable of delocalizing into the π-system. The production and reactivity of such systems are investigated and their biological significance discussed.

1. Introduction

1.1. Aromatic and Antiaromatic Systems

Recent theoretical concepts teach that the number and orbital interaction of cyclically delocalized electrons are of considerable significance for the stability of molecular ground states and the energy content of transition states. The Hückel rule and the Woodward-Hoffmann rules, confirmed by numerous experimental examples, provide impressive support for these concepts.

Thus calculations of the resonance energy per π-electron for annulenes and 1*H*-1-azaannulenes (see Fig. 1), relative to the corresponding acyclic conjugated planar systems, reveal: $(4n+2)\pi$-systems are stabilized by resonance and the corresponding $4n\pi$-systems, with which this report is concerned, are destabilized[2].

Studies on cyclobutadiene[3] and on cyclopropenyl anions[4, 5] (4π-systems) show that these systems do indeed have a higher energy content than comparable open-chain systems. *Breslow*[5] and *Dewar*[6] therefore propose the use

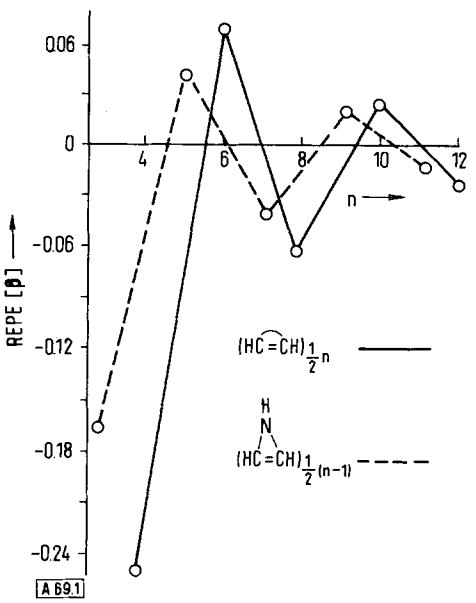


Fig. 1. Resonance energy per π-electron (REPE) for annulenes (——) and 1*H*-1-azaannulenes (– – –). *n* = number of ring members [2].

[*] Prof. Dr. R. R. Schmidt
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
7 Stuttgart 80, Pfaffenwaldring 55 (Germany)

of the terms "aromatic" and "antiaromatic" in characterizing this phenomenon of alternating energy content in formally related systems, and classification of the corresponding acyclic reference system as "nonaromatic". Thus defined, these terms provide a qualitative description of an important ordering principle in the chemistry of cyclically conjugated systems and are of theoretical and practical utility. Since a clear-cut answer to the important question of the reference system is not always available, a formalistic and noncritical usage of the terms "aromatic" and "antiaromatic" has repeatedly aroused opposition[7-9].

1.2. 8π-Systems in Heterocycles

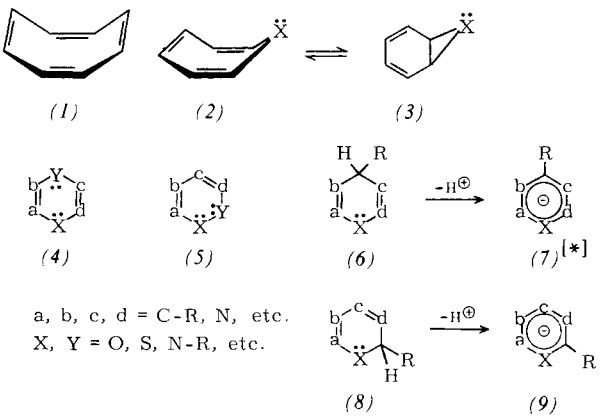
The agreement observed between calculation and experimental results in the case of cyclobutadiene no longer exists on going to cyclooctatetraene *(1)*; typically olefinic character is found[10]. The reason lies in the molecular geometry. An important prerequisite for electron delocalization is not satisfied, *i.e.* planarity of the molecular skeleton. π-Conjugation of the cyclic 8π-system, and hence electron delocalization, is thwarted by the angular skeleton. The dihedral angle between the π-bonding planes is about 90°[11]; localized π-bonds are present.

Replacement of an ethylene group of cyclooctatetraene *(1)* by a hetero atom bearing a free electron pair leads to the seven-membered heterotropilidenes (hetero-π-homobenzenes) *(2)*, which are likewise potential 8π-electron systems[12, 13] with antiaromatic character (see Fig. 1). Nor are these systems planar[14]. The more or less pronounced valence isomerization to the hetero-σ-homobenzenes *(3)* has at least three reasons: a) steric reasons—nonplanarity leads to spatial proximity of the atoms forming the new π-bond; b) differing strength of the new σ-bond—this phenomenon can be rationalized according to *Hoffmann*[15] and *Günther*[16] with the aid of the Walsh MO model, thus leading to the prediction that the new σ-bond will be the stronger the more electronegative the hetero atom happens to be; c) the hitherto little-discussed electronic destabilization of the 8π-system[12, 17]. This destabilization becomes clearly apparent on comparison of the hetero-system with cyclooctatetraene and cycloheptatriene; it is seen as an enhanced reactivity which manifests itself in valence isomerizations, rearrangements, and additions[12, 13].

Replacement of two ethylene groups in cyclooctatetraene, each by a hetero atom having a free electron pair, will yield the six-membered potential 8π-systems *(4)* and *(5)*, which should be essentially planar with bond angles of about 120 According to MO calculations[18, 19] these are particularly favorable models displaying electronic destabilization. Compounds of this type do indeed show remarkable behavior in their reactions[1, 20].

Even more reactive potential cyclic 8π-systems should arise on replacement of X or Y in *(4)* or *(5)* by a carbanion center, as in *(7)* and *(9)*; their tendency to stabilize the negative charge raises the electronic destabilization. Such systems are accessible by deprotonation of suitable dihydroheterocycles like *(6)* or *(8)*[1, 20].

The significance of the heterotropilidenes such as *(2)* has been underlined above all by the work of *Vogel*, *Hafner*, *Prinzbach*, and their respective co-workers[12, 13]. This progress report will be concerned in particular with the generation and properties of six-membered anionic and also neutral potential 8π-systems—systems of considerable significance in the biological sector. Furthermore, a brief account of seven-membered anionic systems will also be presented.



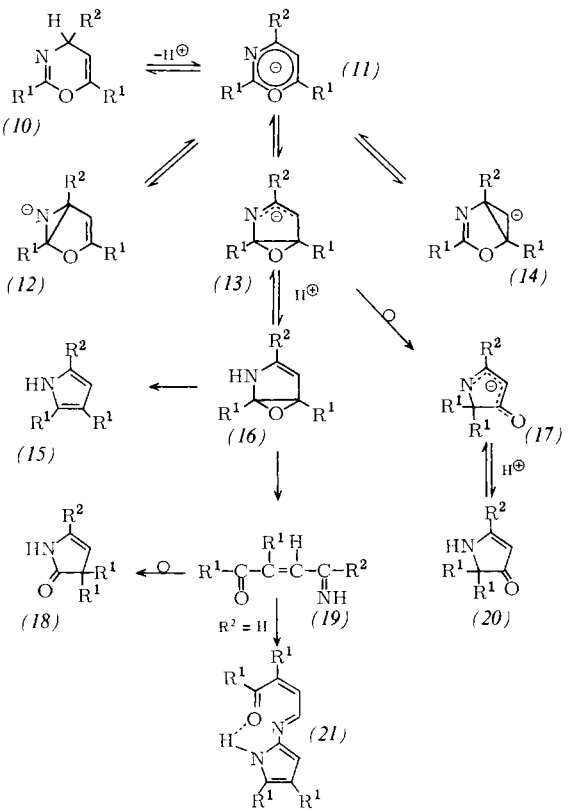
(1) *(2)* *(3)* *(4)* *(5)* *(6)* *(7)*[*] *(8)* *(9)*

2. Six-Membered Heterocyclic Systems with Eight π-Electrons

2.1. Systems Analogous to Oxepin

2.1.1. 1,3-Oxazinyl Anions

Our work on six-membered anionic 8π-systems began with the study of 4*H*-1,3-oxazines *(10)*[21, 22], which are readily accessible by polar cycloaddition[23, 24]. Reaction of *(10)*, $R^1 = R^2 =$ aryl, with strong bases at low temperatures (up to



(10) *(11)* *(12)* *(13)* *(14)* *(15)* *(16)* *(17)* *(18)* *(19)* *(20)* *(21)*

Scheme 1

[*] Anionic systems having eight delocalizable π-electrons will be depicted in this manner.

$-120\,^{\circ}C$) in THF yields a dark blue solution. This color is attributed to the 1,3-oxazinyl anion *(11)* (Scheme 1). However, the rapid disappearance of the color suggests *(11)* to contain so much energy that it rapidly transforms into a ring-strained, valence-isomeric bicyclic compound, even at $-120\,^{\circ}C$.

The oxazinyl anion *(11)* possesses ambivalent character and can undergo valence isomerization to the oxaazabicyclo[3.1.0]hexenyl anions *(12)*—*(14)*, forming a new sigma bond at the price of two π-electrons. Theory of valence isomerization of heterotropilidenes *(2)*⇌*(3)*[15, 16] clearly favors the "pyrrole oxide" anion *(13)*, whose negative charge is not localized in the three-membered ring and which also forms the highly stable 1-azaallyl anion system[22]. This situation is confirmed by analysis of the molecular orbitals of the reactant *(11)* and the products *(12)*—*(14)*[22] and by calculating the energy profile of the valence isomerizations. Reaction simulation leads to the curve shown in Figure 2. Accordingly, valence isomerization of *(11)* to *(13)* not only requires a lower activation energy than valence isomerization of *(11)* to *(12)* or *(14)*, but the anion *(13)* also has a lower energy than the anions *(11)*, *(12)*, and *(14)*; *i.e.* kinetic and thermodynamic arguments favor formation of *(13)*.

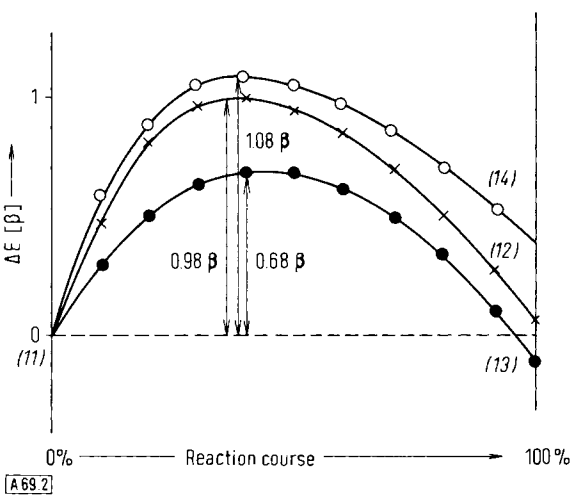


Fig. 2. Electrocyclic ring contraction of the 1,3-oxazinyl anion *(11)*. Energy profile calculation by reaction simulation.

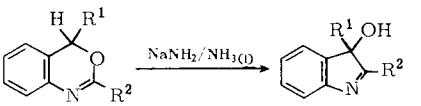
Base treatment of *(10)* affords weakly yellow compounds that are labile in protic media; spectroscopic findings and the molecular orbital calculations mentioned above do indicate the pyrrole oxide structure *(16)*. Moreover, this structure also derives support from the chemical reactions shown in Scheme 1[22]. The action of triethyl phosphite and triphenylphosphane converts *(16)* into the pyrrole *(15)*. In a protic medium, rapid cycloreversion of *(16)* to the imino ketone *(19)* is observed. The latter compound is transformed into 2-pyrrolin-5-one *(18)* on heating[25]; *(18)* can be obtained directly from *(16)* in a thermal reaction, the UV spectrum indicating intermediacy of the imino ketone *(19)*.

Anion *(13)* rearranges to anion *(17)* above $0\,^{\circ}C$[22]; delocalization of the negative charge over five centers to form a resonance system having terminal sites of high electronegativity probably favors this reaction course. Protonation furnishes the less well known 2-pyrrolin-4-ones *(20)*[26].

The low activation energy of the above thermal reactions suggests that they are symmetry-allowed pericyclic processes[27]. The intramolecular nature of the rearrangements *(19)*→*(18)* and *(13)*→*(17)* and the modest dependence of the cycloreversion *(16)*→*(19)* upon pH and substituent effects likewise support this assumption[22, 28].

Oxazines *(10)*, $R^2=H$, devoid of substituents in position 4 furnish unstable aldimino ketones *(19)* by proton-catalyzed ring cleavage of the intermediate pyrrole oxides *(16)*. Dimerization and dehydration leads to azamerocyanines *(21)* ($R^1=C_6H_5$; $\lambda_{max}=456$ nm; $\log\varepsilon=3.82$)[29].

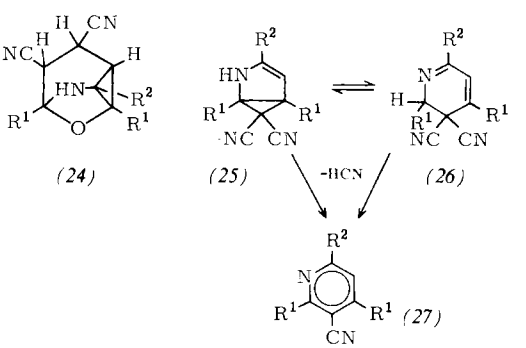
4*H*-3,1-Benzoxazines *(22)* are transformed into 3*H*-indole derivatives *(23)* on base treatment[30]; a common feature of this reaction and the rearrangement *(13)*→*(19)* is the rupture of the C—O bond. Intramolecular rearrangement of the R^2 group does not occur, owing to the energetics of benzoannelation.



(22) *(23)*

Attempts to trap the oxazinyl anion *(11)* or the valence isomers *(12)*—*(14)* by anionic polar cycloaddition[23, 31] with electron deficient olefins lead to interesting reactions. Reaction of *(10)* or *(16)* with fumaronitrile in the presence of butyllithium/THF affords compounds whose spectroscopic data indicate the tricyclic structure *(24)*[28]. Both *(11)* and *(14)* represent potential starting compounds for this anionic cycloaddition.

Under the same conditions, reaction with tetracyanoethylene gives good yields of 2-azabicyclohexenes *(25)*, which exist in solvent-dependent equilibrium with 2,3-dihydropyridines *(26)*[29]. This unusual reaction of tetracyanoethylene[32] is possibly preceded by an oxidation to tetracyanoethylene oxide with the anion *(13)* acting as oxidizing agent; the pyrrolyl anions react with tetracyanoethylene oxide with formal loss of mesoxalonitrile to form the compounds *(25)* and/or *(26)* which eliminate hydrogen cyanide and quantitatively give 3-pyridinecarbonitrile *(27)*[29].



(24) *(25)* *(26)* *(27)*

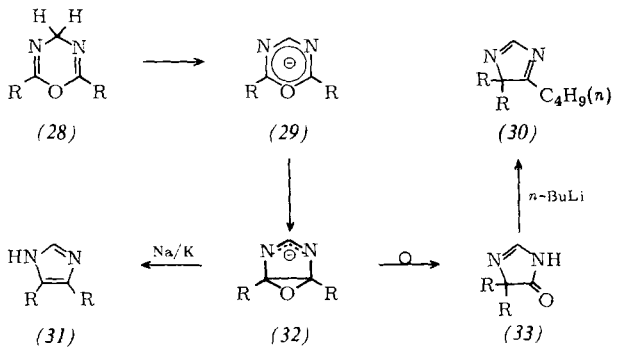
These reactions convey an idea of the high energy content of the oxazinyl anion *(11)* which on protonation undergoes stepwise transformation into the four isomers of greater thermodynamic stability *(16)*, *(18)*, *(19)*, and *(20)*.

The pronounced nucleophilic character of the 8π-system *(11)* is also suspended by a two-electron transfer. Such electron transfer was observed during the action of *(11)* on benzaldehyde. Apart from the products of the base-catalyzed Canizzaro reaction, an excess of benzyl alcohol and, after aqueous work-

up, the hydrolysis product of 1,3-oxazinium salt[24, 28] are obtained.

2.1.2. 1,3,5-Oxadiazinyl Anions

Basically comparable reactions are observed on anion formation from the 4*H*-1,3,5-oxadiazines *(28)*, readily obtained by polar cycloaddition[23] (Scheme 2)[28]. Reaction with *n*-butyllithium in THF at −80 °C proceeds *via* the 1,3,5-oxadiazinyl anion *(29)* and the anion *(32)*, formed especially rapidly owing to its 1,3-diazaallyl anion structure, to give the rearranged imidazolinones *(33)* or the 4*H*-imidazole *(30)* arising therefrom by action of excess *n*-butyllithium; on reaction of *(28)* with Na/K alloy, *(32)* is reduced to the 1*H*-imidazole *(31)*[28]. Thus the additional nitrogen atom favors ring contraction of *(29)* to *(32)* and subsequent reactions, although the charge density at C^2 and C^6 does not differ in anion *(29)*.

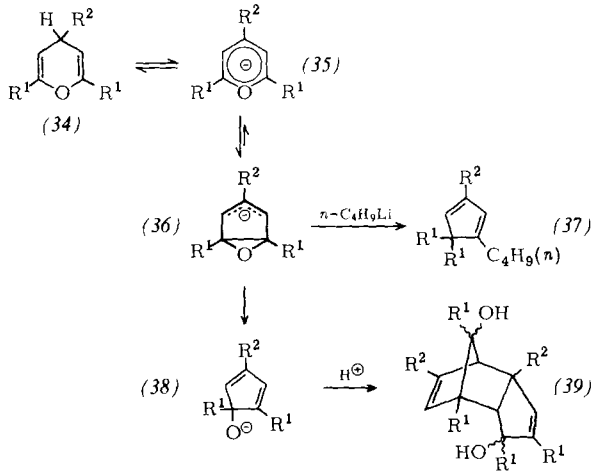


Scheme 2

2.1.3. Pyranyl Anions

How effectively the bicyclic compounds with 1-azaallyl anion or 1,3-diazaallyl anion systems stabilize the negative charge (see Schemes 1 and 2) is underlined by the behavior of 4*H*-pyrans *(34)* towards strong bases[33] (Scheme 3). Action of butyllithium/THF on *(34a)* at −80 to −120 °C produces only slight amounts (less than 3%) of the pyranyl anion *(35a)* as a stable blue-violet solution. A low yield of the cyclopentadiene derivative *(37a)* is formed, presumably *via* the anion *(36a)*, with a large excess of butyllithium. Only on use of lithium diisopropylamide as base is an equilibrium concentration of anion *(35a)* formed (detectable by deuteration). Thence a pK_a value of 37 ± 2 can be deduced for the triphenylated pyran *(34a)*[34, 73].—The 2,6-diphenylated 4*H*-pyran *(34b)* still affords the blue anion *(35b)* with lithium diisopropylamide; it could be detected by deuteration (3—5%). Anion formation from unsubstituted 4*H*-pyran *(34c)* could not be detected even by UV spectroscopy.

This result clearly illustrates the low tendency of 4*H*-pyrans *(34)* to transform into systems formally containing eight π-electrons. This phenomenon is so striking because ring strain and formation of an allyl anion system[35] rule out valence isomerization of *(35)* to *(36)* as an energetic alternative. Only when reaction is carried out at −30 °C and above does the activation energy suffice for irreversible subsequent reactions starting from *(35a)* and *(35b)*; the resulting cyclopentadiene dimers *(39a)* and *(39b)*, respectively, are formed *via* *(38)*.



(a), $R^1 = R^2 = C_6H_5$; *(b)*, $R^1 = C_6H_5$; $R^2 = H$; *(c)*, $R^1 = R^2 = H$;

Scheme 3

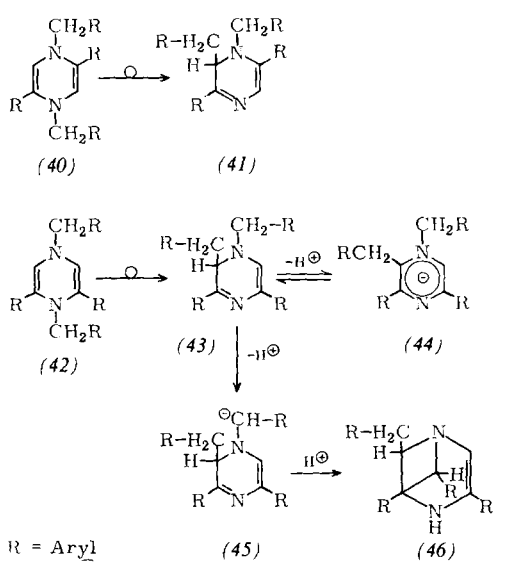
Thus it becomes obvious that these oxepin-analogous anionic systems have only a slight formation tendency and a high reactivity, provided they do not possess any special structural[36], and hence energetic, features. Valence isomerizations affording systems analogous to benzene oxides are directed by electronegative ring members of appropriate ligands.

2.2. Azepine-Analogous Systems

2.2.1. 1,4-Dihydropyrazines and Dihydropyrazinyl Anions

1,4-Dihydropyrazine is isoelectronic with cyclooctatetraene and 1*H*-azepine. As long ago as 1893, *Mason* and *Winder*[37] thought they had synthesized the *N,N'*-dibenzylated 1,4-dihydropyrazines *(40)* and *(42)* (Scheme 4). *Chen* and *Fowler*[38] were able to show, however, that 1,2-dihydropyrazines *(41)* and *(43)* must have been formed. The electronic destabilization of 1,4-dihydropyrazines is clearly removed by a 1,3-rearrangement[39]. This process is probably facilitated by the high migratory aptitude of the benzyl group.

The rearranged compounds *(41)* and *(43)* should be convertible into anionic 8π-systems by the action of bases, leading



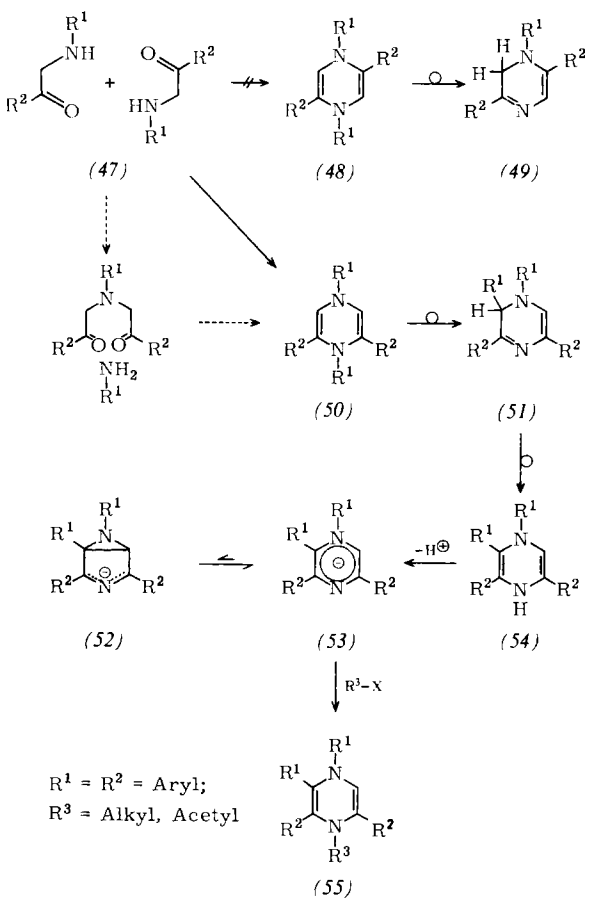
Scheme 4

to loss of the proton attached to the quaternary ring C atom. In fact, treatment of, *e.g. (43)*, with butyllithium initially produces a dark red solution from which a yellow compound isomeric with the starting compound is obtained; however, this product has the diazabicycloheptene structure *(46)*[40].

The color of the reaction solution can be taken as indicating generation of a small amount of the expected dihydropyrazinyl anion *(44)*. However, since the negative charge is not favorably delocalized in a possible subsequent product, no further regrouping occurs. Instead, a benzyl anion system *(45)* is produced in an equilibrium mixture; after intramolecular nucleophilic addition giving *(46)* the negative charge is stabilized in a 1-azaallyl anion.

In order to suppress formation of the benzyl anions *(45)*, an attempt was made to produce the 1,2-dihydropyrazines *(49)* similarly by dimerizing condensation of arylaminoketones *(47)* *via* the 1,4-dihydropyrazines *(48)* (Scheme 5). However, depending upon the aryl substituent, one surprisingly obtains 1,4-dihydropyrazines *(50)* or the 1,4-dihydropyrazines *(54)* by double substituent shift with *(51)* as likely intermediate[40-42].

Formation of *(50)* is due to production of diphenacylaniline from *(47)*. The reason underlying the double rearrangement *(50)* → *(54)* has not yet been established. Steric constraints probably play a crucial role. Regeneration of the 1,4-dihydropyrazine system *(54)* from *(51)* show the formation tendency and thermal stability of the resulting 1,4-dihydropyrazines *(50)* and *(54)* to be fairly high, and synthesis of further 1,4-dihydropyrazines substantiates this conclusion. Thus derivatives of 1,4-dihydropyrazine have been prepared by *Chen* and *Fowler*[43] using electron-withdrawing substituents, by *Sulzbach* and *Iqbal*[44] employing trimethylsilyl substituents, and by *Lown* and *Akhtar*[45] mainly by use of relatively immobile alkyl groups on the two nitrogen atoms. The last-mentioned research group has recently also shown that the 1,3-rearrangement is to be classed as an antara-suprafacial [1,3]-sigmatropic shift[46,47].



Scheme 5

The reason for this unexpected stability can only lie in a special conformation opposing cyclic delocalization of the eight electrons. This was confirmed by X-ray structural analysis of a compound of structure *(50)*[48] (see Figure 3).

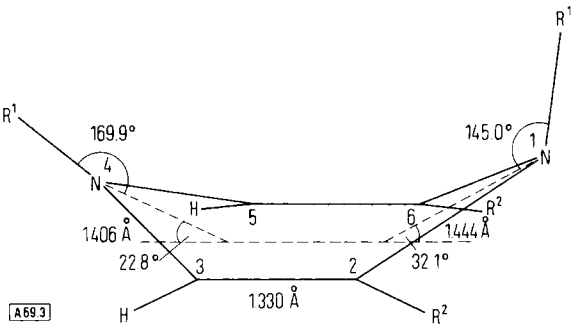
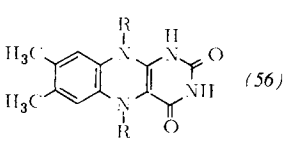


Fig. 3. X-ray data of 1,4-bis(4-chlorophenyl)-2,6-diphenyl-1,4-dihydropyrazine *(50)*, R^1 = 4-chlorophenyl, R^2 = phenyl [48].

According to Figure 3, the four C atoms of the 1,4-dihydropyrazine skeleton form a plane while the two nitrogen atoms (N^1, N^4) are arranged at different distances above this plane; the overall skeleton consequently has a quasi-boat shape. Nevertheless, deviations from planarity are not so pronounced as to largely preclude π- and n-electron delocalization[49]. The position of the aryl ligand on N^1 leads, however, to a separation of the electronic system into a delocalized, possibly homoaromatic system of six π-electrons (C^2, C^3, N^4, C^5, C^6) and an almost orthogonal lone pair on N^1. This structural finding gives grounds for suspecting that six-membered, formally antiaromatic ring systems can counteract electronic destabilization by ligand conformations which substantially reduce or eliminate delocalization of the eight π-electrons. Thus a state is approached such as is attainable only by skeletal bending in the case of eight-membered rings. This ligand-control of stability of 1,4-dihydropyrazines[1,42] should play a greater role than the deviations of the cyclic skeleton from planarity[47,50]. Confirmation of this result is provided by investigations of conformation and nitrogen inversion in 1,5-dihydroisoalloxazines *(56)*—models for dihydroflavin—and is not a consequence of bulky ligands attached to the pyrazine skeleton[51] (see also Section 4).


(56)

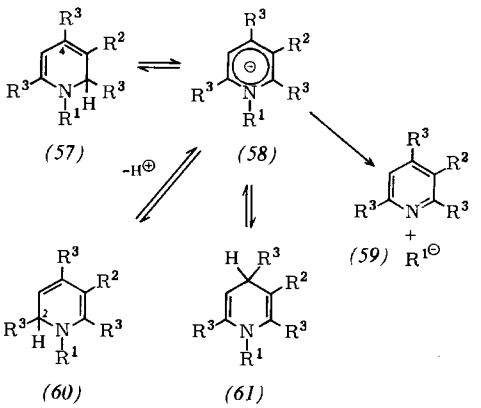
The doubly rearranged *N*-aryl-1,4-dihydropyridines *(54)* (see Scheme 5) are suitable for anion formation. The anions obtained by treatment with strong bases at low temperature are dark red. However, they do not display rearrangement or valence isomerization to form *(52)*. Formation of a 2-azaal-

lyl anion system and the fact that the new σ-bond—as in the case of azepine[15, 16, 52]—is unstable give reason for expecting this finding. The dihydropyrazinyl anions *(53)* undergo *N*-alkylation and *N*-acylation at low temperature; the reaction products are 1,4-dihydropyrazines *(55)*.

2.2.2. Dihydropyridyl and Dihydroquinolyl Anions

The results obtained for the pyrans (see Section 2.1.3) suggest that dihydropyridines[53], having no ligands capable of stabilizing negative charges, will not display any pronounced tendency to form anions. This was also observed (Scheme 6). The triphenylated dihydropyridine *(57a)* could not be demonstrably converted into the anion *(58)*[54] by lithium diisopropylamide at low temperature; *i.e.* the pK_a value of *(57a)* is greater than 40. A comparably low acidity is found for the *N*-dimethylamino-compound *(57b)*; above −20 °C, however, it decomposes irreversibly *via* the anion *(58b)* into lithium dimethylamide and the pyridine derivative *(59b)*.

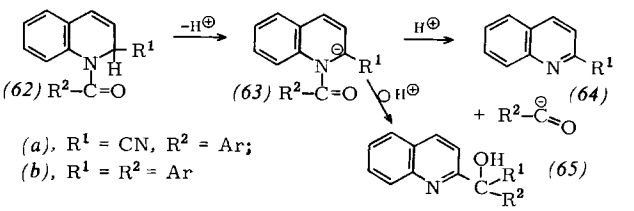
Under drastic reaction conditions the *C*-unsubstituted dihydropyridines *(57c)*, *(57d)*, *(61c)*, and *(61d)* are transformed into the equilibrium mixture by potassium *tert*-butoxide in DMSO at elevated temperature[54, 55]. However, this reaction might proceed with participation of DMSO anion in a multicenter process[56]. Surprisingly *N*-phenyl-1,2-dihydropyridine *(57d)* can also be deprotonated at the methylene group to a slight extent by lithium diisopropylamide in THF at low temperature. The phenyl ligand may play an important part in the reaction.



	R^1	R^2	R^3
(a)	CH_3	H	C_6H_5
(b)	$N(CH_3)_2$	H	C_6H_5
(c)	CH_3	H	H
(d)	C_6H_5	H	H
(e)	CH_3	CN	H
(f)	CH_3	$CON(CH_3)_2$	H

Scheme 6

Annelation of a benzene ring significantly raises the acidity of the dihydropyridine system[57]. This acidification should be especially pronounced in the Reissert compounds *(62a)* when induced by the *N*-acyl and 2-cyano group (Scheme 7). The tendency to regenerate the quinoline system *(64)* [see also the cleavage of *(57b)*] makes the anions *(63)* suitable for use as reagents for nucleophilic acylation. The simplest case would be synthesis of aldehydes with protons. Although aldehydes or their derivatives have not yet been detected during anion formation in protic media[58], an intramolecular nucleophilic acylation has nevertheless been observed. In this way the quinolylmethanols *(65b)* have been obtained from *(62b)*[59].



Scheme 7

Apart from acidification by benzoannelation and by electron-withdrawing ligands at the centers 2, 4, and 6 cumulating negative charge in the anion, results gathered for the 1,3-oxazines and 1,3,5-oxadiazines (Sections 2.1.1 and 2.1.2) have shown that anion formation will be promoted by electron-withdrawing ligands in positions 3 and 5 above all when valence isomerization to a bicyclo[3.1.0]hexenyl anion ensues. Since Nature employs such a system for hydrogen transfer in NADH it seemed logical to examine whether deprotonation and electron transfer should be considered as a valid alternative to the generally accepted hydride transfer mechanism[60].

For this purpose the dihydropyridines *(57e)*, *(60e)*, *(60f)*, *(61e)*, and *(61f)* were treated with lithium diisopropylamide (Scheme 6) and lithium salt formation detected by deuteration and alkylation[54]. It could be unequivocally shown that these lithium salts are not formed by deprotonation at the methylene group and prototropism; instead direct exchange of H^2 occurs with *(60e)*, *(60f)*, *(61e)*, and *(61f)*, and direct exchange of H^4 in the case of *(57e)*. The adjacent location of the nitrile or carboxamide group assists this process by complex formation—a phenomenon that has also been observed in other systems[61]. Hence a further argument is obtained for the hydride transfer mechanism[60]. The very modest tendency to undergo valence isomerization to give a bicyclic system, which is even more pronounced for the dihydropyridyl anions *(58)*, owing to the negative charge and the greater ring strain, than for the azepines should be the principle cause for the very slight inclination to form *(58)*.

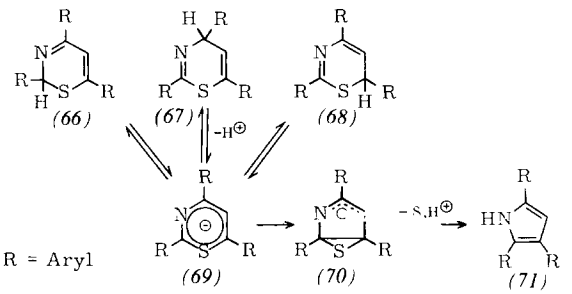
2.3. Systems Analogous to Thiepin

2.3.1. 1,3-Thiazinyl Anions

Thiepin-like six-membered 8π-systems warrant particular attention since they should provide further information about the stability and possible synthesis of the difficultly accessible thiepins[62]. Systems isoelectronic with the thiepins can be obtained in the form of 1,3-thiazinyl anions *(69)* as highly unstable dark violet solutions by the action of strong bases on the 1,3-thiazines *(66)*—*(68)*; however, their reaction products are not the anion *(70)* but the pyrrole *(71)* (Scheme 8)[40, 63]. Indoles are formed in like manner from 4*H*-3,1-benzothiazines by action of a base[64].

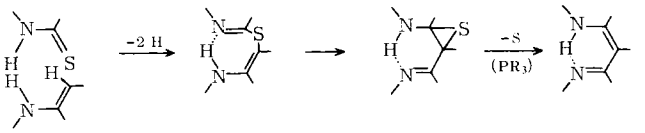
This result accords with expectations. On going from the 1,3-oxazinyl (see Section 2.1.1) to the 1,3-thiazinyl anion, electronic destabilization should increase owing to the lower electronegativity of the sulfur provided the sulfur makes no particular contribution to stabilization of the negative charge[65]. The high associated energy content of *(69)* and the modest

stability of the episulfide bond in the anion *(70)* lead even at very low temperature to a fast irreversible elimination of sulfur. Apparently the thiazinyl anions *(69)* behave like the thiepins, whose synthesis is so difficult precisely because of this rapid desulfuration.



Scheme 8

The charge density distribution (see Figure 4) partly explains the facile intramolecular linkage of a new CC bond. However, consideration of the formally close resemblance of this reaction to the important method of CC bond formation developed by *Eschenmoser*[66] (Scheme 9), which requires a phosphane and generally higher temperature, clearly reveals the high energy content of *(69)* promoting the reaction.



Scheme 9

The thiazinyl anions *(69)* can be obtained as essentially stable solutions below $-100\,°C$. They can be quantitatively deuterated, alkylated, and acylated at $-100\,°C$[28, 41, 63]. Their stability and their ambivalent character depend not only on the base ratio[40, 63, 67] but also on salt additives and above all on added complexing agents for the cations. The reason lies in the presence of more or less intimate ion pairs or free ions. In accord with the charge density distribution (Fig. 4), however, the 6-substituted 6*H*-thiazine *(68)* is the major product. On addition of crown ethers for cation complexation, the free anions are generally transformed quantitatively into the 6-substituted 6*H*-thiazines *(68)*. This is particularly significant for the utilization of *(69)* in synthetic methods[1].

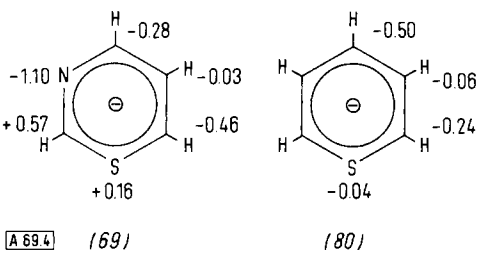
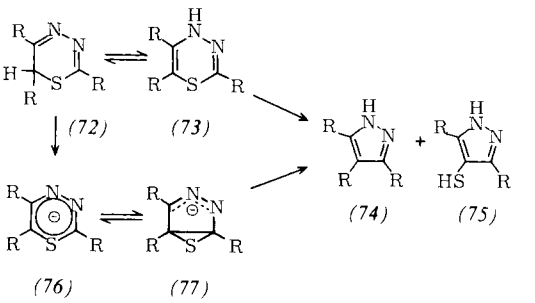


Fig. 4. Charge density calculations for the 1,3-thiazinyl anion *(69)* and the thiopyranyl anion ("thiabenzene anion") *(80)* [68].

2.3.2. Thiadiazinyl Anions

Acid-catalyzed ring contraction of 6*H*-1,3,4-thiadiazines *(72)* generally requires elevated reaction temperatures; sulfur-free pyrazoles *(74)* and 4-pyrazolethiols *(75)* are obtained (Scheme 10)[69]. The high-energy 4*H*-1,3,4-thiadiazines *(73)* occur as intermediates[70].

An analogous result can be accomplished by formation of the anion *(76)* at considerably lower temperatures[70]. Temperature variations indicate that the 1,3-thiazinyl anions *(69)* are not stabilized to the 8π-anion *(76)* by introduction of the additional nitrogen atom in position 4 although MO calculations on *(69)* (see Fig. 4) attribute a large partial negative charge to this center. Anion formation is rate determining; valence isomerization to *(77)* and elimination of sulfur or episulfide ring opening to give *(74)* or *(75)* follow rapidly. The various conditions of pyrazole formation on action of acids and bases show the 1,3,4-thiadiazinyl anions *(76)* to have a very high energy content.



Scheme 10

Synthesis of imidazoles from 4*H*-1,3,5-thiadiazines *via* the corresponding anions proceeds with comparable ease[71].

2.3.3. Thiopyranyl Anions ("Thiabenzene Anions")

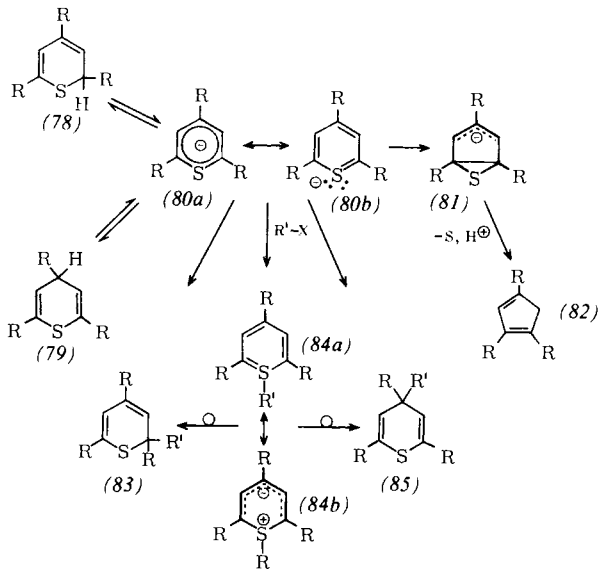
In contrast to the thiazinyl and thiadiazinyl anions, the thiopyranyl anions *(80)* do not possess an electronegative element—apart from the sulfur atom—for acceptance and stabilization of negative charge. Moreover, there is no charge density difference (see Fig. 4) at C^2 and C^6 which would promote formation of a new CC bond to give the anion *(81)*. Irreversible sulfur elimination from *(81)* to yield the low-energy cyclopentadiene *(82)* should nevertheless favor this reaction course.

The thiopyranyl anion *(80)* displays an entirely new behavior on reaction (Scheme 11)[72, 73]. Starting, *e.g.* from the triphenyl substituted thiopyran *(78)* or *(79)*, $R = C_6H_5$, even moderately strong bases lead to a solution of the ambivalent anion *(80)* which is stable in an inert atmosphere and is dark red at room temperature.

Hence a pK_a value of 19.5 ± 1 is derived (see Table 1)[73]. Only on action of triphenylphosphane at room temperature can the sulfur-free cyclopentadiene *(82)* be produced. Deuteration to give 2-deuteriothiopyran *(83)*, $R' = D$, and likewise the alkylation and acylation proceed smoothly, generally affording 4-substituted thiopyrans *(85)*[72]. Reaction with "hard" alkylating reagents particularly at low temperatures (diphenyliodonium salts, methyl fluorosulfate) furnishes a stable red solution which according to UV measurements contains a high proportion of $1\lambda^4$-thiabenzene *(84)*[28, 73].

Thiabenzenes were produced by *Price et al.*[74], *Hortmann et al.*[75], and *Mislow et al.*[76] by another route. Possibly, reaction of *(80)* with electrophiles leads to transient formation of the easily rearrangeable thiabenzenes *(84)* in other cases too. Calculations of charge distribution (see Fig. 4) and investi-

gations on the phosphabenzene anion[77, 98] could provide support for a reaction course of this kind.



Scheme 11

The unexpectedly high acidity of thiopyran, which is also observed for 2*H*-thiochromene and for phosphacyclohexadiene[77-79] and the non-occurrence of spontaneous ring contraction to give cyclopentadiene probably have the following explanation: thiopyranyl anions *(80)* are not cyclic 8π- but cyclic 6π-systems, as shown by the resonance structure *(80b)* having an electron decet and negative charge at the sulfur, *i.e. (80)* is better described as a thiabenzene anion[72]. According to *Dewar*[80], the thiabenzene system is non-aromatic; its energy lies between those of the aromatic 6π and antiaromatic 8π-systems. In this model (see Fig. 5) two orthogonal d-orbitals of the sulfur are delocalized into the π-system, affording a cyanine anion system whose termini lie in the sulfur atom. Other models agree less well with the observations mentioned[74, 75]. Formation of thiabenzenes *(84)* from the thiabenzene anions *(80)* is not entirely compatible with the ylide structure derived for thiabenzenes by *Hortmann et al.*[75] and *Mislow et al.*[76].

The pK_a values and the half-wave potentials in Table 1 clearly demonstrate the anion-stabilizing effect of sulfur atoms, which has been interpreted in various ways. The low-lying d-orbitals[81] or antibonding σ-orbitals[82] might possibly take up the excess electron pair. Since the oxygen and nitrogen atoms do not possess such orbitals the anionic cyclic 8π-system will have a higher energy content in this case.

However, a difference of *ca.* 17 pK_a units between the analogous oxygen and sulfur system is so exceptional[5, 83] that different electronic configurations must be assigned—as suggested—to the two systems. In this context, all available evidence indicates the concept of more or less pronounced cyclic delocalization of eight π-electrons in systems with first-row ring members to be the principal factor. Contrary to expectation, however, the thiazine system is less acidic and the second half-wave potential is more negative than in the corresponding thiopyran system although the more electronegative nitrogen is present as ring member.

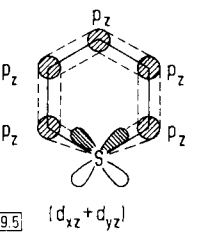


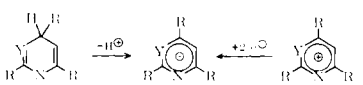
Fig. 5. Model for electronic configuration of thiabenzene according to *Dewar* [80].

3. Seven-Membered Anionic Systems Having Eight π-Electrons

A considerably lower electronic destabilization is expected for seven-membered 8π-systems than for six-membered 8π-systems (see Section 1.1). The cycloheptatrienyl anion[85] and its heptaphenyl derivative[86] were generated a long time ago; they proved to be thermally unstable[12]. Furthermore, unsubstituted cycloheptatriene (having a pK_a value of +36) is far less acidic than cyclopentadiene (pK_a = +18)[85, 87].

In the case of the 4*H*-1,2-diazepines *(86)*, which do not undergo valence isomerization[88], transformation into 1,2-diazepinyl anions *(87)* is again seen to be difficult[17]. Thus on treatment with *n*-butyllithium and *tert*-butyllithium at low temperature, *(86)* does not yield the expected anions *(87)* but products of addition to the C^3N^2 double bond. This is a clear indication of the low acidity of the 4*H*-1,2-diazepines *(86)*. Partial anion formation only becomes possible with lithium diisopropylamide, a compound exhibiting pronounced

Table 1. pK_a values (in THF) [73] and polarographic half-wave potentials (reference electrode, calomel electrode (saturated); solvent, acetonitrile; supporting electrolyte, tetramethylammonium tetrafluoroborate) [28].

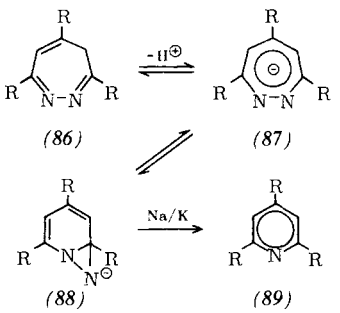


Anion	R	X	Y	pK_a	$E^1_{1/2}$ [V]	$E^2_{1/2}$ [V]
(58a)	C_6H_5	N—CH_3	CH	>40 [a]	—	—
(35a)	C_6H_5	O	CH	37±2 [a]	−0.336	−1.51
Type *(11)*	C_6H_5	O	N	—	−0.015	— [c]
Type *(80a)*	C_6H_5	S	CH	19.5±1 [a, b]	−0.231	−1.31
Type *(69)*	C_6H_5	S	N	22.5±1 [b]	+0.050	−1.37
Type *(80a)*	H	S	CH	32±1 [b]	—	—

[a] Thermodynamic acidity.
[b] Kinetic acidity.
[c] Cyclic voltammetry also field to give a reversible redox potential [84].

steric hindrance; hence it can be deduced that the pK_a value of compounds *(86)* is greater than +30.

In accord with the theory of *Hoffmann*[15] and *Günther*[16] no valence isomerization could be observed on anion formation. Only on coupling with pyridine formation to give *(89)*, *i.e.* by reaction with Na/K alloy, can intermediate valence isomerization be forced to occur. Thus the 1,2-diazepine anions *(87)* behave similarly to *C*-unsubstituted 1*H*-1,2-diazepines, which suffer comparable irreversible changes on heating[89, 90]. Consequently the effect of electronic destabilization on the anions *(87)* cannot be neglected.



(86) *(87)* *(88)* *(89)*

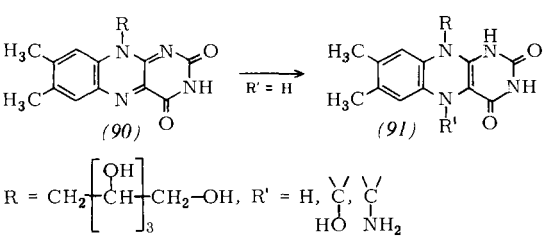
R = Aryl

Apart from the above reactions, seven-membered heterocycles and particularly the intensively studied benzodiazepines exhibit numerous interesting valence isomerizations and rearrangements[91] to which the cyclic delocalization of eight π-electrons must make a significant contribution.

4. Biological Systems

The question of the stability of six-membered heterocycles containing eight delocalizable π-electrons not only possesses purely chemical interest but is also of considerable significance for the transfer of a formal hydride equivalent from the CH substrate onto heteroaromatic coenzymes such as flavin *(90)* and nicotinamide adenine dinucleotide (NADH) and its resolution into one-electron equivalents must necessarily involve a formal 8π intermediate[42, 92].

Flavin coenzyme catalyzed hydrogen transfer from substrates of CH active hydroxy and amino compounds leads to products of addition to the 1,4-diazadiene system of oxidized flavin *(90)*. In this reaction a 1,4-dihydropyrazine system is generated transiently in the dihydroflavin *(91)*, which is transformed into oxidized flavin and a carbonyl compound

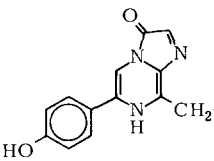


(90) *(91)*

R = CH_2–[CH(OH)]$_3$–CH_2–OH, R' = H, C(OH)(HO)(C(NH$_2$)(NH$_2$))

by dehydrogenation[92]. As in the 1,4-dihydropyrazines (Section 2.2.1), the stability of *(91)* is largely dependent on the planarity and especially on the positions[51, 93] of the *N*- and *N'*-ligands. In this way the wide range of potentials open to the flavoproteins is subject to control—which is of particular biological significance[51, 92]. In addition, a possible explanation of the surprisingly high O_2 affinity of such potentially antiaromatic systems is suggested: reaction of organic singlet compounds with triplet oxygen is known to be spin-forbidden and is therefore slow provided it does not proceed *via* radicals. However, radicals have never been observed in biological flavin-dependent O_2 activation[92, 94].

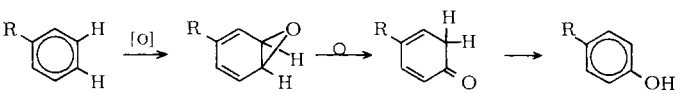
Some bioluminescing organisms contain luciferins which formally display cyclic 8π-systems[95]. As an example we can consider the luciferin *(92)* from *Renilla reniformis*. It has not yet been established, however, whether the dihydropyrazine system possesses specific biological significance for the luminescence property beyond its enhanced electron donor character.



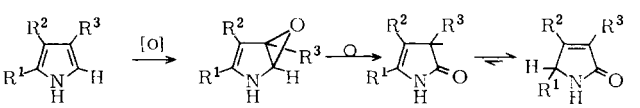
(92)

In dihydronicotinamide, NADH possesses a system which could transform into a cyclic 8π-system *via* deprotonation. Studies performed on model compounds (see Section 2.2.2) nevertheless suggest that such a reaction fails to occur, owing to the high energy of the dihydropyridyl anion, and direct hydride transfer to the substrate with formation of NAD^+ is unequivocally favored, *i.e.* the carboxamide group in position 3 stabilizes the labile dihydropyridine.

Studies on the benzene oxide-oxepin problem acquired a new dimension when it was discovered that the oxidative metabolism of arenes proceeds *via* benzene oxide-oxepin intermediates (see Scheme 12)[96, 97]. Recently, *Frydmann et al.*[98, 99] found that the enzymatic oxidation of porphobi-

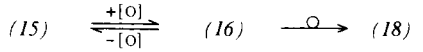


Scheme 12



(93) *(94)* *(95a)* *(95b)*

$R^1 = CH_2NH_2$, $R^2 = CH_2$–COOH, $R^3 = CH_2$–CH_2–COOH



(15) *(16)* *(18)*

linogen *(93)*, the key intermediate in porphyrin and corrin syntheses, leads to the tautomeric pyrrolinones *(95a)* and/or *(95b)*. Comparison of this reaction with the enzymatic oxidation of arenes reveals a close structural analogy. It seems obvious to conclude that the pyrrole oxide *(94)* is the reaction intermediate[100]. Supporting evidence comes from the rearrangements observed with the 1,3-oxazinyl anion *(11)*. Facile rearrangement of the pyrrole oxides *(16)* to the pyrrolinone *(18)* related to *(95)* and the possible reduction of *(16)* to the pyrroles *(15)* follow parallel courses (Section 2.1.1). The marked hydrolytic lability of the pyrrole oxides *(16)* and *(94)* in comparison with the benzene oxides will disfavor direct detection of *(94)* as an intermediate of porphobilinogen oxidation.

5. Summary and Outlook

Available factual material shows: negatively charged six-membered and presumably also seven-membered cyclic 8π-systems are destabilized by resonance if the ring is composed of first row atoms. Destabilization is manifested in reduced acidity of the starting materials and enhanced reactivity of the anions. The thiopyranyl and phosphabenzene anion show that ring members from the second row can, at least partly, accommodate the excess electron pair in a low-lying orbital. The overall system thus experiences considerable stabilization. A significant role in determining the observed reactions is played by electron-withdrawing sites in or attached to the ring. In the specific case of uncharged six-membered cyclic 8π-systems, of which only 1,4-dihydropyrazine has been considered in this article, electronic destabilization is probably reduced by ring deformations and particular ligand conformations.

The more or less enhanced energy content of these systems permits surprising valence isomerizations, rearrangements, fragmentations, and reactions with electrophiles at very low temperatures. Only few of the resulting preparative pathways have so far been implemented. Furthermore, anion formation and the reactivity of the resulting anions have not yet been examined in many cases. Nor has any work been done on the possible stabilization of these systems by transition metals. The occurrence of special ring inversion barriers could be important in the future investigation of spectroscopic properties[51, 101].

Some of these systems are excellent models for biologically relevant systems. Further model studies should help us to answer questions of electron-transfer properties and proclivity to radical formation, as well as those concerning the influence of ligands and conformations on redox properties, to mention just a few.

I am particularly indebted to my co-workers mentioned in the bibliography for their assistance in the investigations described, to Prof. R. Gleiter and Prof. P. Hemmerich for stimulating discussions, and the Gesellschaft Deutscher Chemiker for their recognition of these studies. Thanks are also due to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

Received: December 30, 1974 [A 69 IE]
German version: Angew. Chem. 87, 603 (1975)

---

[1] Based on a lecture delivered at the Chemiedozententagung, Stuttgart, April 1974.—Heterocyclic 8π-Systems, Part 9.—Part 8: ref. [42].

[2] *B. A. Hess* and *L. J. Schaad*, J. Amer. Chem. Soc. *93*, 305, 2413 (1971); J. Org. Chem. *36*, 3418 (1971); *L. J. Schaad* and *B. A. Hess*, J. Amer. Chem. Soc. *94*, 3068 (1972); *B. A. Hess, L. J. Schaad*, and *C. W. Holyoke*, Tetrahedron *28*, 3657, 5299 (1972).

[3] *G. Maier*, Angew. Chem. *86*, 491 (1974); Angew. Chem. internat. Edit. *13*, 425 (1974).

[4] *R. Breslow*, Accounts Chem. Res. *6*, 393 (1973); Pure Appl. Chem. *28*, 111 (1971), and literature cited therein.

[5] *R. Breslow*, Angew. Chem. *80*, 573 (1968); Angew. Chem. internat. Edit. *7*, 565 (1968).

[6] *M. J. S. Dewar*, Angew. Chem. *83*, 859 (1971); Angew. Chem. internat. Edit. *10*, 761 (1971); *M. J. S. Dewar, M. C. Kolm*, and *N. Trinajstić*, J. Amer. Chem. Soc. *93*, 3437 (1971).

[7] *J. F. Labarre* and *F. Crasnier*, Fortschr. Chem. Forsch. *24*, 33 (1971).

[8] *G. Binsch*, Naturwissenschaften *60*, 369 (1973).

[9] *E. Heilbronner*, Lecture at the Chemiedozententagung, Universität Stuttgart, April 1974.

[10] *R. A. Raphael* in *D. Ginsburg*: Nonbenzenoid Aromatic Compounds. Interscience, New York 1959, p. 465; *G. Schröder*: Cyclooctatetraen. Verlag Chemie, Weinheim 1965.

[11] *I. L. Karle*, J. Chem. Phys. *20*, 65 (1952).

[12] *K. Hafner*, Angew. Chem. *75*, 1041 (1963); Angew. Chem. internat. Edit. *3*, 165 (1964).

[13] Surveys: *E. Vogel* and *H. Günther*, Angew. Chem. *79*, 429 (1967); Angew. Chem. internat. Edit. *6*, 385 (1967); *G. Maier*, Angew. Chem. *79*, 446 (1967); Angew. Chem. internat. Edit. *6*, 402 (1967); *L. A. Paquette*, Angew. Chem. *83*, 11 (1971); Angew. Chem. internat. Edit. *10*, 11 (1971); *H. Kessler* in Houben-Weyl-Müller: Methoden der organischen Chemie. 4th Edit., Thieme, Stuttgart, Vol. V/1, p. 305.

[14] *I. C. Paul, S. M. Johnson, L. A. Paquette, J. H. Barrett*, and *R. J. Haluska*, J. Amer. Chem. Soc. *90*, 5023 (1968); *L. A. Paquette* in *P. Snyder*: Nonbenzenoid Aromatics. Academic Press, New York 1969, pp. 259ff.

[15] *R. Hoffmann*, Tetrahedron Lett. *1970*, 2907; *R. Hoffmann* and *W. D. Stohrer*, J. Amer. Chem. Soc. *93*, 6941 (1971).

[16] *H. Günther*, Tetrahedron Lett. *1970*, 5173; *H. Günther, J. B. Pawliczek, B. D. Tunggal, H. Prinzbach*, and *R. H. Levin*, Chem. Ber. *106*, 984 (1973).

[17] *R. R. Schmidt* and *H. Vatter*, Tetrahedron Lett. *1972*, 4891.

[18] *H. U. Wagner*, Universität München, personal communication, see also refs. [15, 16].

[19] *W. D. Hobey*, J. Org. Chem. *37*, 1137 (1972).

[20] The author has reported on this in several lectures, the first time on June 14, 1971, Chemisches Kolloquium, Universität München.

[21] *R. R. Schmidt*, Angew. Chem. *83*, 622 (1971); Angew. Chem. internat. Edit. *10*, 572 (1971).

[22] *R. R. Schmidt, W. J. W. Mayer*, and *H. U. Wagner*, Liebigs Ann. Chem. *1973*, 2010.

[23] *R. R. Schmidt*, Angew. Chem. *85*, 235 (1973); Angew. Chem. internat. Edit. *12*, 212 (1973).

[24] *R. R. Schmidt*, Synthesis *1972*, 333.

[25] *R. Japp* and *J. Klingemann*, J. Chem. Soc. *57*, 692 (1890).

[26] *G. Rio* and *D. Masure*, Bull. Soc. Chim. Fr. *1972*, 4598.

[27] *R. B. Woodward* and *R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).

[28] *R. R. Schmidt*, unpublished investigations.

[29] *R. R. Schmidt* and *H. Huth*, unpublished investigations.

[30] *D. Lednicer* and *D. E. Emmett*, J. Heterocyl. Chem. *7*, 575 (1970).

[31] *Th. Kauffmann*, Angew. Chem. *86*, 715 (1974); Angew. Chem. internat. Edit. *13*, 627 (1974).

[32] *P. Laszlo*, Tetrahedron Lett. *1972*, 3625.

[33] *R. R. Schmidt* and *R. Prewo*, unpublished investigations.

[34] See *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965.

[35] Difference in resonance energy between the allyl- and 1-azaallyl anion: *ca.* 0.5β [22].

[36] *S. V. Krivun, S. N. Baranov*, and *O. F. Voziyanova*, Zh. Obshch. Khim. *43*, 359 (1973).

[37] *A. T. Mason* and *G. R. Winder*, J. Chem. Soc. *63*, 1355 (1893).

[38] *S.-J. Chen* and *F. W. Fowler*, J. Org. Chem. *35*, 3987 (1970).

[39] A comparable stabilization process has also been observed in an *N*-alkylated azepine: *K. Hafner*, Technische Hochschule Darmstadt, personal communication.

[40] *M. Dimmler*, Diplomarbeit, Universität Stuttgart 1971; *R. R. Schmidt* and *M. Dimmler*, to be published.

[41] *M. Dimmler*, Dissertation, Universität Stuttgart 1974.

[42] *R. R. Schmidt, M. Dimmler*, and *P. Hemmerich*, to be published.

[43] *S.-J. Chen* and *F. W. Fowler*, J. Org. Chem. *36*, 4025 (1971).

[44] *R. A. Sulzbach* and *A. F. Iqbal*, Angew. Chem. *83*, 145 (1971); Angew. Chem. internat. Edit. *10*, 127 (1971).

[45] *J. W. Lown* and *M. H. Akhtar*, J. C. S. Chem. Comm. *1972*, 829; J. C. S. Perkin I *1973*, 683.

[46] *J. W. Lown* and *M. H. Akhtar*, J. C. S. Chem. Comm. *1973*, 511.

[47] *J. W. Lown, M. H. Akhtar*, and *R. S. McDaniel*, J. Org. Chem. *39*, 1998 (1974).

[48] *J. Stezowski*, Crystal Struct. Commun., in press.

[49] *E. Heilbronner* and *H. Bock*: Das HMO-Modell und seine Anwendung—Grundlagen und Handhabung. Verlag Chemie, Weinheim 1968, p. 285.

[50] *H. Kohn* and *R. A. Olofson*, J. Org. Chem. *37*, 3504 (1972).

[51] *L. Tauscher, S. Ghisla*, and *P. Hemmerich*, Helv. Chim. Acta *56*, 630 (1973).

[52] *W. D. Stohrer*, Chem. Ber. *106*, 970 (1973).

[53] Review on dihydropyridines: *U. Eisner* and *J. Kuthan*, Chem. Rev. *72*, 1 (1972).

[54] *R. R. Schmidt* and *G. Berger*, to be published.

[55] *F. W. Fowler*, J. Amer. Chem. Soc. *94*, 5926 (1972).

[56] Radical components could not be detected by ESR spectroscopy; see *B. Schroeder, W. P. Neumann, J. Hollaender*, and *H. P. Becker*, Angew. Chem. *84*, 894 (1972); Angew. Chem. internat. Edit. *11*, 850 (1972).

[57] *R. R. Schmidt, J. Talbiersky*, and *H. von Benda*, unpublished experiments.
[58] *F. D. Popp*, Advan. Heterocycl. Chem. *9*, 1 (1968).
[59] *C. E. Crawforth* and *O. Meth-Cohn*, J. C. S. Chem. Comm. *1972*, 865.
[60] *K. Wallenfels, W. Ertel*, and *K. Friedrich*, Liebigs Ann. Chem. *1973*, 1663, and references cited therein.
[61] *P. Puck, R. Gleiter*, and *G. Köbrich*, Chem. Ber. *103*, 1431 (1970), and references cited therein.
[62] *L. Field* and *D. L. Tulem* in *A. Weissberger* and *E. C. Taylor*: The Chemistry of Heterocyclic Compounds. Wiley, New York 1972, Vol. 26, p. 574.
[63] *R. R. Schmidt* and *M. Dimmler*, Chem. Ber. *107*, 3800 (1974).
[64] *D. Lednicer* and *D. E. Emmert*, J. Heterocycl. Chem. *8*, 903 (1971).
[65] Owing to the pronounced acidifying effect of divalent sulfur, however, this has to be assumed in many cases: see *D. Seebach*, Angew. Chem. *81*, 690 (1969); Angew. Chem. internat. Edit. *8*, 639 (1969); Synthesis *1969*, 17.
[66] *Y. Yamada, D. Diljbovic, P. Wehrli, B. Golding, P. Löliger, R. Keese, K. Müllen*, and *A. Eschenmoser*, Angew. Chem. *81*, 301 (1969); Angew. Chem. internat. Edit. *8*, 343 (1969).
[67] Pyrrole formation is promoted by nucleophilic attack of the base at the episulfide atom; see also *B. M. Trost* and *S. D. Ziman*, J. Org. Chem. *38*, 933 (1973).
[68] Calculations by the extended Hückel method without 3d-orbital participation: *R. Gleiter*, Technische Hochschule Darmstadt.
[69] *H. Beyer*, Z. Chem. *9*, 361 (1969), and references cited therein; *H. Beyer, H. Honeck*, and *L. Reichelt*, Liebigs Ann. Chem. *741*, 45 (1970).
[70] *R. R. Schmidt* and *H. Huth*, Tetrahedron Lett., in press.
[71] *C. Giordano*, personal communication.
[72] *R. R. Schmidt* and *U. Burkert*, Tetrahedron Lett. *1973*, 4355.
[73] *U. Burkert*, Dissertation, Universität Stuttgart 1974.
[74] *M. Polk, M. Siskin*, and *C. C. Price*, J. Amer. Chem. Soc. *91*, 1206 (1969), and references cited therein.
[75] *A. G. Hortmann* and *R. L. Harris*, J. Amer. Chem. Soc. *92*, 1803 (1970).
[76] *G. H. Senkler, J. Stackhouse, B. E. Maryanott*, and *K. Mislow*, J. Amer. Chem. Soc. *96*, 5648 (1974), and references cited therein.
[77] *G. Märkl* and *A. Merz*, Tetrahedron Lett. *1971*, 1215.
[78] *K. Dimroth*, Fortschr. Chem. Forsch. *38*, 1 (1973).
[79] *I. Murata, T. Tatsuoka*, and *Y. Sugihara*, Tetrahedron Lett. *1973*, 4261; Angew. Chem. *86*, 161 (1974); Angew. Chem. internat. Edit. *13*, 142 (1974).
[80] *M. J. S. Dewar*: The Molecular Orbital Theory of Organic Chemistry. McGraw-Hill, New York 1969, pp. 430—436.
[81] *W. G. Salmond*, Quart. Rev. (Chem. Soc.) *22*, 253 (1968); *R. Gleiter* and *R. Hoffmann*, Tetrahedron *24*, 5899 (1968), and references cited therein.
[82] *S. Wolfe, A. Rank*, and *I. G. Csizmadia*, J. Amer. Chem. Soc. *91*, 1567 (1969); *N. D. Epiotis, F. Bernardi*, and *S. Wolfe*, VI. International Symposium on Sulphur Chemistry, Bangor, July 1974.
[83] *S. Oae, W. Tagaki*, and *A. Ohno*, Tetrahedron *20*, 417 (1964); *R. L. Slaugh* and *E. Bergman*, J. Org. Chem. *26*, 3158 (1961); *R. Breslow* and *E. Mohacsi*, J. Amer. Chem. Soc. *85*, 431 (1963).
[84] We are grateful to Professor Dr. *S. Hünig*, Universität Würzburg, for performing these studies.
[85] *H. J. Dauben* and *M. Rifi*, J. Amer. Chem. Soc. *85*, 3041 (1963).
[86] *R. Breslow* and *H. W. Chang*, J. Amer. Chem. Soc. *84*, 1484 (1962).
[87] *R. Breslow* and *K. Balasubramanian*, J. Amer. Chem. Soc. *91*, 5182 (1969); *R. Breslow* and *W. Chu, ibid. 92*, 2165 (1970); *95*, 411 (1973).
[88] *O. Buchardt, C. L. Pedersen, U. Svanholm, A. M. Duffield*, and *A. T. Balaban*, Acta Chem. Scand. *23*, 3125 (1969).
[89] *R. Allmann, A. Frankowski*, and *J. Streith*, Tetrahedron *28*, 581 (1972).
[90] *J. Streith, J. P. Luttringer*, and *M. Nastasi*, J. Org. Chem. *36*, 2962 (1971).
[91] *N. W. Gilman, J. F. Blount*, and *L. H. Sternbach*, J. Org. Chem. *37*, 3201 (1972); *A. Nabeya, K. Kurita*, and *J. A. Moore, ibid. 38*, 2954 (1973), and references cited therein.
[92] *P. Hemmerich* and *M. Schumann-Jorns* in: Enzymes: Structure and Function. FEBS-Symposia, Amsterdam, North Holland 1972, Vol. 29, p. 95.
[93] *R. Norrestam, M. von Glehn, L. O. Hagmann*, and *P. Kierkegaard*, Acta Chem. Scand. *23*, 2199 (1969), and references cited therein.
[94] *V. Massey* and *P. Hemmerich* in *P. D. Boyer*: The Enzymes. Third Edition, Volume on Oxidation and Reduction. Academic Press, New York, in press.
[95] *W. Adam*, Chem. Uns. Zeit *7*, 182 (1973); *K. Hori, J. E. Wampter*, and *J. M. Cornier*, J. C. S. Chem. Comm. *1973*, 492; *F. McCapra* and *M. J. Manning, ibid. 1973*, 467.
[96] *H. J. Altenbach* and *E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. internat. Edit. *11*, 937 (1972).
[97] *D. M. Jerina, H. Yagi*, and *J. W. Dally*, Heterocycles *1*, 267 (1973).
[98] *R. B. Frydman, M. L. Tomaro, A. Wanschelbaum*, and *B. Frydman*, FEBS Lett. *26*, 203 (1972); *M. L. Tomaro, R. B. Frydman*, and *B. Frydman*, Biochemistry *12*, 5263 (1973).
[99] *R. B. Frydman, M. L. Tomaro, A. Wanschelbaum, E. M. Andersen, J. Awruch*, and *B. Frydman*, Biochemistry *12*, 5253 (1973).
[100] *R. R. Schmidt*, Lecture, Chemisches Kolloquium, Universität Würzburg, November 1973; see ref. [99].
[101] *C. J. Finder, D. Chung*, and *N. L. Allinger*, Tetrahedron Lett. *1972*, 4677.

The Pyruvate Dehydrogenase Multienzyme Complex

By Ferdinand Hucho[*]

The three enzymes pyruvate dehydrogenase, dihydrolipoamide transacetylase, and dihydrolipoamide dehydrogenase constitute the pyruvate dehydrogenase multienzyme complex of *E. coli*; in mammals the complex also contains a kinase and a phosphatase. Multienzyme complexes are structural, functional, and regulatory units enabling the organism to operate more economically than with single enzymes. The pyruvate dehydrogenase multienzyme complex may stand at the switch-point between energy metabolism and gluconeogenesis.

1. Introduction

Multienzyme complexes are proteins in which several noncovalently bonded enzymes in constant relative amounts form a stable and highly ordered association. The enzyme constituents of the complex often catalyze successive steps in a metabolic sequence. Multienzyme complexes occupy an intermediate position between cooperating but structurally independent "soluble" enzymes on the one hand and membrane-bound insoluble enzyme systems on the other, and can thus serve as models for both groups. Typical examples from the group of structurally independent soluble enzyme systems are the enzymes of glycolysis or of the tricarboxylic acid cycle, while the insoluble enzymes include the respiratory chain proteins of the mitochondrial membrane or the photosynthesis proteins of the chloroplast membrane. Examples of multienzyme complexes are the α-keto acid dehydrogenases, fatty acid synthetase, and the enzyme complexes that take part in the synthesis of aromatic amino acids.

[*] Univ.-Doz. Dr. F. Hucho
Fachbereich Biologie der Universität
D-2775 Konstanz, Postfach 733 (Germany)

The boundary between the three groups is not sharp. Even though the number of multienzyme complexes discovered so far is limited, we can speculate that some of the "soluble enzymes" do not occur wholly disordered in the cell but

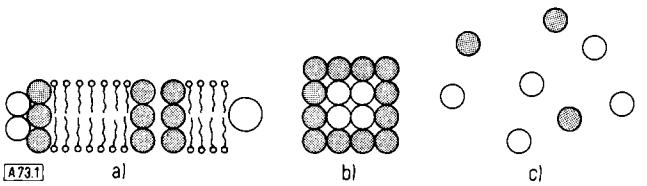


Fig. 1. Multienzyme complexes (b) as a state between membrane-bound (a) and "soluble" enzymes (c).

form complexes with other enzymes[1, 2]. Less stable complexes are probably destroyed by the classical methods of protein purification. Conversely, it cannot be ruled out that some enzymes occurring separately in the cell aggregate during isolation, so that the purified multienzyme complex is an artefact (see Section 5.1).

Multienzyme complexes are structural, functional, and probably also regulatory units made up of several enzymes. Their investigation can help in particular in the solution of the following problems:

1) How are structures of higher order built up from protein molecules?

2) How do enzymes that catalyze successive steps in a metabolic process cooperate?

3) How is the activity of a system of several enzymes regulated in the cell?

Pyruvate dehydrogenase will be discussed here with reference to these aspects. Three enzymes are directly involved in the oxidation of pyruvic acid in mitochondria (Fig. 2): pyruvate dehydrogenase (E_1), dihydrolipoamide transacetylase (E_2), and dihydrolipoamide dehydrogenase (E_3) which is a flavoprotein[3][*].

They catalyze the reaction

$$CH_3—CO—COOH + NAD^+ + HS—CoA \rightarrow CH_3—CO—S—CoA + CO_2 + NADH + H^+ \quad (1)$$

which occurs in several steps (see Sections 3.1—3.3)[4]:

$$\text{Pyruvate} + \text{TPP-}E_1 \rightarrow CO_2 + \text{Hydroxyethyl-TPP-}E_1 \quad (2)$$

$$\text{Hydroxyethyl-TPP-}E_1 + \text{Lipoyl-}E_2 \rightarrow \text{S-Acetyldihydrolipoyl-}E_2 + \text{TPP-}E_1 \quad (3)$$

$$\text{S-Acetyldihydrolipoyl-}E_2 + \text{CoA} \rightarrow \text{Acetyl-CoA} + \text{Dihydrolipoyl-}E_2 \quad (4)$$

$$\text{Dihydrolipoyl-}E_2 + \text{FAD-}E_3 \rightarrow \text{Lipoyl-}E_2 + \text{reduced FAD-}E_3 \quad (5)$$

$$\text{Reduced FAD-}E_3 + NAD^+ \rightarrow NADH + H^+ + \text{FAD-}E_3 \quad (6)$$

The three enzymes, plus two more in higher organisms (see Section 4.5), form the pyruvate dehydrogenase multienzyme complex. The object of the present review is to demonstrate that E_1, E_2, and E_3 in the multienzyme complex form a structural, functional, and regulatory unit in accord with the criteria set out above.

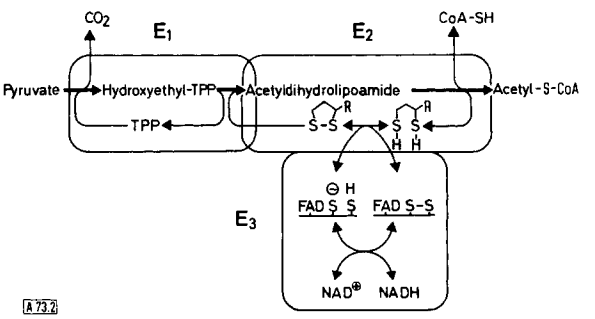


Fig. 2. Schematic representation of the pyruvate dehydrogenase multienzyme complex (for explanation see text). E_1 = pyruvate dehydrogenase: E_2 = dihydrolipoamide transacetylase, E_3 = dihydrolipoamide dehydrogenase. In the formulas under "Acetyldihydrolipoamide", left, lipoamide; right, dihyrolipoamide; $R = (CH_2)_4CONH_2$.

Table 1. Properties of pyruvate dehydrogenase multienzyme complexes.

Organisms	Polypeptide chains						Electron microscopy				Ref.
	E_1		E_2		E_3		Mol. wt. of	Diameter [Å] of		Geometry of	
	Number	Mol. wt.	Number	Mol. wt.	Number	Mol. wt.	the complex	the complex	E_2	E_2	
Mammals [a]	α 60 β 60	41000 36000	60	52000	10—12	55000	7.6×10^6	400—450	210	pentagonal dodecahedron	[45, 46, 74]
Yeast [b]	?	100000	?	80000	?	61000	5×10^6— 7.4×10^6	350	220	pentagonal dodecahedron	[12]
Neurospora crassa [c]										pentagonal dodecahedron	[9, 10]
E. coli [d]	16	96000	16	80000	16	54000	3.75×10^6	300—430		cube	[27, 28]
	24	100000	24	78000	12	56000	4.6×10^6				[26]
Azotobacter [e]										cube	[7]

[a] In addition to E_1, E_2, and E_3 the complex contains a kinase and a phosphatase (interconversion).
[b] Interconversion not detectable.
[c] Interconversion demonstrated for strain L74.
[d] No interconversion.
[e] Complex may contain phosphotransacetylase.

[*] Abbreviations:
E_1: Pyruvate dehydrogenase (EC 1.2.4.1)
E_2: Dihydrolipoamide transacetylase (EC 2.3.1.12)
E_3: Dihydrolipoamide dehydrogenase (EC 1.6.4.3)
TPP: Thiamine pyrophosphate
CoA: Coenzyme A
FAD: Flavin adenine dinucleotide
NAD^+, NADH: Nicotinamide adenine dinucleotide, oxidized and reduced forms.

Pyruvate dehydrogenase multienzyme complexes have been isolated from numerous organisms, *e. g.* from *Escherichia coli*[5, 6], *Azotobacter*[7], *Streptococcus*[8], *Neurospora crassa*[9, 10], Yeast[11-13], potatoes[14], pigeon breast muscle[15-18], skin fibroblasts[19], and several mammalian organs[20-24] (Table 1). This review is restricted to the enzymes from *E. coli* and from mammals, since these have been particularly thoroughly investigated.

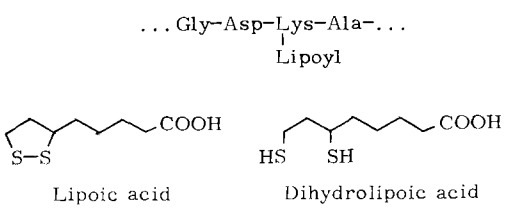
2. Composition and Structure of the Pyruvate Dehydrogenase Multienzyme Complex

2.1. The Multienzyme Complex from *Escherichia coli*

By definition, multienzyme complexes contain the component enzymes in definite and constant proportions. The numerical relationships are determined by the complex geometry. Conversely, if one wishes to obtain an idea of the geometric structure of the complex one must determine the proportions of the constituent enzymes and the number of the subunits. The rate of synthesis, controlled by the genome, of the various polypeptide chains must be suited to the geometric demands of the complex if the cell is not to produce an "excess" of polypeptide chains. Knowledge of the stoichiometry of the complex is thus as important for the question of genetic control of the synthesis of the constituent enzymes as it is for questions concerning structure and function. The experimental findings on this point still fail to give a uniform picture:

It was first postulated that the complex from *E. coli* contained the polypeptide chains of the three constituent enzymes in the ratio of 1 : 1 : 1, 24 polypeptide chains of each enzyme[25]. However, a later analysis gave the ratio as 1 : 1 : 0.5[26], *i.e.* two polypeptide chains of E_1 and E_2 were found for each polypeptide chain of the flavoprotein E_3; the molecular weight of the complete complex was given as 4.6×10^6 dalton[26]. Other authors confirmed the ratio of 1 : 1 : 1, but found only 16 polypeptide chains for each enzyme, and therefore only 3.75×10^6 dalton as the molecular weight of the complex[27,28][*]. Small-angle X-ray scattering confirms this value[29,29a]. The discrepancy may be due to use of different bacterial strains.

The native enzymes E_1[26,30] and E_3[26,31,32] are dimeric. The molecular weights of the constituent enzymes E_1, E_2, and E_3 are respectively 100000, 80000, and 56000 dalton [26–28,30,31]. The multienzyme complex contains, besides the three enzymes, six cofactors: TPP, Mg^{2+}, lipoic acid, coenzyme A, FAD, and NAD^+[25,34]. One of these, lipoic acid, is bonded covalently to the protein through the ε-amino group of a lysine residue[35,36]. This amide bond is formed enzymatically, with consumption of ATP, in the presence of an enzyme isolated from *E. coli* and *Streptococcus*[37]. A further enzyme, a lipoamidase[38,39], effects the hydrolytic removal of the lipoic acid from the protein. The amino-acid sequence in the neighborhood of the lipoic acid[40] clearly differs from that at the lipoic acid bonding site of the otherwise very similar α-ketoglutaric acid dehydrogenase multienzyme complex.



Biochemical and electron-microscopic investigations, in particular those by *Reed*'s group at the University of Texas, have shown that the multienzyme complex has an ordered symmetric structure. The information about this structure is contained in the primary structure of the constituent enzymes, for if the complex is decomposed and the purified enzymes E_1, E_2, and E_3 are brought together then, *in vitro* and spontaneously (*i.e.* without the help of a further biological factor in the cell) they form an active complex of almost unchanged structure and activity[5,33,41]. Furthermore, E_2 can be split reversibly into its subunits[42]. Such reconstitution experiments are important for understanding the processes that afford complicated cell structures from simple building units; they show that not only the secondary and tertiary structure but also the quaternary structure and structures of higher order, such as multienzyme complexes, are determined by primary structure of the protein.

E_1 and E_3 do not associate with one another, yet both are bound by E_2[5]. The dihydrolipoamide transacetylase (E_2) appears to exert a structure-forming function as well as a catalytic function. It forms the nucleus of the complex, being surrounded by E_1 and E_3 subunits.

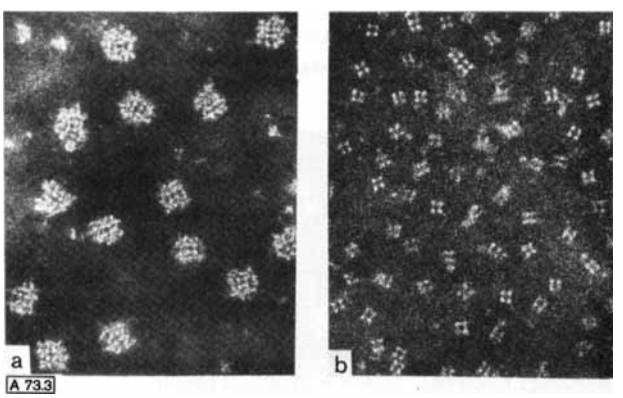


Fig. 3. Electron micrographs of (a) pyruvate dehydrogenase multienzyme complex and (b) dihydrolipoamide transacetylase (E_2) from *E. coli*. Magnification 200000 [43].

The impressive electron micrographs published by *Reed* and *Oliver*[43] show that this nucleus has cubic symmetry (Fig. 3). *Henning* therefore proposes a model in which the 16 E_2 subunits in the complex isolated by him are situated in pairs at the eight corners of a cube[27].

The electron micrographs do not give a clear indication of the arrangement of E_1 and E_3 on the cube surface, but it can be imagined that every subunit of the transacetylase (E_2) binds one polypeptide chain of E_1 and one of E_2, so that each corner of the cube is formed from two elementary complexes that severally consist of one subunit of E_1, E_2, and E_3. On the basis of the electron micrographs the diameter of the complete complex is estimated at 300 Å[43], but investigation by small-angle X-ray scattering indicates a maximal diameter of 430 Å[29,29a].

2.2. The Multienzyme Complex from Mammals

The mammalian pyruvate dehydrogenase multienzyme complex, first isolated from pig heart muscle[20,21], is nowadays available in very pure form and in substantial quantities[24]. Like the *E. coli* complex, it consists of the three enzymes pyruvate dehydrogenase (E_1), dihydrolipoamide transacetylase (E_2), and dihydrolipoamide dehydrogenase (E_3), which on being brought together reassociate spontaneously to form

[*] This "nuclear complex" is, however, able to bind further E_1 molecules *in vitro*. The bonding may be nonspecific, the molecules that are thus bound taking no part in the catalysis [28].

the original active multienzyme complex[44, 45]. Its molecular weight amounts to at least 7.6×10^6 dalton[45], but it must be borne in mind that a portion of the subunits may be lost during isolation and purification of the enzyme.

The nucleus of the complex is formed here too by the transacetylase (E_2), which consists of sixty probably identical polypeptide chains having a molecular weight of 52000 dalton[46]. Each of these subunits contains one covalently bound molecule of lipoic acid.

If one starts, as in the *E. coli* complex, with a ratio of 1:1:1 for the three constituent enzymes and adds thereto equal proportions of the two regulatory enzymes pyruvate dehydrogenase kinase and phosphatase (see Section 4.5), one obtains a molecular weight of 16×10^6 dalton. There is, however, no evidence that these assumptions are in fact realistic. The stoichiometry of the complex is still not clear. Its size is similar to that of the ribosomes and is thus not unusual for cell particles. *Reed* estimates that in bovine kidneys approximately 15 molecules of this complex are present per mitochondrion. *Srere* has shown that the concentration of such molecules in the cell is of the order of 10^{-5} mol/l[47].

The pyruvate dehydrogenase (E_1) has a molecular weight of 154000 dalton and consists of two subunits of molecular weight 41000 and two of molecular weight 36000 dalton ($\alpha_2\beta_2$)[46]. There are indications that the two types of subunit exert different functions (see Section 3.1). The complex probably contains 60 molecules of type $\alpha\beta$, *i.e.* one molecule of each type per subunit of E_2.

The flavoprotein E_3 has a molecular weight of 110000 dalton and contains two probably identical polypeptide chains, each of which contains one molecule of FAD[48, 49]. The purified complex contains only 10—12 polypeptide chains of the flavoprotein[24]. The sequence of polypeptide chains is known for the neighborhood of the SH groups important for the catalysis[49a, 49b].

As already mentioned, the mammalian complex contains a kinase and a phosphatase[50, 51]; the functions of these are discussed in Section 4.5. The kinase (molecular weight 100000 dalton[24] is relatively strongly bound to the transacetylase (E_2). The phosphatase (molecular weight also 100000[24]) exists in an association-dissociation equilibrium with the complex; it is not known at which position it is bound in the complex. Only a few of these two regulatory enzymes occur in the complex, perhaps only about five; it is, however, possible that the native complex contains a larger number of kinase and phosphatase molecules, some of which are lost during the purification (see Section 4.5)[52, 53].

The transacetylase (E_2) in the mammalian complex, as in the *E. coli* complex, functions both catalytically and in determining the structure. It forms the nucleus of the complex, the other enzymes being arranged on its surface. Electron microscopic investigations have shown that its symmetry differs considerably from that of the *E. coli* transacetylase (Figs. 4b—4d); the pictures do not show a cube, as in the latter case, but are instead better interpreted as pentagonal-dodecahedra[43, 54]; the diameter has been given as 210 Å[43] and as 230—240 Å[54]. The diameter of the whole complex is *ca.* 400—450 Å[43, 54]. The electron-microscopic pictures of the whole complex indicate an icosahedral structure (Fig. 4a)[54].

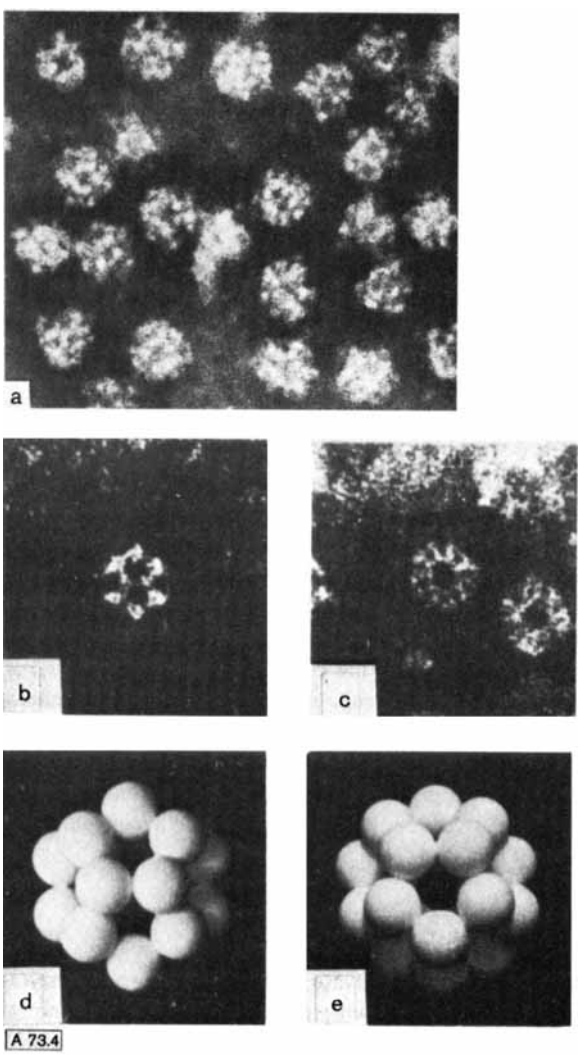


Fig. 4. Electron micrographs of a) mammalian pyruvate dehydrogenase multienzyme complex and b) c) of dihydrolipoamide transacetylase (E_2) [43]. d) and e) are models that interpret Figs. 4b) and 4c), respectively, as pentagonal dodecahedra [43]. Magnification 200000. Photograph a) was kindly placed at our disposal by Dr. *E. Junger* and Prof. *H. Reinauer*, Düsseldorf.

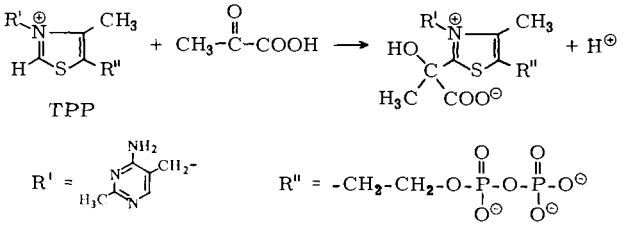
3. Mechanism of the Enzyme Catalysis

No review of the extensive literature dealing with the mode of action of the coenzymes that take part in pyruvate oxidation will be given here; instead, the reader is referred to specialized reviews: for TPP[55, 56], for FAD[57–62], for NAD^+[63–65], for coenzyme A[66], and for lipoic acid[67]. Except for E_3, little is known about the role of the proteins in catalysis of reactions (2)—(5); thus, only a few important aspects will be mentioned, though unsolved problems will be pointed out.

3.1. Pyruvate Dehydrogenase (E_1)

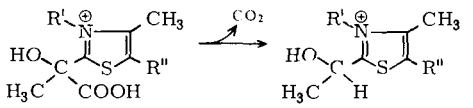
Pyruvate dehydrogenase (E_1) is not just a decarboxylase, as the widely used name "pyruvate decarboxylase" mistakenly suggests—it is correctly assigned to the dehydrogenases. Thus, reactions (2) and (3) also occur with lipoic acid that is not bound to protein[67]. Hexacyanoferrate(III) can also act as an electron acceptor in the oxidation of pyruvate to acetate by E_1, *i.e.* after separation from E_2 and E_3[68]; however, the reaction rate is then only *ca.* 1% of that with the whole complex.

Decarboxylation of the pyruvate is initiated by its attachment to the 2-position of the thiazole ring of TPP.



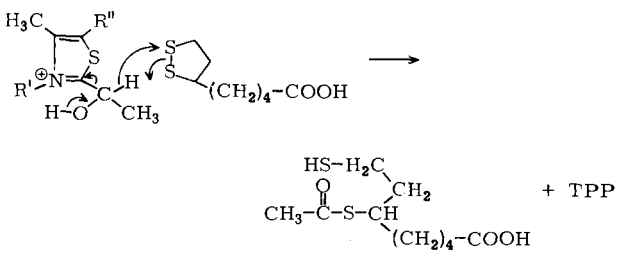
TPP

The loss of CO_2 leads to hydroxyethyl-TPP[55, 56], an intermediate that *Holzer* isolated and named "active acetaldehyde" by analogy with "active acetic acid" (acetylcoenzyme A)[20, 69].



The reaction depends on the acidity of the hydrogen in position 2 of the thiazole ring of TPP[55, 70]. The cofactor in the enzyme reaction is magnesium, which also accelerates the corresponding nonenzymatic hydrogen-isotope exchange with water[71].

The next step is oxidation of the hydroxyethyl group and transfer of the resulting acetyl residue to the lipoic acid of E_2. This dehydrogenase and transferase activity is also localized in E_1[67, 68]. Free lipoic acid can function as an acceptor for the acetyl group in the absence of E_2, as can water in the presence of an electron acceptor such as hexacyanoferrate(III). The reaction occurs approximately as shown in the scheme below.



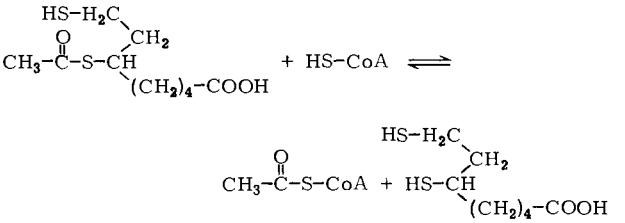
The acetyl group is found as substituent of the secondary SH group of the dihydrolipoic acid[72]. The course proposed for the reaction is supported by inhibition of the reaction by arsenite[73] since arsenite inactivates the enzyme only in the presence of pyruvate and coenzyme A; in this reaction dihydrolipoic acid is formed, which with arsenite forms a cyclic thioarsenite.

There are indications that with the enzyme from mammalian organs the decarboxylase reaction and the dehydrogenase-transferase reaction are catalyzed by different subunits of E_1[74]. With the *E. coli* complex the two types of catalytic activity are probably localized on one polypeptide chain which is about twice as long as the α- or β-chain of the mammalian enzyme. Bromopyruvate[75] and mercury compounds[76] inactivate E_1.

3.2. Dihydrolipoamide Transacetylase (E_2)

The lipoic acid is covalently linked to the transacetylase E_2 by an amide bond. E_2 catalyzes the next step of the reaction, which is transfer of the acetyl group of the dihydrolipoic acid to coenzyme A.

The reaction is reversible, and this reversibility has been used as a test for E_2 in the absence of E_1 and E_3[6]. Acetyl-CoA inhibits the reaction. Little work has been done on the mode of the action or the catalytic role of the protein[77].

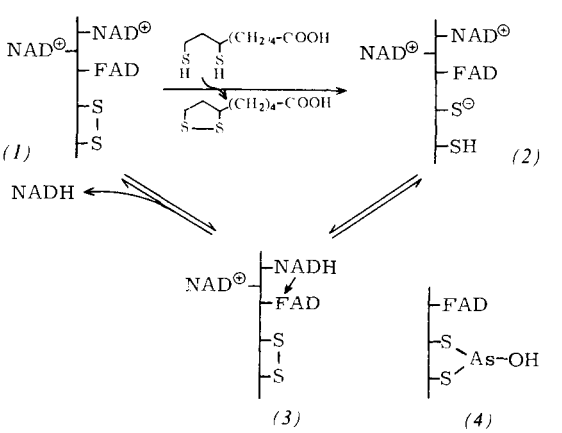


3.3. Dihydrolipoamide Dehydrogenase (E_3)

The function of the dihydrolipoamide dehydrogenase (E_3) in the multienzyme complex is to regenerate E_2 and thus to make possible the next reaction cycle. This occurs by the transfer of two electrons from dihydrolipoic acid to NAD^+, a reaction in which two molecules of NAD^+, one molecule of FAD, and one disulfide group of the protein take part *(1)*. The disulfide group is reduced in an intermediate stage and stabilizes the FAD in a redox state *(2)* that corresponds to a flavosemiquinone[78, 79]. The structure of this state could not as yet be clarified, but the diradical previously suggested by *Massey*[78] as a possibility has been excluded. *(2)* does indeed show the absorption at 530 nm characteristic of radicals, but it is ESR-inactive and diamagnetic. The long-wave absorption speaks against covalent linkage of the protein-sulfur to position 4a of the flavin[80], but no ionic or charge-transfer interaction can be unambiguously detected.

Participation of the disulfide group has, however, been made certain. Reduction of the enzyme by NADH increases the number of SH groups per polypeptide chain by two[81, 82, 60]. Arsenite inhibits the enzyme activity in the presence of NADH by the formation of the cyclic compound *(4)*; this inhibition can be removed by 2,2-dimercaptopropanol (BAL)[78, 81].

If the enzyme is treated with *p*-(chloromercuri)benzenesulfonate, which is a reagent for sulfide groups, the characteristic absorption at 530 nm disappears[83]. Participation of an SH



group in the intermediate *(2)* is thus proved, and it is equally certain that the enzyme is reduced by only two reduction equivalents. The appearance of a form of the enzyme completely reduced by four equivalents is irreversible, and this form is therefore catalytically inactive; in *Massey*'s view it is pre-

vented by the second NAD molecule bound to the enzyme, because the latter is an essential cofactor in oxidation of NADH by dihydrolipoamide dehydrogenase (E_3)[78]. The reader is referred to specialized publications for further details of the reaction kinetics[84, 85].

The disulfide group is intramolecular, *i.e.* it does not link the two polypeptide chains of the dimeric enzyme. These chains are kept together by hydrophobic interaction and not by covalent bonding[86], since, for instance, they can be separated from one another by dilution of the protein[87], whereby they are inactivated. These polypeptide chains are inactive.

3.4. Cooperation of the Enzymes in the Multienzyme Complex

There are still hardly any experimental answers to the questions posed below. It is still largely unknown how the many components in such a complicated system cooperate. If, for example, one starts with lipoic acid, the following problem arises: The lipoic acid is bound covalently to E_2, and is thus fixed in space. It must, however, enter into interaction with hydroxyethyl-TPP (E_1), coenzyme A (E_2), and the disulfide group or the FAD of the dihydrolipoamide dehydrogenase (E_3) during a reaction cycle. In other words, the same lipoamide molecule simultaneously—or at the most within a very short time—acts as a cosubstrate for three enzymes. If we regard the proteins concerned as rigid molecules, this makes almost insuperable demands on the spatial arrangement of the system. The three active sites of the enzyme concerned must form a single large active site containing the six cofactors (TPP, Mg^{2+}, lipoic acid, CoA-SH, FAD, and NAD^+—in the last case probably two molecules per polypeptide chain), because, except for acetyl-CoA, the intermediates in the reaction sequence do not leave the protein and are thus also unable to diffuse from one active site to the next.

Seeking a way out of this dilemma, *Reed* points out that, even if the coenzyme is covalently bound to the enzyme, the reactive group of the lipoic acid obtains a certain flexibility in that it is bound to the protein by a "long arm". If one includes the lysine residue to whose ε-amino group the lipoic acid is attached as an amide, this arm is about 14 Å long and can thus perhaps swing backward and forward between the prosthetic groups of E_1 and E_3[1]. Admittedly the distance of TPP from FAD is estimated as 30—60 Å on the basis of fluorescence energy-transfer measurements[87a].

Lazdunski[88] proposes that the polypeptide chains of the complex can change their conformations by a kind of flip-flop mechanism, and thus the functional groups and the coenzymes may assume such spatial positions during the reaction cycle that they can react with one another and with the substrate. Such conformational changes should be detectable by biophysical methods, so that this hypothesis can be tested within the foreseeable future.

It is especially necessary to postulate flexibility of the proteins concerned when the constituent enzymes (and their coenzymes) do not occur in the ratio 1:1:1. Thus, the complex isolated from mammalian organs contains relatively few molecules of E_3 (FAD). It may be that each of these molecules reoxidizes several dihydrolipoamide molecules.

The same problem arises with the inactivation of the mammalian pyruvate dehydrogenase complex by pyruvate dehydrogenase kinase (see Section 4.5). This enzyme too is a constituent of the multienzyme complex, is bonded relatively strongly to E_2, and from that position phosphorylates at least two serine-OH groups per polypeptide chain of E_1. Since only a few—perhaps only five—kinase molecules occur in the isolated complex, each of these molecules must phosphorylate several E_1 chains without, for example, being able to approach them successively by diffusion. Here too one must assume conformational changes based on the flexibility of the molecules concerned, although there is as yet no experimental indication of this. The pyruvate dehydrogenase phosphatase, which reactivates the complex by dephosphorylation, does not pose this problem, since it occurs in relatively loose association-dissociation equilibrium with the multienzyme complex.

The dihydrolipoamide transacetylase (E_2) probably plays a considerable part in cooperation of the component enzymes in the complex. E_1 and E_3 are evidently brought into a sterically favorable position relative to one another on the surface of E_2. There are less demanding systems in which the acetyl residue is directly transferred to coenzyme A without the aid of lipoic acid, *e.g.* the pyruvate-ferredoxin-oxidoreductase from *Clostridium acidiurici*[89], and moreover the pyruvate oxidase from *E. coli* catalyzes the oxidative decarboxylation of pyruvate without the participation of lipoic acid[90, 91], *i.e.* with only the cofactors TPP, Mg^{2+}, and FAD. This route is not followed in the case of the multienzyme complex, since the reaction does not occur if one blocks the lipoic acid[73] or E_2 as a whole[3]. There is as yet no experimental evidence with the aid of which to recognize the advantages of the route taken by the pyruvate dehydrogenase multienzyme complex.

4. Regulation of the Enzyme Activity

4.1. Pyruvate Metabolism

The metabolism of an organism can be regulated by intracellular and by extracellular processes. Hormonal regulation, for instance, is extracellular. The following three classes belong to intracellular regulation:

1) Regulation of the amount of enzyme on the chromosomal level by induction and repression of enzyme synthesis.

2) Regulation of the enzyme activity by "feedback" or "feedforward" action of the metabolites on the enzyme (also simple product inhibition, substrate activation, and similar processes).

3) Regulation of the enzyme activity by enzymatically catalyzed activation and inactivation of enzymes (interconversion).

All these processes take part in regulation of pyruvate dehydrogenase; least is known about the extracellular factors.

The complexity of the control of the enzymatic activity arises from the position of pyruvate dehydrogenase in metabolism (Fig. 5). The enzyme is at the switchpoint of several metabolic routes. Pyruvate is formed in glycolysis from glucose, from lactate, and from amino acids such as alanine or cysteine. At the same time, it is the starting point of two important metabolic routes:

1) Pyruvate can be oxidatively degraded to acetyl-CoA, whereby NADH and finally, through the tricarboxylic acid cycle and by oxidative phosphorylation, ATP are formed.

2) However, pyruvate can also be carboxylated to give oxalacetate and thus can be the starting point of gluconeogenesis.

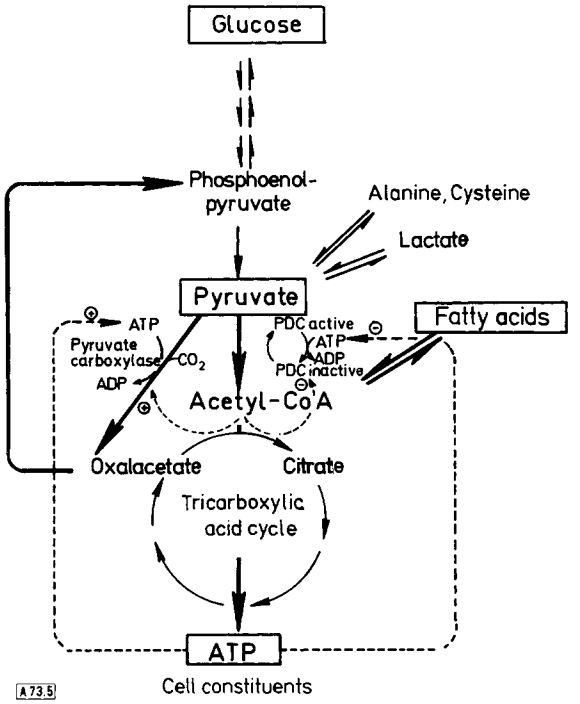


Fig. 5. Simplified scheme of pyruvate metabolism. The broken arrows show activation (+) or inhibition (−) of pyruvate carboxylase and the pyruvate dehydrogenase multienzyme complex (PDC) by acetyl-CoA and ATP.

The key enzyme for the first route is the pyruvate dehydrogenase multienzyme complex, and for the second it is the pyruvate carboxylase.

4.2. Regulation on the Chromosomal Level

In *E. coli* the synthesis of the multienzyme complex is subject to genetic regulation[92]. It is true that it is independent of 3',5'-cyclic AMP[93], but it can be induced by the substrate of the complex, namely pyruvate[94]. The amount of enzyme synthesized can be varied by a factor of ten according to the inducer. Moreover, it has proved possible to isolate constitutive mutants capable of producing about twice as much pyruvate dehydrogenase complex as in the "fully induced" synthesis[95]. Special importance for the synthesis of the whole complex is ascribed to the structural gene for the pyruvate dehydrogenase components. The gene for dihydrolipoamide dehydrogenase (E_3) has not yet been found; that for the other two component enzymes of the complex lie close together (ace-locus)[92].

There is also evidence of a genetic control of the enzyme synthesis in mammals[96–98].

4.3. Hormonal Regulation

If the adipose tissue of normally fed rats is incubated with insulin in the presence of lactate, a marked increase in the pyruvate dehydrogenase activity is observed[99–101]. Thus, insulin exerts a stimulating action at at least two points in the conversion of glucose into fatty acid: it increases not only the glucose transport in the cell but also the oxidation of pyruvate. It is still unknown what chemical reactions underlie this second action, but at least part of the effect is due to a change in the proportion of phosphorylated inactive to dephosphorylated active pyruvate dehydrogenase complex[102–105]. Calcium ions may mediate the hormone effect[106] since, as effectors of phosphatase[107, 108], they increase its affinity for the phosphorylated enzyme[106]. In addition, *Cuatrecasas* found that insulin increases the concentration of the whole enzyme[109].

4.4. "Feedback" and "Feed-forward" Regulation.—Product Inhibition

E_1 is the point of attack by most of the factors that regulate the activity of the pyruvate dehydrogenase multienzyme complex. This appears logical, since E_1 catalyzes the first, almost irreversible, and probably also rate-determining step in the reaction sequence. Glycolysis intermediates have an activating effect on the *E. coli* enzyme, most strongly fructose 1,6-di(phosphate) but also fructose 6-phosphate, glyceraldehyde 3-phosphate, phosphoenol pyruvate[110], dihydroxyacetone phosphate, and glucose 6-phosphate[111]. Acetyl-CoA inhibits[110, 112] with negative cooperativity, whereas positive cooperativity was found for the pyruvate substrate[113] GTP[114] (but not ATP[111, 115] or other nucleotides) inhibits the pyruvate dehydrogenase complex from *E. coli*[114].

Along with the "feedback" inhibition by acetyl-CoA and the "feedforward" activation by glycolysis products, product inhibition of the *E. coli* enzyme by NADH has been described[112]. NADH inhibits E_3, and it appears that the complex is very much more sensitive to NADH than acetyl-CoA.

The multienzyme complex from mammalian organs is also subject to "feedback" or product inhibition by numerous metabolites[116–123] (see Tables 2 and 3). However it appears, in contrast to the situation with the *E. coli* enzyme, that

Table 2. Kinetic parameters of mammalian pyruvate dehydrogenase multienzyme complex. (For details about Mg^{2+} see Table 3.)

Substance	Michaelis or inhibition constants [mol/l]	Binding site	Remarks
Pyruvate	$K_m = 4 \times 10^{-5}$ (kidney and heart)	E_1	substrate
	$K_i = 9 \times 10^{-4}$ (kidney)	?	inhibits the interconversion
	$K_i = 8 \times 10^{-5}$ (heart)	?	inhibits the interconversion
Coenzyme A	$K_m = 3 \times 10^{-6}$	E_2	substrate
Acetyl-CoA	$K_i = 5 \times 10^{-6}$	E_2	competitive inhibitor (not competitive with pyruvate)
NAD^+	$K_m = 2.5 \times 10^{-5}$	E_3	substrate
NADH	$K_i = 2 \times 10^{-6}$	E_3	competitive inhibitor
Nucleotides	$K_{m(ATP)} = 2 \times 10^{-5}$	kinase	substrate of the kinase
	$K_{i(ADP)} = 1 \times 10^{-4}$	kinase	competitive inhibitor

Table 3. Comparison of the Michaelis constants of the enzymes of the pyruvate dehydrogenase complex requiring Mg^{2+} with the physiological Mg^{2+} concentration.

Enzyme	K_m [mol/l]	Ref.
Phosphatase		
(in phosphate buffer)	2×10^{-2}	[139]
(in imidazole buffer)	3×10^{-3}	[107]
Kinase	2×10^{-5}	[107]
Pyruvate dehydrogenase multienzyme complex	5×10^{-6}	[74]
Physiological Mg^{2+} concentration (free Mg^{2+})	1×10^{-3}	[143]

here the ratio NADH/NAD^+ is of greater importance than the ratio acetyl-CoA/CoA in the cell for regulation of the enzyme activity[118]. Short-chain acyl-CoA esters are stronger inhibitors than long-chain ones[119]. All the intermediates of the tricarboxylic acid cycle inhibit pyruvate oxidation[120–122], for instance citrate by influencing the interconversion[123].

ATP inhibits the pyruvate dehydrogenase complex from mammalian organs by the conversion of E_1 into a phosphorylated inactive form (see Section 4.5).

4.5. Interconversion[*]

The activity of the pyruvate dehydrogenase complex from mammalian organs is regulated by two enzymes which are both components of the multienzyme complex. A kinase inactivates the complex by phosphorylation in the presence of ATP, and the reactivation is effected by a phosphatase that dephosphorylates the system[50]. Pyruvate dehydrogenase is thus included among the interconvertible enzymes. This interconversion has been found in all the mammalian organs examined: in the kidney[50], in heart muscle[51, 127], in the liver[50, 51], in the brain[128, 129], and in adipose tissue[130, 131]. No difference in principle was found between cattle, pigs, and rats in this respect[129]. The phosphatases and the kinases of the organs and organisms are interchangeable. *E. coli* enzyme does not show this interconversion, but it occurs in at least one strain of *Neurospora*[10]. It is not known whether there is any relationship between the evolutionary level and the presence of this regulatory mechanism.

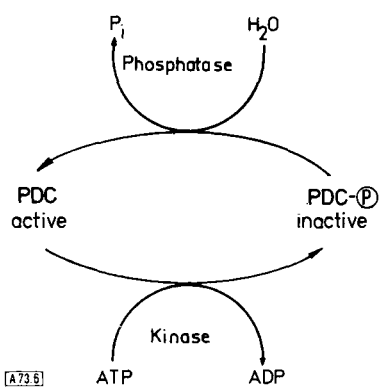


Fig. 6. Scheme for the interconversion of the pyruvate dehydrogenase multienzyme complex (PDC) from mammalian organs. A kinase phosphorylates and inactivates the enzyme, a phosphatase dephosphorylates and reactivates it.

The interconversion was discovered for the purified enzyme *in vitro*[50, 51] but could also be demonstrated in the living organ[132–135].

The site of phosphorylation by the kinase is the pyruvate dehydrogenase (E_1)[50]. By tryptic degradation a tetradecapeptide was isolated that contains two phosphorylated serine groups and the following sequence[136, 137]:

Tyr-His-Gyl-His-Ⓟ-Ser-Met-Ser-Asn-Pro-Gly-Val-Ⓟ-Ser-Tyr-Arg

Of the two different polypeptide chains of pyruvate dehydrogenase (E_1), only that with the higher molecular weight, the α-chain, is phosphorylated[136].

The kinase is strongly bound to the dihydrolipoamide transacetylase (E_2)[24, 51]. The site of the binding of the phosphatase is unknown; it is much more loosely bound than the kinase, so that an association-dissociation equilibrium is set up between it and the complex[24, 106, 138].

It has not yet been made clear why phosphorylation of the pyruvate dehydrogenase (E_1) leads to its inactivation.

The inactivation and reactivation by pyruvate dehydrogenase kinase and phosphatase are under metabolic control. Two classes of compounds in particular merit discussion in this connection: the α-keto acids as substrates or substrate analogs of the pyruvate dehydrogenase[107], and the adenine nucleotides, *e.g.* ATP, as the end product of the metabolic sequence introduced by the multienzyme complex[139].

α-Keto acids: Pyruvic acid and to a smaller degree oxobutyric acid and phenylpyruvic acid protect the pyruvate dehydrogenase from phosphorylation and inactivation by the pyruvate dehydrogenase kinase[51, 107]. This protection by pyruvate is considerably more powerful for the heart enzyme ($K_i = 0.08$ mmol/l) than for the kidney enzyme ($K_i = 0.9$ mmol/l)[107]. Kinetic studies have shown that there is a regulatory bonding site for α-keto acids that probably does not coincide with the substrate bonding site of E_1 or with the bonding site of the ATP of the pyruvate dehydrogenase kinase[107, 140].

The protective effect of the pyruvate can be physiologically meaningful: *Krebs* has shown that the reduction equivalents necessary for gluconeogenesis must be produced by oxidation of pyruvate in the mitochondria when lactate is not the starting material for gluconeogenesis[141, 142]. After loading of the organism the pyruvate concentration *in vivo* can rise to 0.5 mmol/l. Under these conditions gluconeogenesis by way of oxalacetate is possible only if part of the pyruvate is oxidized so as to provide the NADH necessary for this purpose. Pyruvate itself makes this possible by protection of the pyruvate dehydrogenase against inactivation by the kinase.

In the heart, on the other hand, any factor that favors cell respiration is welcome. Here the protective effect of pyruvate is much more marked than in the kidney in order that oxidation of the pyruvate cannot be blocked by the ATP formed.

[*] In enzymology interconversion is understood to mean modification of an enzyme which thereby appreciably changes its activity or its regulatory properties. The concept is used in the narrower sense particularly when the modification is catalyzed enzymatically and leads to the formation or cleavage of covalent bonds to the enzyme. The importance of enzyme-catalyzed chemical modification of enzymes as a regulatory mechanism was recognized only in recent years (for reviews see [124—126]).

Adenine nucleotides: ATP is essential as a substrate of kinase for interconversion. ADP is a relatively weak competitive kinase inhibitor, while AMP, cyclic AMP, and many other nucleotides have no significant influence on the regulation[107]. The Michaelis constant of ATP is low, so that in all metabolic states of the cell the ATP concentration suffices for saturation of the kinase. On the other hand, because of their weak inhibitory effect, ADP and still more AMP are ineffective as regulatory variables for the kinase. The nucleotides mentioned have no direct influence worth mentioning on the pyruvate dehydrogenase phosphatase, so that it is not clear how interconversion corresponding to the demands of the cell can be introduced for regulation of the pyruvate dehydrogenase activity. In the absence of interaction with metabolic variables the phosphorylation-dephosphorylation cycle is a waste of ATP, since the kinase and the phosphatase together exert the action of an ATPase. (However, the amount of ATP consumed in this way is not very large.)

A solution appears if we bring magnesium ions into the discussion[139]. Comparison of the Michaelis constants of the enzyme components of the complex for Mg^{2+} (Table 3)[139] shows that in the physiological concentration range only the phosphatase fails to be saturated with magnesium ions. A variation of this concentration *in vivo* should thus influence the phosphatase activity.

Model experiments *in vitro* have shown that such variation can be produced by fluctuations in the composition of the adenine nucleotide pool. About 90% of the magnesium in the cell is bound by the complex of cell constituents, a third of it by the adenine nucleotides alone[143]. ATP again complexes Mg^{2+} about ten times more strongly than does ADP, so that the composition of the adenine nucleotide pool—the concentration ratios of ATP, ADP, and AMP—can influence the concentration of magnesium ions that are free, *i.e.* not bound in a complex, within the cells[144]. At a high energy charge[145], *i.e.* when very much more ATP than AMP is present, more magnesium is bound than at a low energy charge. However, as shown above, the concentration of free magnesium ions in the cell influences the phosphatase activity and thus the activity of the whole multienzyme complex. The energy charge of the cell varies only within relatively narrow limits, but these fluctuations suffice[139] to vary the activity of the pyruvate dehydrogenase multienzyme complex appreciably by means of the mechanism outlined above (Fig. 7). Similar considerations may apply to calcium, which perhaps plays a central role.

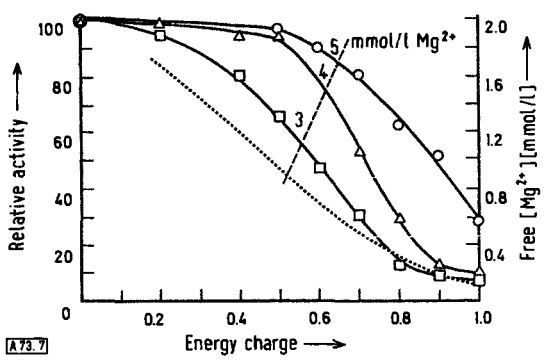


Fig. 7. Dependence of the activity of mammalian pyruvate dehydrogenase multienzyme complex on the energy charge and the Mg^{2+} concentration. The curves describe experiments at a total Mg^{2+} concentration of 3, 4, and 5 mmol/l. The broken curve shows the concentration of free Mg^{2+}, *i.e.* that not bound in a complex, at a total concentration of 4 mmol/l. At energy charge 1 the adenine nucleotide pool contains only ATP, and at energy charge 0 it contains only AMP. ATP binds Mg^{2+} *ca.* ten times as strongly as does AMP. The activity of the enzyme decreases with increasing energy charge because the Mg^{2+} required for reactivation by the phosphatase is complexed by ATP. The energy charge is defined as

$$\frac{1}{2}\left(\frac{[ADP] + 2[ATP]}{[AMP] + [ADP] + [ATP]}\right).$$

Atkinson has shown that other metabolic effectors may also considerably increase the dependence of an enzyme on the energy charge[145]. While experiments with intact mitochondria confirm the importance of the energy charge (the ATP/ADP quotient) for the activity of the complex, doubt has been cast on whether divalent ions in fact exert this effect *in vivo*[146]; nevertheless, experiments by *Schuster* and *Olson*[147, 148] and more recently by *Chiang* and *Sacktor*[149] with heart mitochondria confirm our model.

4.6. Summary of the Regulation Mechanisms

The studies carried out so far on regulation by interconversion permit the conclusion that in an energy-consuming organ such as the heart it operates more strongly in the direction of activation of pyruvate dehydrogenase, but in a gluconeogenetic organ such as the kidney it operates in the direction of inactivation[51]. This is shown by the higher phosphatase and lower kinase activity of the purified heart enzyme and also by the fact that there the protective effect of pyruvate against inactivation is considerably stronger than in the kidney[107]. Nevertheless, it is still unclear whether we are dealing here with a quantitative or a qualitative difference, *i.e.* whether in the heart multienzyme complex the kinase molecules are present in larger amount or whether they are simply more active.

Reed has drawn attention[50] to an interesting reciprocal relationship between pyruvate dehydrogenase and pyruvate carboxylase: The inhibitors of one enzyme—ATP and coenzyme A—are essential cofactors of the other. It is thus conceivable that the concentration of these metabolites exerts an influence on whether pyruvate is used for energy metabolism by means of the tricarboxylic acid cycle or for gluconeogenesis by way of oxalacetate (see Fig. 5). Admittedly, the available data are quite insufficient to explain quantitatively the many regulation mechanisms that affect the pyruvate dehydrogenase multienzyme complex or to estimate their importance for the activity of the enzyme *in vivo*; many of the experiments discussed in this review have been carried out with the purified enzyme in a test tube and await confirmation by experiments with living organisms. For the present, the interpretation that we have here the switchpoint between energy metabolism and gluconeogenesis remains speculative, and the relation to fatty acid metabolism is still largely unclear. Therefore, the present review will not go beyond a summary of the most important kinetic data (Tables 2 and 3) and the indications of Fig. 5.

We could further speculate whether, through the three planes of regulation described above (Section 4.1), we are not approaching a division of labor, perhaps in the sense that each plane is responsible for a different time scale. The chromosomal plane regulates the enzyme activity slowly, in a matter of hours and days; regulation by feedback is achieved rapidly, within seconds or even milliseconds. Interconversion fills the gap in the minute range, so that the rate of pyruvate oxidation

can be adjusted both to the short-term and to the long-term changes of the demands for metabolism.

5. Concluding Remarks

5.1. The Multienzyme Complex—An Artefact?

In the Introduction we indicated the possibility that several proteins might agglomerate into a multienzyme complex during isolation of the enzyme, *i. e.* that the multienzyme complex is a preparation artefact. In favor of this is the failure to detect the pyruvate dehydrogenase complex, in spite of its size, in mitochondria by electron microscopy. However, the following arguments speak against this hypothesis:

1) The association of the enzymes concerned is highly specific. For example, it is impossible to form hybrid complexes with the constituent enzymes of the otherwise very similar α-ketoglutaric acid complex (provided that one takes no account of E_3, the flavoprotein, which is the same in both complexes).

2) Electron micrographs of the purified complex and of the constituent enzymes show that the geometry of the complexes is specific to the organism. (Since the data obtained from them agree with measurements of small-angle X-ray scattering they are also not artefacts of fixation or staining.) Hybrids from complexes of different organisms are not formed.

3) The activity of the enzyme is greater in the complex than in the isolated state. For example, E_2 considerably stimulates the phosphorylation of E_1 by pyruvate dehydrogenase kinase[107]. Furthermore, the kinase is associated with E_2 but its substrate is E_1. Both make complex formation also *in vivo* probable.

However, a final proof of presence of the complex *in vivo* is still lacking.

5.2. Biological Importance of a Multienzyme Complex

Are there any advantages for metabolism if several enzymes come together to form a multienzyme complex? This question can here be touched on from only two points of view.

1) A multienzyme complex catalyzes several reaction steps without the need for the intermediates to leave the enzyme and diffuse to the next enzyme in the metabolic sequence. This is a kinetic advantage and it also prevents another enzyme from competing for one of the intermediates and thus causing "branching". The complex "channels" the substrate in a particular direction.

2) Association of identical polypeptide chains to form oligomeric enzymes is a widely occurring principle. Almost all allosterically regulated enzymes are built up of several polypeptide chains. The multienzyme complex is perhaps only a further development of this principle. The importance of "protein-protein interactions" for the regulation of enzyme activity can be supported by many examples, and early indications for this are available also for the pyruvate dehydrogenase complex (see Section 5.1, paragraph 3).

If we are perhaps convinced of the concept of multienzyme complexes by these two arguments, the size of the unit structure still remains a riddle. Why, instead of one polypeptide chain of each constituent enzyme in one complex, are there 18 identical chains *(E. coli)* or even up to 60 (mammals)? Does the resulting geometry provide a particularly favorable steric arrangement of the active sites of the enzyme? The experimental data so far available do not suffice to answer these questions.

Received: April 2, 1974;
in abbreviated form: January 21, 1975 [A 73 IE]
German version: Angew. Chem. *87*, 614 (1975)
Translated by Express Translation Service, London

[1] *L. J. Reed* and *D. J. Cox*, Annu. Rev. Biochem. *35*, 57 (1966).
[2] *H. Sund* and *K. Weber*, Angew. Chem. *78*, 217 (1966); Angew. Chem. internat. Edit. *5*, 231 (1966).
[3] *M. Koike, L. J. Reed*, and *W. R. Carroll*, J. Biol. Chem. *238*, 30 (1963).
[4] *I. E. Gunsalus* in *W. B. McElroy* and *H. B. Glass:* The Mechanism of Enzyme Action. John Hopkins Press, Baltimore 1954, p. 545.
[5] *M. Koike, L. J. Reed*, and *W. R. Carroll*, J. Biol. Chem. *235*, 1924 (1960).
[6] *L. J. Reed* and *C. R. Willms* in *W. A. Wood:* Methods in Enzymology. Academic Press, New York 1966, Vol. IX, p. 247.
[7] *T. W. Brestens, J. Krul, P. C. Scheepens*, and *C. Veeger*, FEBS-Lett. *22*, 305 (1972).
[8] *L. J. Reed, F. R. Leach*, and *M. Koike*, J. Biol. Chem. *232*, 123 (1958).
[9] *R. W. Harding, D. F. Caroline*, and *R. P. Wagner*, Arch. Biochem. Biophys. *138*, 653 (1970).
[10] *O. H. Wieland, U. Hartmann*, and *E. A. Siess*, FEBS-Lett. *27*, 240 (1972).
[11] *U. Wais, U. Gillmann*, and *J. Ullrich*, Hoppe-Seylers Z. Physiol. Chem. *354*, 206 (1973).
[12] *U. Wais, U. Gillmann*, and *J. Ulrich*, Hoppe-Seylers Z. Physiol. Chem. *354*, 1378 (1973).
[13] *E. Junger, H. Reinauer, U. Wais*, and *J. Ullrich*, Hoppe-Seylers Z. Physiol. Chem. *354*, 1655 (1973).
[14] *M. Crompton* and *G. G. Laties*, Arch. Biochem. Biophys. *143*, 143 (1971).
[15] *V. Jagannathan* and *R. S. Schweet*, J. Biol. Chem. *196*, 551 (1952).
[16] *R. S. Schweet, B. Katchman, R. M. Bock*, and *V. Jagannathan*, J. Biol. Chem. *196*, 563 (1952).
[17] *A. A. Glemzha, L. S. Zilber*, and *S. E. Severin*, Biokhimiya *31*, 1033 (1966).
[18] *S. E. Severin. L. S. Hylova*, and *V. S. Gomazkova*, Abstracts, 8th International Congress of Biochemistry, Interlaken 1970, p. 117.
[19] *J. P. Blass* and *S. Cederbaum*, Abstracts, 9th International Congress of Biochemistry, Stockholm 1973, p. 361.
[20] *P. Scriba* and *H. Holzer*, Biochem. Z. *334*, 473 (1961).
[21] *T. Hayakawa, H. Muta, M. Hirashima, S. Ide, K. Okabe*, and *M. Koike*, Biochem. Biophys. Res. Commun. *17*, 51 (1964).
[22] *T. Hayakawa, M. Hirashima, S. Ide, M. Hamada, K. Okabe*, and *M. Koike*, J. Biol. Chem. *241*, 4694 (1966).
[23] *E. Ishikawa, R. M. Oliver*, and *L. J. Reed*, Proc. Nat. Acad. Sci. USA *56*, 534 (1966).
[24] *T. C. Linn, J. W. Pelley, F. H. Pettit, F. Hucho, D. D. Randall*, and *L. J. Reed*, Arch. Biochem. Biophys. *148*, 327 (1972).
[25] *L. J. Reed* and *D. J. Cox* in *P. D. Boyer:* The Enzymes. Academic Press, New York 1970, p. 213.
[26] *M. H. Eley, G. Namihira, L. Hamilton, P. Munk*, and *L. J. Reed*, Arch. Biochem. Biophys. *152*, 655 (1972).
[27] *O. Vogel, B. Hoehn*, and *U. Henning*, Proc. Nat. Acad. Sci. USA *69*, 1615 (1972).
[28] *O. Vogel, B. Hoehn*, and *U. Henning*, Eur. J. Biochem. *30*, 354 (1972).
[29] *H. Durchschlag*, Hoppe-Seylers Z. Physiol. Chem. *354*, 205 (1973).
[29a] *H. Durchschlag*, Biophys. Struct. Mechanism *1*, 153, 169 (1975).
[30] *O. Vogel* and *U. Henning*, Eur. J. Biochem. *18*, 103 (1971).
[31] *R. N. Perham* and *J. O. Thomas*, FEBS-Lett. *15*, 8 (1971).
[32] *O. Vogel, H. Beikind, H. Müller*, and *U. Henning*, Eur. J. Biochem. *20*, 169 (1971).
[33] *C. R. Willms, R. M. Oliver, H. R. Henney, B. B. Mukherjee*, and *L. J. Reed*, J. Biol. Chem. *242*, 889 (1967).
[34] *J. C. Gunsalus*, Fed. Proc. *13*, 715 (1954).
[35] *M. Koike* and *L. J. Reed*, J. Biol. Chem. *235*, 1931 (1960).
[36] *H. Nawa, W. T. Brady, M. Koike*, and *L. J. Reed*, J. Amer. Chem. Soc. *82*, 896 (1960).
[37] *L. J. Reed, M. Koike, M. E. Levitch*, and *F. R. Leach*, J. Biol. Chem. *232*, 143 (1958).
[38] *K. Suzuki* and *L. J. Reed*, J. Biol. Chem. *238*, 4021 (1963).
[39] *G. R. Seaman* and *M. D. Naschke*, J. Biol. Chem. *213*, 705 (1955).
[40] *K. Daigo* and *L. J. Reed*, J. Amer. Chem. Soc. *84*, 606 (1962).
[41] *H. Fernandez-Moran, L. J. Reed, M. Koike*, and *C. R. Willms*, Science *145*, 930 (1964).
[42] *E. R. Schwartz* and *L. J. Reed*, J. Biol. Chem. *244*, 6074 (1969).

[43] *L. J. Reed* and *R. M. Oliver*, Brookhaven Symp. Biol. *21*, 397 (1968).
[44] *T. Hayakawa* and *M. Koike*, J. Biol. Chem. *242*, 1356 (1967).
[45] *T. Hayakawa, T. Kanzaki, T. Kitamura, Y. Fukuyoshi, Y. Sakurai, K. Koike, T. Suematsu*, and *M. Koike*, J. Biol. Chem. *244*, 3660 (1969).
[46] *C. R. Barrera, G. Namihira, L. Hamilton, P. Munk, M. E. Eley, T. C. Linn*, and *L. J. Reed*, Arch. Biochem. Biophys. *148*, 343 (1972).
[47] *P. A. Srere*, Science *158*, 936 (1967).
[48] *V. Massey, T. Hofmann*, and *G. Palmer*, J. Biol. Chem. *237*, 3820 (1962).
[49] *J. Visser* and *C. Veeger*, Biochim. Biophys. Acta *159*, 265 (1968).
[49a] *J. P. Brown* and *R. N. Perham*, Biochem. J. *138*, 505 (1974).
[49b] *R. G. Matthews, L. D. Arscott*, and *C. H. Williams*, Biochim. Biophys. Acta *370*, 26 (1974).
[50] *T. C. Linn, F. H. Pettit*, and *L. J. Reed*, Proc. Nat. Acad. Sci. USA *62*, 234 (1969).
[51] *T. C. Linn, F. H. Pettit, F. Hucho*, and *L. J. Reed*, Proc. Nat. Acad. Sci. USA *64*, 227 (1969).
[52] *T. E. Roche, J. W. Pelley, D. D. Randall, M. W. Burgett*, and *L. J. Reed*, Fed. Proc. *30*, 1175 (1971).
[53] *H. Reinauer*, personal communication.
[54] *E. Junger* and *H. Reinauer*, Biochim. Biophys. Acta *250*, 478 (1971).
[55] *R. Breslow*, J. Amer. Chem. Soc. *80*, 3719 (1958).
[56] *A. Schellenberger*, Angew. Chem. *79*, 1050 (1967); Angew. Chem. internat. Edit. *6*, 1024 (1967).
[57] *P. Hemmerich, C. Veeger*, and *H. C. S. Wood*, Angew. Chem. *77*, 699 (1965); Angew. Chem. internat. Edit. *4*, 671 (1965).
[58] *G. R. Penzer* and *G. K. Radda*, Quart. Rev. Chem. Soc. *21*, 43 (1967).
[59] *P. Hemmerich, G. Nagelschneider*, and *C. Veeger*, FEBS-Lett. *8*, 69 (1970).
[60] *E. C. Slater:* Flavins and Flavoproteins. Elsevier, Amsterdam 1966.
[61] *K. Yagi:* Flavins and Flavoproteins. University of Tokyo Press, Tokyo 1968.
[62] *H. Kamin:* Flavins and Flavoproteins. University Park Press, Baltimore 1971.
[63] *H. Sund* in *T. P. Singer:* Biological Oxidations. Interscience, New York 1968, p. 603.
[64] *K. A. Schellenberg* in *H. Sund:* Pyridine Nucleotide-Dependent Dehydrogenases. Springer, Berlin 1970, p. 15.
[65] *K. Wallenfels* in *H. Sund:* Pyridine Nucleotide-Dependent Dehydrogenases. Springer, Berlin 1970, p. 31.
[66] *P. Goldman* and *P. R. Vagelos* in *M. Florkin* and *E. H. Stotz:* Comprehensive Biochemistry. Elsevier, Amsterdam 1964, Vol. 15, p. 71.
[67] *L. J. Reed* in *M. Florkin* and *E. H. Stotz:* Comprehensive Biochemistry. Elsevier, Amsterdam 1966, Vol. 14, p. 99.
[68] *M. L. Das, M. Koike*, and *L. J. Reed*, Proc. Nat. Acad. Sci. USA *47*, 753 (1961).
[69] *H. Holzer* and *K. Beaucamp*, Angew. Chem. *71*, 776 (1959).
[70] *J. Ulrich* and *A. Mannschreck*, Biochim. Biophys. Acta *115*, 46 (1966).
[71] *A. Schellenberg, A. Kolbe*, and *G. Hübner*, Hoppe-Seylers Z. Physiol. Chem. *341*, 22 (1965).
[72] *J. C. Gunsalus, L. S. Barton*, and *W. Gruber*, J. Amer. Chem. Soc. *78*, 1763 (1956).
[73] *O. K. Reiss*, J. Biol. Chem. *233*, 789 (1958).
[74] *T. E. Roche* and *L. J. Reed*, Biochem. Biophys. Res. Commun. *48*, 840 (1972).
[75] *M. E. Maldonado, K.-J. Ok*, and *P. A. Frey*, J. Biol. Chem. *247*, 2711 (1972).
[76] *E. R. Schwartz* and *L. J. Reed*, J. Biol. Chem. *245*, 183 (1970).
[77] *E. R. Schwartz* and *L. J. Reed*, J. Biol. Chem. *243*, 639 (1968).
[78] *V. Massey* and *C. Veeger*, Biochim. Biophys. Acta *48*, 33 (1961).
[79] *V. Massey* in *P. D. Boyer, H. Lardy*, and *K. Myrbäck:* The Enzymes. Academic Press, New York 1963. Vol. 7, p. 275.
[80] *W. H. Walker* and *P. Hemmerich*, Eur. J. Biochem. *13*, 258 (1970).
[81] *R. L. Searls, J. M. Peeters*, and *D. R. Sanadi*, J. Biol. Chem. *236*, 2317 (1961).
[82] *G. Palmer* and *V. Massey*, Biochim. Biophys. Acta *58*, 349 (1962).
[83] Cited in [67], p. 114.
[84] *J. Visser, H. Voetberg*, and *C. Veeger* in *H. Sund:* Pyridine Nucleotide-Dependent Dehydrogenases. Springer, Berlin 1970, p. 359.
[85] *H. van Muiswinkel-Voetberg* and *C. Veeger*, Eur. J. Biochem. *33*, 285 (1973).
[86] *J. F. Kalse* and *C. Veeger*, Biochim. Biophys. Acta *159*, 244 (1968).
[87] *H. van Muiswinkel-Voetberg, J. Visser*, and *C. Veeger*, Eur. J. Biochem. *33*, 265 (1973).
[87a] *O. A. Moe, D. A. Lerner*, and *G. G. Hammes*, Biochemistry *13*, 2552 (1974).
[88] *M. Lazdunski*, Curr. Top. Cell. Regul. *6*, 267 (1972).
[89] *K. Uyeda* and *J. C. Rabinowitz*, J. Biol. Chem. *246*, 3111 (1971).
[90] *F. R. Williams* and *L. P. Hager*, Arch. Biochem. Biophys. *116*, 168 (1966).
[91] *C. O. Cunningham* and *L. P. Hager*, J. Biol. Chem. *246*, 1583 (1971).
[92] *U. Henning, G. Dennert, R. Hertel*, and *W. S. Skipp*, Cold Spring Harbor Symp. Quant. Biol. *31*, 227 (1966).
[93] *M. Engel-Rae* and *U. Henning*, Biochem. Biophys. Res. Commun. *53*, 812 (1973).
[94] *J. Dietrich* and *U. Henning*, Eur. J. Biochem. *14*, 258 (1970).
[95] *J. E. Flatgaard, B. Hoehn*, and *U. Henning*, Arch. Biochem. Biophys. *143*, 461 (1971).
[96] *H. Reinauer, G. Grassow*, and *S. Hollmann*, Hoppe-Seylers Z. Physiol. Chem. *349*, 969 (1968).
[97] *H. Reinauer* and *S. Hollmann*, Hoppe-Seylers Z. Physiol. Chem. *350*, 40 (1969).
[98] *H. Reinauer, W. Janssen*, and *S. Hollmann*, Hoppe-Seylers Z. Physiol. Chem. *352*, 125 (1971).
[99] *R. L. Jungas*, Fed. Proc. *29*, 891 (1970).
[100] *R. L. Jungas*, Endocrinology *86*, 1368 (1970).
[101] *R. M. Denton, H. G. Coore, B. R. Martin*, and *P. J. Randle*, Nature New Biol. *231*, 115 (1971).
[102] *L. Weiss, G. Löffler, A. Schirmann*, and *O. Wieland*, FEBS-Lett. *15*, 229 (1971).
[103] *O. Wieland, E. Siess, H. J. v. Funcke, C. Patzelt, A. Schirmann, G. Löffler*, and *L. Weiss* in *O. Wieland, E. Helmreich*, and *H. Holzer:* Metabolic Interconversion of Enzymes. Springer, Berlin 1972.
[104] *O. Wieland, C. Patzelt*, and *G. Löffler*, Eur. J. Biochem. *26*, 426 (1972).
[105] *C. Patzelt, G. Löffler*, and *O. Wieland*, Eur. J. Biochem. *33*, 117 (1973).
[106] *R. M. Denton* and *P. J. Randle*, Abstracts, 9th International Congress of Biochemistry, Stockholm 1973, p. 351.
[107] *F. Hucho, D. D. Randall, T. E. Roche, M. W. Burgett, J. W. Pelley*, and *L. J. Reed*, Arch. Biochem. Biophys. *151*, 238 (1972).
[108] *H. G. Coore, R. M. Denton, B. R. Martin*, and *P. J. Randle*, Biochem. J. *125*, 115 (1971).
[109] *V. Sica* and *P. Cuatrecasas*, Biochemistry *12*, 2282 (1973).
[110] *E. R. Schwartz, L. O. Old*, and *L. J. Reed*, Biochem. Biophys. Res. Commun. *31*, 495 (1968).
[111] *L. C. Scheu* and *D. E. Atkinson*, J. Biol. Chem. *245*, 5974 (1970).
[112] *R. G. Hansen* and *U. Henning*, Biochim. Biophys. Acta *122*, 355 (1966).
[113] *H. Bisswanger* and *U. Henning*, Eur. J. Biochem. *24*, 376 (1971).
[114] *E. R. Schwartz* and *L. J. Reed*, Biochemistry *9*, 1435 (1970).
[115] *L. C. Shen, L. Fall, G. M. Walton*, and *D. E. Atkinson*, Biochemistry *7*, 4041 (1968).
[116] *P. B. Garland* and *P. J. Randle*, Biochem. J. *91*, 6c (1964).
[117] *F. Hucho*, unpublished results.
[118] *J. Bremer*, Eur. J. Biochem. *8*, 535 (1969).
[119] *J. D. Erfle* and *F. Somer*, Biochim. Biophys. Acta *178*, 441 (1969).
[120] *R. J. Haslam* and *H. A. Krebs*, Biochem. J. *86*, 432 (1963).
[121] *T. König* and *G. Szabados*, Acta Biochim. Biophys. Acad. Sci. Hung. *2*, 253 (1967).
[122] *C. K. Silert* and *D. B. Martin*, Biochem. Biophys. Res. Commun. *31*, 818 (1968).
[123] *W. M. Taylor* and *M. L. Halperin*, J. Biol. Chem. *248*, 6080 (1973).
[124] *H. Holzer* and *W. Durtze*, Annu. Rev. Biochem. *40*, 345 (1971).
[125] *A. Sols* and *C. Gancedo* in *E. Kun* and *S. Grisolia:* Biochemical Regulatory Mechanisms in Eukaryotic Cells. Wiley, New York 1972.
[126] *O. Wieland, E. Helmreich*, and *H. Holzer:* Metabolic Interconversion of Enzymes. Springer, Berlin 1972.
[127] *O. Wieland* and *B. von Jagow-Westermann*, FEBS-Lett. *3*, 271 (1969).
[128] *O. Wieland, B. von Jagow-Westermann*, and *B. Stukowski*, Hoppe-Seylers Z. Physiol. Chem. *350*, 329 (1969).
[129] *M. W. Burgett*, PhD Thesis, University of Texas, Austin, Texas 1972.
[130] *R. L. Jungas*, Metabolism *20*, 43 (1971).
[131] *H. G. Coore, R. M. Denton, B. R. Martin*, and *P. J. Randle*, Biochem. J. *125*, 115 (1971).
[132] *A. Corsi, M. Zatti, M. Midrio*, and *A. L. Granata*, FEBS-Lett. *11*, 65 (1970).
[133] *H. D. Söling, B. Willms*, and *G. Janson*, FEBS-Lett. *11*, 324 (1970).
[134] *H. D. Söling, G. Bernhard*, and *G. Janson*, FEBS-Lett. *13*, 201 (1971).
[135] *C. Patzelt, G. Löffler*, and *O. Wieland*, Eur. J. Biochem. *33*, 117 (1973).
[136] *L. J. Reed, T. C. Linn, F. Hucho, G. Namihira, B. R. Barrera, T. E. Roche, J. W. Pelley*, and *D. D. Randall* in *O. Wieland, E. Helmreich*, and *H. Holzer:* Metabolic Interconversion of Enzymes. Springer, Berlin 1972, p. 281.
[137] *E. T. Hutcheson*, PhD Thesis, University of Texas, Austin, Texas 1971.
[138] *F. Hucho*, unpublished observation.
[139] *F. Hucho*, Eur. J. Biochem. *46*, 499 (1974).
[140] *B. Hoffmann* and *F. Hucho*, FEBS-Lett. *43*, 116 (1974).
[141] *H. A. Krebs, B. M. Notton*, and *R. Hems*, Biochem. J. *101*, 607 (1966).
[142] *H. A. Krebs, T. Gascoyne*, and *B. M. Notton*, Biochem. J. *102*, 275 (1967).
[143] *D. Veloso, R. W. Guynn, M. Oskarsson*, and *R. Veech*, J. Biol. Chem. *248*, 4811 (1973).
[144] *J. McD. Blair*, Eur. J. Biochem. *13*, 384 (1970).
[145] *D. E. Atkinson*, Biochemistry *7*, 4030 (1968).
[146] *E. I. Walajtys, D. P. Gottesman*, and *J. R. Williamson*, J. Biol. Chem. *249*, 1857 (1974).
[147] *S. M. Schuster* and *M. S. Olson*, J. Biol. Chem. *249*, 7151 (1974).
[148] *S. M. Schuster* and *M. S. Olson*, J. Biol. Chem. *249*, 7159 (1974).
[149] *P. C. Chiang* and *B. Sacktor*, J. Biol. Chem. *250*, 3399 (1975).

Painting of Ancient Ceramics[**]

By Walter Noll, Reimer Holm, and Liborius Born[*]

Dedicated to Dr. Werner Heimsoeth on the occasion of his 65th Birthday

The painting of ancient ceramics has been investigated for its morphological characteristics and its elemental and phase composition with the aid of scanning electron microscopy, energy-dispersive and in part wavelength-dispersive X-ray microanalysis, X-ray diffraction, and electron spectroscopy. Some conclusions about the methods of production can be drawn from these results. It transpires that the painting of ancient ceramics constitutes an extremely important document for the history of chemical technology. The findings bring to light the wealth of experience acquired by the craftsmen and artists of the time and their knowledge of the mineral raw material and their possible utilization. The facts thus obtained are of great value for problems in archaeology and prehistory and at the same time open up new prospects for interdisciplinary collaboration.

1. Introduction

"In the beginning were ceramics"—these could be the introductory words of a chapter in a treatise on the history of mankind dealing with the development of artificial wares; for ceramics were the first products to liberate man from total dependence on natural materials. So far as we know at present, this important step was made in the seventh millenium B. C. in Iraq. Up to this day ceramics play an important role, no matter how primitive or how developed a culture may be.

As old as the discovery of the ceramic vessel, is Man's desire to decorate its surface, and this decoration has always constituted an extremely fruitful field of research for prehistorians, archaeologists, and art historians alike—it provides evidence of the artistic achievement and of the culture-historical position of ancient peoples, and is thus also a valuable aid in dating the objects in question.

To scientists who have also recently turned their attention to the painting of ceramics the interest lies in a different direction. The painting provides evidence of an industrial finishing process representative of the degree of experience and knowledge of raw materials possessed by the ancient cultures.

The present contribution has been planned in this last sense. Its objectives have been in the first place to identify the chemical and mineralogical content of the paintings and then to reconstruct the manufacturing processes, when necessary with the aid of results from simulation experiments.

2. Previous Investigations

Of the wealth of material offered by ancient ceramic activity, only a relatively small—although important—part has previously been placed under the searchlight of the scientific method, namely the Attic black and red figure painting [1–15, 19]. The following findings, accumulated from attempts stretching over 40 years to clarify the techniques used, should be borne in mind, for these will also be important regarding further considerations.

Red and black colors were produced side by side by the use of aqueous slurries or iron-rich clays as "paint slips" and by varying the atmosphere in the furnace in which the pots were fired. Potassium-rich illitic and therefore readily sintering clays were selected for those parts of the painting that were to be black, while for the red areas, if these were not afforded by the ceramic body itself, potassium-poor kaolinitic, and thus difficultly sintering clays, were used. The firing was first essentially oxidizing[*], up to a maximum temperature of about 850 °C, and the conditions were then made reducing. At this stage the entire painting became black as a result of partial reduction of the ferruginous clay minerals to iron(II)-iron(III) oxides. During cooling large amounts of air were admitted, and now the only parts of the painting that had sintered slightly and remained porous and permeable to the altered furnace atmosphere became oxidizied and thus red. In contrast, the more strongly compacted paint strokes remained black. In view of the decisive steps in the firing technique, this method of working is described below as the "reduction-reoxidation technique".

The important point to note is that no color-forming pigments were introduced with the paint slips, but were first produced during the firing. This was recognized as early as 1929 by *Binns* and *Fraser*[1][**]. Hematite (α-Fe_2O_3) is formed as the red pigment; the black pigment was first identified by *U. Hofmann* as hercynite ($FeO \cdot Al_2O_3$)[9–12]. Its black color can, however, be understood only if iron(III) ions are also present, *e.g.* as a solid solution with magnetite ($FeO \cdot Fe_2O_3$).

Attic painting is further characterized by its high luster. This was achieved by particularly careful slurrying of the clay. Only the finest fractions, enriched in clay minerals, were

[*] Prof. Dr. W. Noll, Dr. R. Holm, and Dr. L. Born
Mineralogisch-Petrographisches Institut der Universität
5 Köln 1, Zülpicher Strasse 49 (Germany)

[**] After a lecture given by *W. Noll* at Mannheim on September 20, 1974 at the conference of the GDCh "Analytical Chemistry" group.

[*] According to *A. Winter*, the oxidation during heating was interrupted by periods of reduction, since after each stoking with further fuel the flame at first tended to "smoke".

[**] "The essential points of the present study are, first, that the formation of the black color in the glaze took place in the fire and there only, and, second, that while the reducing fire also blackened the body, this was reoxidized and reddened during the cooling".

used for the painting. When the paint was applied the flaky clay minerals arranged themselves more or less parallel to one another and to the vessel surface. Moreover, since the temperatures were never raised so high that the structure of the particles and the texture of their attachment were lost by abundant melt formation, the surface received a luster that could not be equalled in any other way, even by total melting. This process has been described as "Glanzton" technique.

3. Methods of Investigation

In our work we used scanning electron microscopy (SEM) to elucidate the structure of the paint layers and the morphology of the constituent particles; energy-dispersive X-ray microanalysis for the determination of the elementary composition and for semiquantitative estimations; and X-ray powder diffraction (Debye-Scherrer method) for characterizing the structure of the crystalline phases. This combination of approaches has proved extremely fruitful for the investigation of paint layers on ceramics[16–24]. Because of its great depth of focus, the scanning electron microscope[25, 26] provides sharp pictures of even greatly uneven surfaces as they were produced by breaking the potsherds, being the only means of obtaining reliable information about morphological details; the combination of SEM and energy-dispersive X-ray microanalysis makes it possible to interpret the composition of the surface chemically and indeed to analyze single grains. Finally, minute quantities of a substance (a few tenths of a milligram) can be identified by X-ray powder diffraction. If X-ray microanalysis is carried out on the same sample, the investigation can be effected almost non-destructively, a feature that is often desirable in view of the object's value. Since energy-dispersive X-ray microanalysis detects only elements with an atomic number greater than 10, the ESCA method (*E*lectron *S*pectroscopy for *C*hemical *A*nalysis as introduced by *K. Siegbahn*) is also used for special cases such as the detection of boron or carbon. On occasions the distribution of elements in the sample surface is also investigated by the electron microprobe, thus supplementing the energy-dispersive measurements.

4. The Objects

The aim of our work was to study the ceramic techniques used over a much wider region and in much older times than had been previously attempted. The choice of the objects was concentrated on finds from the eastern Mediterranean area and the cultures that enriched them, notably Anatolia and Mesopotamia. The time span stretched from the classical Attic period back to the beginnings of painted ceramics in Iraq. The oldest material available to us originated from the sixth millenium B. C.

In that region and at that time black and red paintings are the commonest. The painting on Mesopotamian pottery of the sixth millenium B. C. is at first monochrome, but as early as about 5000 B. C. the two colors appear dichromic side by side. Almost simultaneously white is added to these colors. It is only much later that the palette is enriched by blue and green colors that are much more unusual than the black, red, and white (Egypt, Attic lekythoi). The relevant pigments are illustrated in Table 1.

Table 1. Pigment used in the painting of ancient pottery.

Colors	Pigment phases	Raw materials	Refs.
Black to brownish black	Maghemite [γ-Fe_2O_3] Magnetite [Fe_3O_4] Hercynite [$FeAl_2O_4$] and solid solution $\pm$Hematite [α-Fe_2O_3]	Ferruginous clays Ocherous earths, *etc.*	[9—13, 19, 21] Present work
	Jacobsite [$MnFe_2O_4$] and Mn-contg. spinels Bixbyite [Mn_2O_3] Hausmannite [Mn_3O_4]	MnO_2 minerals: pyrolusite, manganomelane, "umber", *etc.*	[18, 20]
	Soot, graphite	Soot, graphite	[34]
Brown to yellowish brown	Maghemite [γ-Fe_2O_3] Hercynite [$FeAl_2O_4$] and solid solution Hematite [α-Fe_2O_3]	Ferruginous clays Ocher	[21]
Red	Hematite [α-Fe_2O_3] Copper [Cu], coll. dispers.	Ferruginous clays; ocher Basic Cu carbonate	[9—12, 19, 21] [17, 19, 21]
White	Calcite Huntite $CaMg_3[CO_3]_4$ Gypsum and anhydrite [partly + $CaSO_4 \cdot 0.5H_2O$] Metakaolinite [$Al_2O_3 \cdot 2SiO_2$] Protoenstatite [$MgSiO_3$]	Chalk, light-colored limestone Gypsum and anhydrite Kaolinite Talc (steatite, soapstone)	[11] Present work [35] [24] [17, 19, 21] [16, 19, 23]
Blue	Egyptian Blue [$CaCu[Si_4O_{10}]$] Cobalt aluminate $CoAl_2O_4$	Calcite, basic Cu carbonate, quartz, Na carbonate ?	[19, 21] [24, 35]
Green	Copper hydroxychloride $Cu_2(OH)_3Cl$		[37] Present work

Black is the most interesting color, being found everywhere and produced by various techniques. One of these, the iron-reduction technique, achieved a remarkable development in the course of time.

5. Monochrome Painting

5.1. Black by the Iron-Reduction Technique

The process in which black colors are produced in ceramic firing by the reduction of ferruginous clays is widely distributed and very old; according to our present knowledge, it is probably the oldest of all ceramic-decoration processes. During the reduction spinel phases are formed as black pigments, but they are almost invariably accompanied by hematite, which shifts the color toward dark- to pale-brown shades according to the amount present. Its presence may be due to incomplete reduction or to parital reoxidation during cooling. At least in the oldest, and certainly primitively fired, objects both processes will have played a part. In the first place, we shall speak only of a "reduction technique", as long as it cannot be shown that reoxidation was an appreciable and consciously applied stage in the firing, as it became in the Attic period.

The wide distribution of this technique is shown in Fig. 1. On this map the time parameter is indicated by different methods of marking places, always in steps of a thousand years[*]. This shows that the iron-reduction technique must have originated in Iraq.

On the basis of stylistic characteristics three main groups can be distinguished in *Iraq ceramics*, namely: the wares of *Samarra* type (6th millenium B. C.), of *Tell Halaf* type (5th millenium), and of *El Obeid* type (5th to 4th millenium). Surprisingly, the oldest ceramics and their paint layers consist of relatively highly fired and sintered material. The pottery body is always rich in lime and always close to an iron-rich limestone in composition (Fig. 2). The lime is a constituent of the clay. The pottery clays used nowadays in Seleucia and Samarra contain between 16 and 17 % of CaO[27]. The high lime content is important for the color of the burnt clay: although the relationship is still not clear in detail[27, 28], we know that this lightens the color of the clay from brown to yellow, greenish, and finally white.

There are certain differences in detail between the paint layers of the three types of ceramics. A striking feature of the *Samarra ceramics* is their sometimes enormous iron content, which is not to be found in the clays (Fig. 2); ocher must have been used as the raw material. The same is true for the rarer red paintings (Fig. 2) corresponding to the high iron content, the black pigments are maghemite (γ-Fe_2O_3) and magnetite. Hematite, which is almost always present, lightens the color to brownish shades. The paint layer is applied extremely thickly and is rich in cracks and lumps (Fig. 3).

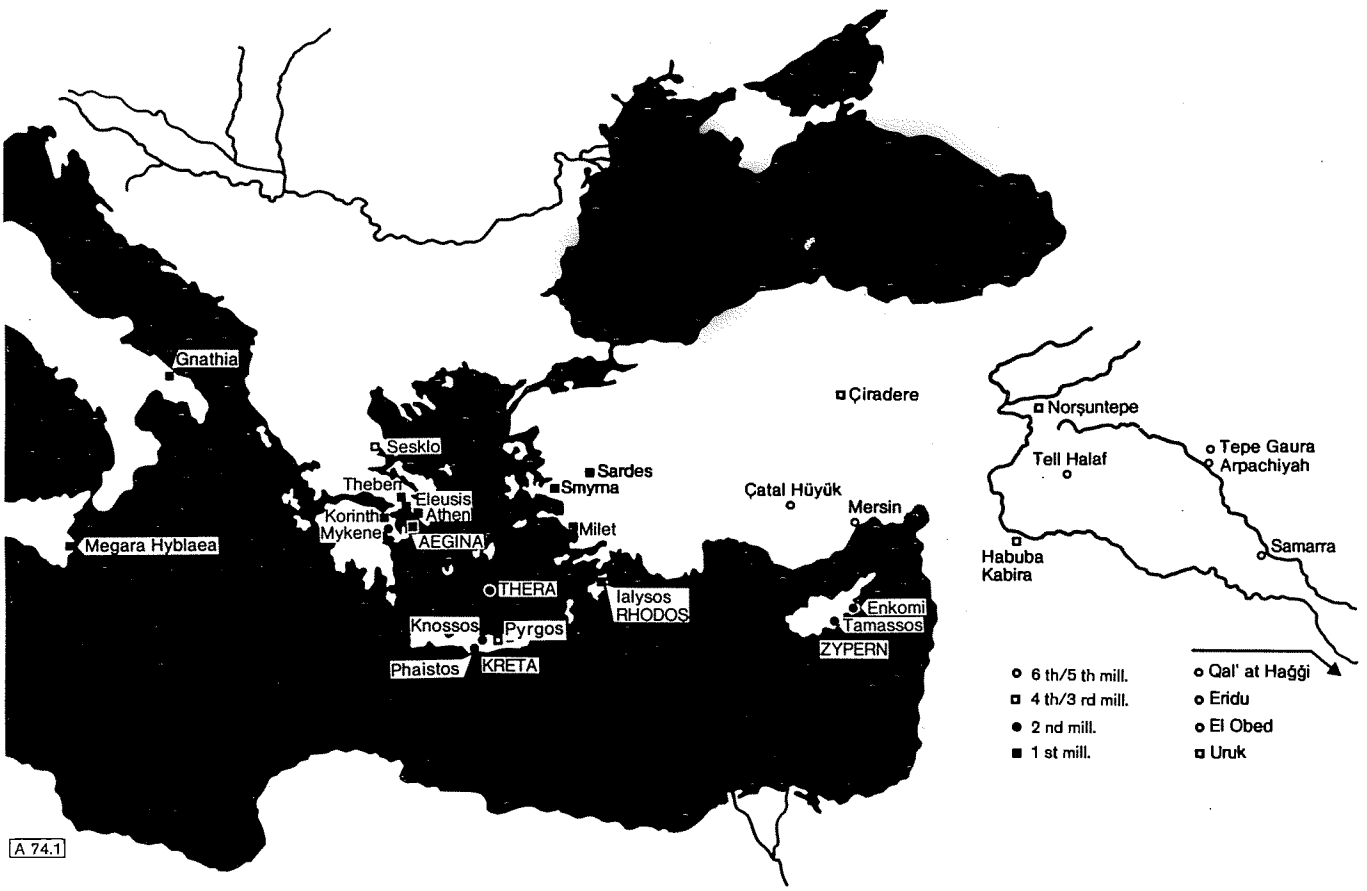


Fig. 1. Spread of the iron-reduction technique during the 6th to the 1st millenium B. C. in the eastern Mediterranean region, Anatolia and Mesopotamia.

The paint mass of *Obeid ceramics* contains titanium and chromium. The local enrichment of these elements and other spectral characteristics indicate that iron ores were mixed with the clays used as the raw material. Apparently the same clays were used for the body and the paint layer, and conse-

[*] Egypt must be left out of account for the moment. A broadly planned investigation of Egyptian pottery painting is currently in progress.

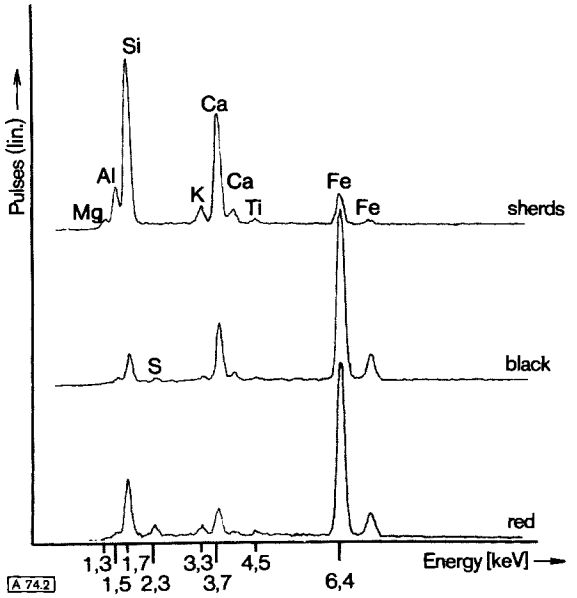


Fig. 2. Energy-dispersive X-ray spectra of sherds and paint layers of Samarra ware, Iraq, 6th millenium B. C.

quently the firing led to a structure in which no difference between the two can be detected (Fig. 4). In the absence of morphological characteristics the thickness of the paint layer can in such cases be established only by means of the titanium content. It must be assumed that titanium participates by spinel formation in production of the black color[28].

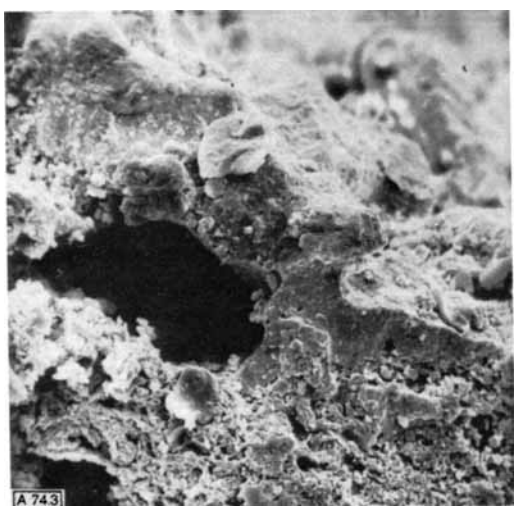


Fig. 3. Black paint layer of a sherd of Samarra ware, Iraq, 6th millenium B. C. Scanning electron microscope, 1 cm = 27 µm.

The paint layers of the *Halaf ware* come closest in their quality to the compositions prepared in later times only from clays. The potassium content is high, that of calcium low. This relationship is reversed within the body of the articles (cf. Fig. 8). In individual cases hercynite is found as a pigment along with hematite and maghemite. The paint layer differs morphologically from the body in being a dense and substantially smooth layer that nevertheless contains bubbles and voids (Fig. 5).

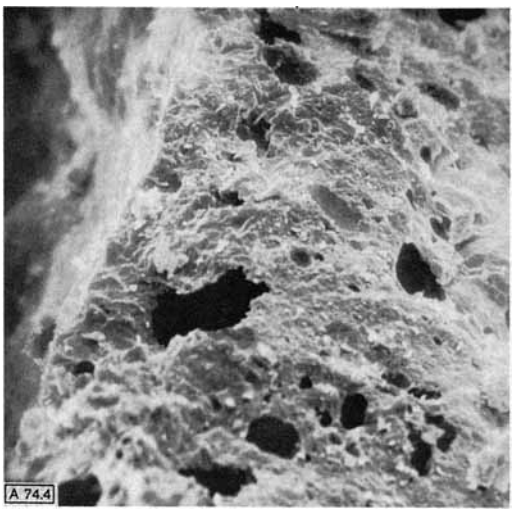


Fig. 4. Black paint layer (left of the markings on the edge) and sherd (right thereof) of Obeid ware, Iraq, 5th to 4th millenium B. C. Scanning electron microscope, 1 cm = 30 µm.

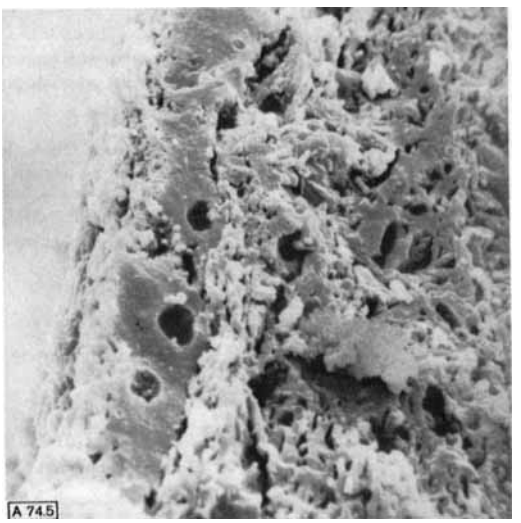


Fig. 5. Black paint layer on a sherd of Halaf ware, Iraq, 5th millenium B. C. Scanning electron microscope, 1 cm = 7.5 µm.

Small contents of chlorine and sulfur were often detected spectroscopically. As shown by X-ray studies, these elements are bound as rocksalt and gypsum, both regular constituents of the clays in the region of the Tigris and the Euphrates[27]. Since chlorine and sulfur are enriched in the paint layers compared with the bodies (Fig. 2), it must be assumed that the dissolved components were drawn into the surface by capillary action when the clay ware was dried, the strong sintering being at least partly a result of a salt glaze effect.

Our views about the firing process itself cannot be too primitive, at least in the case of the oldest wares. Since the oldest potters' furnaces found in Iraq and Iran date back only to the 4th millenium B. C.[29], the firing was presumably carried out at first in dung-charcoal kilns, such as are still used today by potters of that region[27]. The air-dried wares were piled up on a bed of charred fuel and, in the absence of wood, were surrounded by cakes of dried dung. Thus, during the firing the goods are in immediate contact with

oxygen-poor gases and become reduced; only after the fuel has been burnt can air enter and oxidize the porous pottery.

In *Greece* the oldest black paintings made by the iron reduction technique belong to the early Hellenic period in *Aegina* (beginning of the 3rd millenium B. C.). The paint layers are made from ferruginous clays and are strongly sintered; and the almost contemporaneous Early Minoan Pyrgos wares from *Crete* (cf. Table 2) show a similar picture: the homogeneous black layer with which they are covered, and which the archeologists in the absence of closer information called "Firnis" or "Urfirnis", is nothing more than a silicate paint layer prepared from clays by the iron-reduction technique and fired to a high temperature (Fig. 6). The pigment phases are hercynite, maghemite, and hematite. The potters of Middle Minoan time have carried on the Early Minoan tradition. The black priming together with the polychrome painting laid thereon hallmarks the famous *Kamares* ware (cf. Section 6.1).

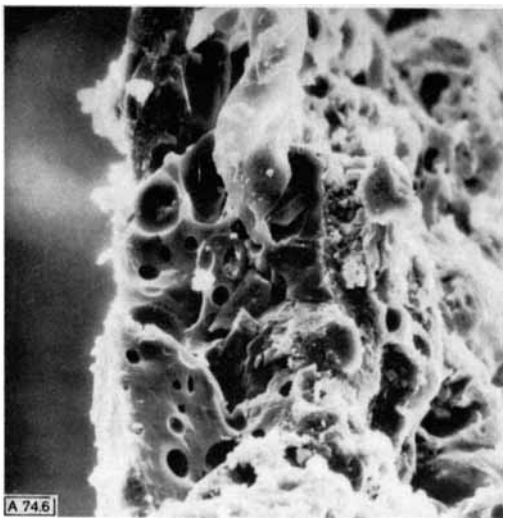


Fig. 6. Black ground ("Urfirnis") on a sherd of Early Minoan Pyrgos ware from Aj. Kyriaki, Crete. Scanning electron microscope, 1 cm = 16.5 μm.

Table 2. Decoration and types of style on Early to Late Minoan ceramics from Crete.

Period B. C.		Execution of the decoration	Style
2800 2500	EM I	Black ware with scratched patterns Red stripes on crude pottery	Pyrgos Hagios Onouphrios
2500 2200	EM II	Mottled ware	Vassiliki
2200 2000	EM III	Black coating ("Urfirnis") white painting thereon	*e.g.* Mochlos
2000 1850	MM I	Black coating ("Urfirnis") white and red painting thereon	Kamares
1850 1700	MM II		
1700 1550	MM III		
1550 1450	LM I	Black and red painting on bare pottery	Floral and sea style
1450 1400	LM II		Palace style
1400 1100	LM III	Black and red painting on bare pottery	Late palace style

It is precisely in Cretan wares that one is struck by the sometimes high content of bubbles in the black paint layer (Fig. 6). These are caused, though perhaps not exclusively, by the fact that during the firing some gases are formed (steam, carbon dioxide) that attempt to escape through the paint layer. Diffusion is possible only as long as this layer remains weakly sintered and porous. At higher temperatures more glass is formed in the paint, the clay becomes more compact, and the gases must now work their way outward as bubbles through the viscous mass; this process becomes "frozen in" during cooling. The large number of bubbles observed in the SEM pictures also indicates a relatively high firing temperature; in the special case of Kamares ceramics this conclusion can be confirmed and indeed the firing temperature can be estimated (Section 6.1).

As suggested by *R. Hampe* of Heidelberg, a suitable name should be found for paint layers of the type just discussed, and the term "*sinter layers*" is now proposed. In contrast to engobes and their special form, the "Glanzton", in the paint layers in question larger amounts of molten phase are formed at the maximum temperature. On the other hand, they differ from glazes in that only part of the mass becomes liquid at the maximum temperature, in our case probably only eutectically melting potassium silicates. The following series is then obtained:

Increasing firing temperature Increasing proportion of molten phase	Engobes esp. "Glanzton" Sinter layers Glazes

The sinter layers then include not only the paint layers of Early and Middle Minoan ceramics but also those of the older black painting described above.

It should be noted in passing that black painting of the same type is found on the pottery of the Minoan settlement on *Thera*[23], analogous to the Kamares ware, and in the Middle Bronze Age on Cyprus[19, 20]. Industrial communication thus appears at least very probable.

The transition from Middle to *Late Minoan* epoch that now follows denotes a change of style (Table 2). The black ground disappears, making way once more for naked clay

on which painting with black and red colors is carried out. The motifs are derived from flora and fauna (the floral and sea styles). It is one of the most interesting results of the present series of investigations that the period of the change in style brings also a decisive alternation in the technical procedure.

This is made clear by scanning electron microscopy (Fig. 7). The quality of the black paint layer has improved considerably. The mass has become homogeneous and free from bubbles, and the surface is remarkably smooth; the boundary between the paint layer and the body is almost a clean line. The painting has a good luster and approaches the quality of a "Glanzton" finish.

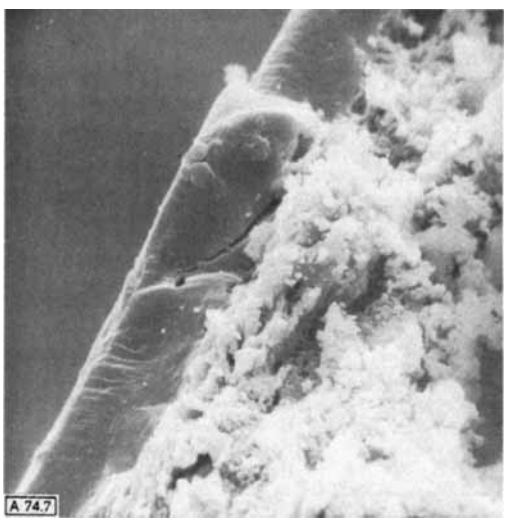


Fig. 7. Black paint layer (left) and sherd (right) of a Late Minoan ceramic (LM IA). Scanning electron microscope, 1 cm = 7.2 μm.

The progress noted here must have been achieved in a very short time, perhaps within a span of 50 years. It coincides with the change from MM III to LM I (Table 2). Transitions can sometimes be recognized by the fact that the painting of a sherd found in LM I bears the characteristics of Kamares ware, but partly also by the fact that white painting typical of the Kamares period was retained for a time in the form of spots and stripes on black and red, only finally to disappear. The same transition, perhaps with a time shift of about 50 years, was undergone by ceramic development on Thera, even though, as will be shown, the potters there also went their way.

From the spectra it follows that the improvements in technique cannot be attributed to changes of a chemical nature (Fig. 8). The difference between the compositions of the paint layers of MM and LM ware from Thera and Crete is not very marked; only the potassium content is a little higher in the Late Minoan ware. For the rest, the spectra show a combination of elements that is quite typical of paints made from clays. The change can thus only have been brought about by changes in the mechanical application of the paint slips or in the firing conditions. Since the quality changes toward a "Glanzton", whose properties, to a considerable extent, are due to finer slurrying, here too this measure must have played an important part. The higher potassium content of Late Minoan black is then explained as due to an enrichment in illitic clay minerals. However, it can also hardly be doubted that the firing temperatures were now reduced to values that appear probable from *Winter*'s experiments[14] on reconstructing true "Glanzton" wares (maximum of ca. 850 °C); as a result, the structure and texture of the small flakes of clay minerals were retained and thus also the permeability of the paint layer to gases. The first step toward the "Glanzton" technique had been taken.

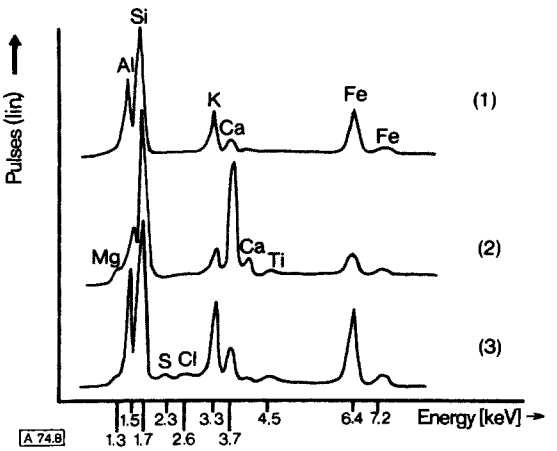


Fig. 8. Energy-dispersive X-ray spectra of sherds (2) and black painting, Minoan ceramic: (1) Thera (Middle Minoan), (3) Crete (Late Minoan).

From this period onward to classical Attic times the development and refinement of the mode of working can be followed in logical manner, *e. g.* to *Mycenean ware* (Fig. 9) or to ceramics of the *geometric epoch.* The highest perfection was reached in the 6th to 5th century B.C. in *Attica* where, in spite of the chemical basis remaining unchanged, the homogeneity of the paint mass and the surface luster are of a quality that cannot be bettered.

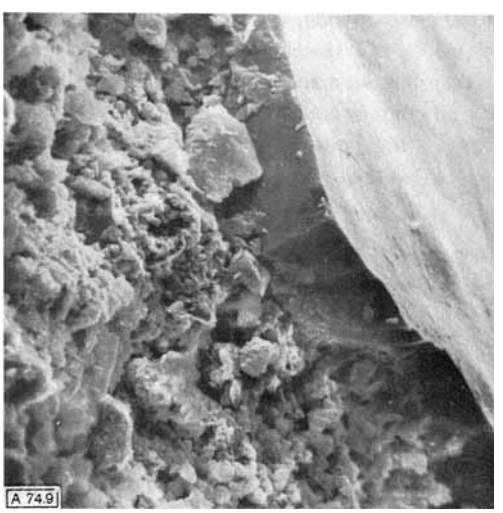


Fig. 9. Black paint layer (middle and right) and sherd (left) of a Mycenean ceramic, about 1200 B.C. Scanning electron microscope, 1 cm = 10.5 μm.

Presentation of this development cannot be concluded without some mention of the ceramic body material itself. The lime content of the ceramics from the eastern Mediterranean, as in the Iraq ware, is high. X-Ray spectroscopic analysis of the body of Kamares ware with the macroprobe gave the following composition (total 99.26 %):

SiO_2	61.2%	CaO	12.6%
TiO_2	0.85%	MgO	3.0%
Al_2O_3	11.5%	BaO	0.03%
Fe_2O_3	7.3%	Na_2O	0.78%
Cr_2O_3	0.03%	K_2O	1.97%

The ancient potters found this material to be advantageous in several respects. A high lime content of the clay means that calcium silicates are formed during firing, and that thus the coefficients of the expansion of the pot mass and the paint layer become more nearly equal. The danger of cracking on cooling is thus decreased, which is especially important if the paint layer is a sinter layer. Furthermore, lime lightens the color of the pottery, as already mentioned, and thus increases the contrast with the painting. On the other hand, the high lime content, doubtless fixed as calcium carbonate in the raw material, leads to the evolution of much CO_2 during firing, and this contributes to the fact that the sinter layers are often permeated by large numbers of bubbles and in some cases become actually foamy.

5.2. Manganese Black Technique

In this process paint slips were prepared that contained larger or smaller additions of manganese oxide minerals as well as the clay. This feature can be derived from the elemental composition which, while typical of clays, includes manganese in concentrations higher than can be found in clays. The manganese raw material also introduced iron. The manganese/iron ratio varies within wide limits; values between 13 and 440 parts to 100 have been measured[20]. *Farnsworth* and *Simmons*[7] became aware as early as 1958 of the importance of manganese content for the color of paintings on ancient ceramics.

Investigation of the phase state showed that here too the painting must have passed through the firing process. It can be assumed that the raw material contained manganese as manganese dioxide, since this is found as an ore in nature (Table 1) and since no anion-forming element other than oxygen has been encountered. However, the paint layers no longer contain an MnO_2 phase. On the contrary, bixbyite (Mn_2O_3) and hausmannite (Mn_3O_4) are found, *i. e.* manganese oxides that are formed when manganese dioxide is heated[30]:

$$MnO_2 \text{ phases} \xrightarrow{450\,^\circ C} \underset{Mn_2O_3}{\text{Bixbyite}} \xrightarrow{900\,^\circ C} \underset{Mn_3O_4}{\text{Hausmannite}}$$

Manganese-iron spinels, which are formed in the system Mn_2O_3/Fe_2O_3 at higher temperatures, are also found[31] and are accompanied by α-Fe_2O_3. The fact that manganese-containing substances are concerned in these spinel phases follows from the lattice constants, which in isolated cases with sufficiently strong back-radiation can be derived from the Debye diagram; the a_0 values are so large that they can be attained only by the introduction of the large manganese ion into the spinel lattice; they fall between the a_0 values for magnetite and jacobsite (Table 3).

Bixbyite, hausmannite, and manganese spinel are formed during the firing in accordance with the Mn/Fe ratio (Table 4). Below about 50% of Mn referred to the sum (Mn+Fe), spinel was formed along with α-Fe_2O_3; above this ratio, hausmannite and bixbyite appear. If the phase combinations found in paint layers are entered on the abscissa of the Fe_2O_3/Mn_2O_3 phase diagram[31], it is found that, with one exception, they correspond to equilibria if the formation temperatures have been between about 900 and 1000 °C (Fig. 10). The question whether conclusions can be drawn from this about the peak temperature of the ceramic firing must, it seems, remain open until the influence of the partial pressure of oxygen on the position of the equilibria has been completely clarified[32].

Table 3. Position of two manganese black spinel phases within the spinel group, lattice constants a_0 [Å].

Spinel phases in manganese black	Limiting types whose cations were detected	
	$MgO \cdot Al_2O_3$	8.080
	$FeO \cdot Al_2O_3$	8.119
	$MnO \cdot Al_2O_3$	8.250
	$MgO \cdot Fe_2O_3$	8.389
	$FeO \cdot Fe_2O_3$	8.396
8.438		
8.444		
	$MnO \cdot Fe_2O_3$	8.511

Table 4. Pigment phases in the manganese black technique in dependence on the Mn/(Mn+Fe) ratio.

Mn/(Mn+Fe) [%]	Phases
11.5	α-Fe_2O_3, a little spinel
20	Spinel, α-Fe_2O_3
25	Spinel
29	Spinel, α-Fe_2O_3
36	Spinel, α-Fe_2O_3
36.5	Spinel, α-Fe_2O_3
50	Hausmannite, spinel, bixbyite
66	Hausmannite, bixbyite
76	Hausmannite, bixbyite
81	Hausmannite, (spinel?)

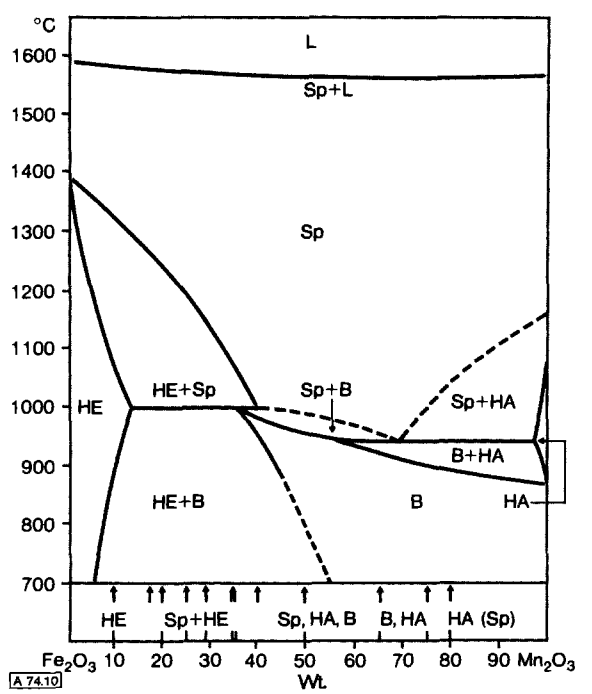


Fig. 10. The Fe_2O_3/Mn_2O_3 system, after [31]. The phase combinations found in paint layers of the manganese black type are entered along the abscissa.

The SEM pictures of manganese black layers generally differ considerably from those of iron-reduction layers. The latter's thickness is variable, being of the order of 20 to 50 µm, while the former are between about 1 and 10 µm. The paint mass consists largely of a loose aggregate of rounded pigment particles with diameters in tenths of a micron (Fig. 11); yet in some places thicker layers are observed whose SEM picture approaches that of the iron-reduction layers. This is the result of different firing techniques and the influence of the raw material composition. In principle, the manganese black layers, unlike the iron-reduction layers, need not be sintered, since they can be fired in an oxidizing atmosphere. From the point of view of the firing technique this method of manufacture is simpler than the iron-reduction technique, but it necessitates a special raw material.

Fig. 11. Manganese-rich pigment "nest" in a black paint layer on a ceramic from Thera, 15th century B.C. Scanning electron microscope, 1 cm = 3 µm.

In the region studied the manganese black technique is not so widespread as the iron-reduction technique (cf. Fig. 12). Its origins lie, so far as we can see at present, in Çatal Hüyük and Mersin in southeast Anatolia and date from the 6th—5th millenium B.C. It is to be found dating from the 4th—3rd millenium in Thrace, Thessaly, and Attica, as well as in the Danube-Moldau region. It crops up, dating from the 2nd millenium, on Aegina (the so-called "matt painting"), on Thera, and in Cyprus. In Cyprus it is relatively late (about 1600 B.C.) despite the local occurrence of manganese ores. In any case, this technique had a long life: as far as is known, it was used until the 7th century B.C.[20].

The procedure is so specialized that it immediately leads to the question of where this knowledge originated. Figure 12 offers an answer. The dates of the finds, starting from southeastern Anatolia where the earliest finds were made, fall in the direction Dikelitash/Thrace, Dimini/Thessaly, and the Balkan region. A similar situation is observed on going from southeastern Anatolia to Cyprus and thence to Thera. It is most remarkable that the movements thus delineated parallel those that *Schachermeyer* derived previously in a completely different way, namely from stylistic elements of the paintings[33] (Fig. 13). Whether these deductions can be interpreted in *Schachermeyer*'s sense as "cultural drifts" must remain undecided. The scientific result itself can be explained by migration and handing on of a technical skill. This is

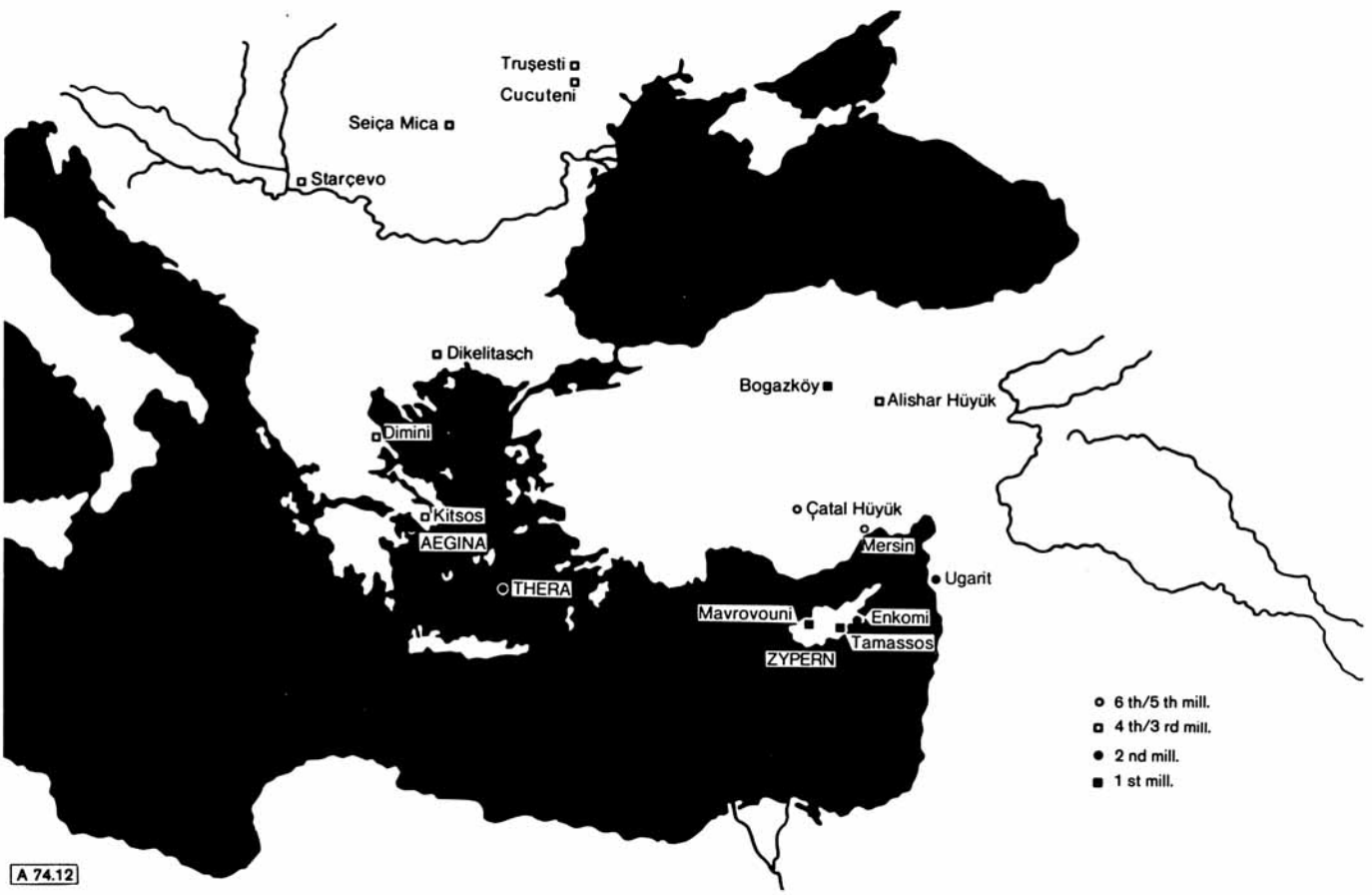


Fig. 12. Spread of the manganese black technique from the 6th to the 1st millenium B.C. to the Balkans and in the eastern Mediterranean area and Anatolia.

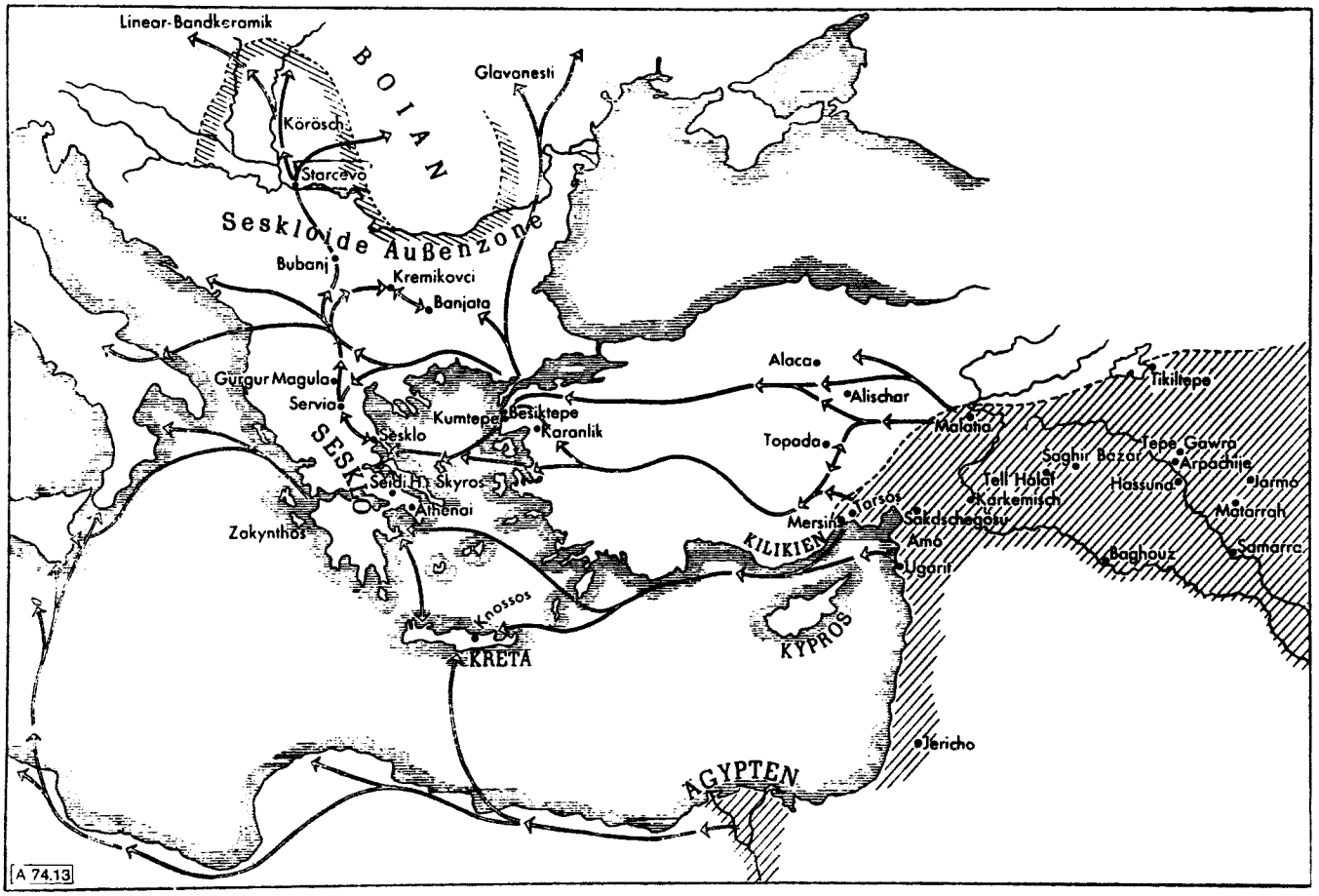


Fig. 13. "Cultural drifts" (see arrows) according to *Schachermeyer* [33] (cf. Fig. 12). ////, approx. region of oriental primary cultures. \\\\, northern boundary of the seskloic zone.

an excellent example of how scientific investigation of ancient objects can assist the work of prehistorians and archaeologists.

Finally it is very informative to have established that the manganese black technique was known in the Minoan settlement on Thera at a time when it cannot be found in Crete itself. This signifies a degree of independent skill among the potters on Thera and also indicates relations with Cyprus, where manganese appears in the paintings approximately simultaneously, about the middle of the 2nd millenium B.C.

Investigations to date on a few samples have shown that the manganese black technique is also encountered in Iran, but further statistical material is required to confirm interpretation of these findings.

5.3. Carbon Black Technique

The surface of a sherd or the complete pot can also be colored black by carbon. There are several ways in which this can be done. Carbon can separate from the flame gases owing to "smoking" during the firing process; clays may be used that are naturally rich in organic substances; the clays may be mixed with oil, animal or vegetable charcoal, soot, or graphite. Graphite is used for actual painting of the surface. In all cases the firing must be conducted under reducing conditions.

There have been hardly any analytical studies of the relationships between the carbon content, the distribution and degree of graphitization of the black pigment on the one hand and the conditions of preparation on the other[35]. Work on this subject has now been commenced.

6. Dichrome and Polychrome Painting

6.1. Black/Red and Black/Red/White

Since *manganese black* can be fired in an oxidizing atmosphere it can easily be combined with iron oxide red to give a dichrome color combination. Such paintings are very old. They have been established on the ceramics of *Iran*, namely from Çašmahi Ali (*ca.* 5000 B.C.) and Tell i Bakun (first half of the 5th millenium B.C.). In the former case the manganese black is laid on a red ground of the clay surface; in the latter, the black and the red are supplemented by white which is laid on as a thick even layer over the pottery and serves as underlayer for chessboard painting. The white covering, which also provides the color of the white fields in the pattern, consists of calcite, the black contains a spinel phase, and the red is hematite.

The *iron-reduction technique* was also used at an early date to produce black and red colors. A fragment of a Halaf ceramic from Arpatchiyeh, *Iraq* (ca. 5000 B.C.), displays red stripes and black dots. The two do not differ appreciably in chemical make-up. The paint slips consisted of clays that are either themselves naturally very rich in iron or were enriched by ferruginous earths. No great difference was detectable in the potassium content, which might have been determinant for varying degrees of compaction during firing conducted in a reducing-oxidizing manner. The decisive difference between the two paint layers lies in their thickness, which is three to four times as great for the black as for the red layers. We thus have here a black/red painting which was fired by

the iron reduction and reoxidation principle, the paint layer intended to remain black being protected against reoxidation simply by being made thicker. This method of working is as primitive as can be imagined and, as proved here, very old. It is found again and again in later periods. Many examples from Late Minoan and Mycenean ceramics show that the painter understood how to influence the thickness of the layer applied, and thus the color, merely by brushwork. The black/red dichromism not only enlivens the picture but also increases its three-dimensional effect.

We cannot exclude the possibility that other artistic tricks were also used to produce the black/red dichromism. On a Mycenean sherd it was shown by ESCA spectroscopy that the boron content was about five times as high in the black as in the surrounding red, while there was no appreciable difference in the potassium content. Thus the boron can have played a part of a sintering aid. It remains an open question whether it was added on purpose or accidentally with the raw material.

Polychrome painting reached its first wonderful degree of perfection in the Middle Minoan times on *Crete*. A vivid color mixture is laid on the black foundation discussed above (Section 5.1): white, yellowish-white, and various shades of red. The paint strokes lie side by side or on top of one another, and generally in the sequence black/white/red. An SEM picture of such layering is shown in Figure 14.

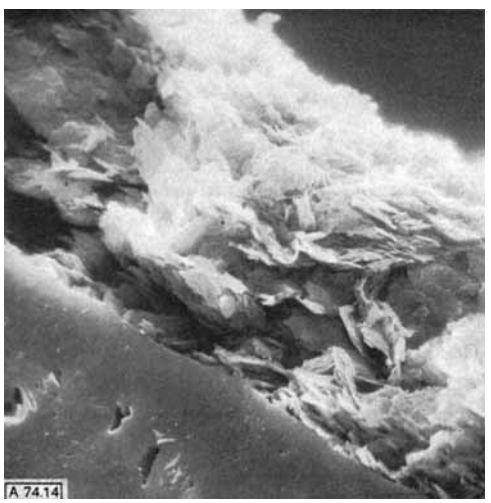


Fig. 14. Color sequence black (bottom, left), white (middle), and red (right, top) of a polychrome-painted Kamares ceramic from Crete. Scanning electron microscope, 1 cm = 7.5 μm.

Investigation of the white pigment has proved to be particularly informative. This pigment is a magnesium silicate with the Mg/Si ratio of talc, the flakes of which can be readily recognized in Fig. 14. Its X-ray diagram, however, shows the interferences of protoenstatite, the thermal transformation product of talc:

$$Mg_3(OH)_2[Si_4O_{10}] \rightarrow 3\,Mg[SiO_3] + SiO_2 + H_2O$$

The pigment on the fired vessel thus consists of pseudomorphs of protoenstatite after talc. Since it is very unlikely that the transformation was effected by heating talc powder *before* the ceramic firing, the appearance of the metasilicate shows that the talc used as the raw material for the white painting passed through ceramic firing. At the same time, the phase change permits the temperature to be estimated. The change first occurs during several hours at about 900 °C; thus, at least this temperature must have been reached at the peak of the firing. Since the development of the protoenstatite lattice increases with rising temperature, the peak temperature can be estimated still more accurately from the number and sharpness of the X-ray interferences. In this way it could be determined that, with some variation in detail from sample to sample, the peak temperatures must have been in the region of about 950 to 1100 °C. This supports the finding based on the morphology that the black ground fired on simultaneously with the white pigment is a sinter layer (Section 5.1).

Temperatures as high as this cannot be achieved by simple wood fires such as are still used by Cretan potters. However, a custom common to many places is to provide the furnace with a final heat impulse by additional firing with olive husks, and, since methods of working have been so conservative over thousands of years, this may be a reflection of an old method.

Talc white is now regarded as a pigment of very indifferent quality. It does not glaze or adhere well. The paint streaks are sensitive to rubbing and the action of water—an indication of the fact that Kamares ceramics were not intended for ordinary use but only for purposes of a cult. It is contact with the black ground that improves the adhesion, for the pigment can sinter onto it.

The use of talc as a white pigment is, so far as we can tell at present, typical of the ceramic finishing in the Middle Minoan period. It was also used on Thera[23]. As a raw material it offered obvious possibilities, since a dense form of talc (soapstone, steatite) was often used by Minoan artists for carving and the residues, not being hard, could be easily pulverized.

All the red paints studied contain hematite. Under the SEM they are found to consist of fine, roughly rounded pigment particles. The raw material was not clay but ocher. Whether this was subjected to the ceramic firing or was applied subsequently in the cold with a bonding material can be decided in the following manner. First, it can be shown that the white pigment consists of pseudomorphs of protoenstatite after talc even in the rare color sequence black/red/white, from which it follows that the red lying under the white must have been fired on[22]. Secondly, a valuable indication was provided by the phase state of mixtures of hematite with talc pigments, by means of which the red shade is varied: in these mixtures the hematite and protoenstatite are accompanied by olivine, which is formed only at higher temperatures by partial reduction of iron(III) to iron(II) oxide and its reaction with the protoenstatite phase that is still very reactive in the nascent condition[22].

$$FeO + Mg[SiO_3] \rightarrow MgFe[SiO_4]$$

It is thus clear that the painters applied all three colors one after the other to the air-dry body of the vessel, allowed each layer to dry on, and finally fired the whole in a single operation.

Black and red, prepared simultaneously and side by side, are here the result of a reduction-reoxidation process in which, as in the classical Attic period, the behavior of the paint layers is controlled by their potassium content during the

alteration of the furnace atmosphere: the black paint is rich in this ion, which acts as a flux (cf. Fig. 8), while the red pigment is almost devoid of it. The only difference from the Attic technique is that ocher and not clay is used for the red. The looser structure of the ocher naturally favored greater porosity, gas permeability, and thus susceptibility of the red paint layer to reoxidation. In Kamares ware we find, according to present knowledge, the oldest examples of a planned reduction-oxidation technique. The process of its manufacture is one—perhaps the first—forerunner of this technique, which was to achieve such great importance in the classical Attic period.

6.2. Polychromism, including Blue and Green

Polychrome painting of vessels reached its highest development in the white-ground Attic lekythoi of the 5th century B.C. It represents a peak not only from an artistic but also from the technical point of view.

The body and shoulder of the vase were covered with a white ground on which black, red, yellow, and brown colors—and sometimes also blue or green—were then painted; this ground is a layer of kaolinite (up to 200 μm thick) which has passed through the fire and has thus been converted into a pseudomorph of metakaolinite after kaolinite (Fig. 15). The spectra show the presence of potassium, which is foreign to the kaolinite structure. Since it is also clearly detectable when X-rays do not detect potassium feldspar as a possible potassium-carrier, its presence can only be ascribed to an addition. As such, only potash comes into question; this could be of value in two ways: as a dispersant during the preparation of the paint slip and as a sintering aid during firing in order to solidify the soft and loose paint slip. As will be shown, it has, however, yet another function.

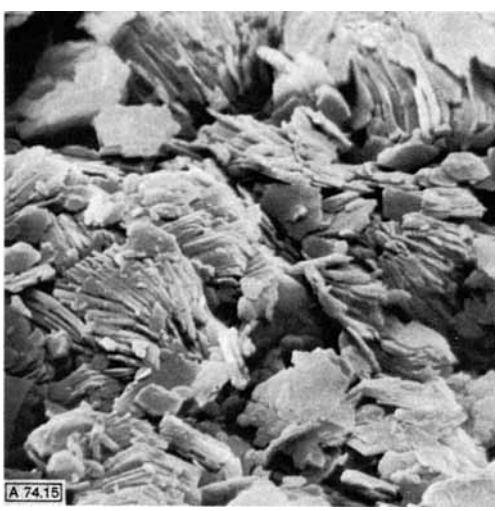


Fig. 15. White ground of an Attic lekythos, 5th century B.C. Flakes and flake stacks of kaolinite (pseudomorphs of metakaolinite after kaolinite). Scanning electron microscope, 1 cm = 3 μm.

On the white ground not only black but also brown and yellowish brown colors are produced by means of ferruginous clay slips, which are fired first in a reducing and then in a reoxidizing atmosphere. The shade of the color is controlled mainly by the potassium content and the layer thickness: the black layers are the thickest and have the highest potassium contents; they contain hercynite and maghemite as the pigments. The brown to yellowish-brown layers contain less potassium and are thinner. The content of hematite increases in the same direction and that of spinel phases decreases.

The most interesting results followed from an investigation of the red paintings. This is unusually rich in shades. The raw material was ocher, which on firing yields relatively dull colors. The paint layers are actually layers of pigment. The particle diameters are of the order of microns, similarly to modern iron oxide pigments (Fig. 16). In addition, however, there is another type of red, which contains colloidal metallic copper as the pigment, and in contrast to the ocher red this pigment does not lie on top of the white ground but is dispersed within it. In general the red color penetrates to about the middle of the white ground. The colloidal particles are too small to be resolved by a scanning electron microscope, *i.e.* they are less than about 250 Å.

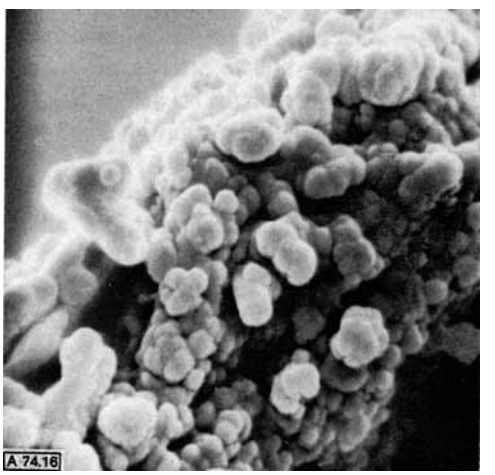


Fig. 16. Iron oxide pigment particles in the red painting on an Attic lekythos. Scanning electron microscope, 1 cm = 1.2 μm.

"Copper red" is known in modern glazing, even if seldom used. It is produced by thermal reduction of copper(II) oxide, and this was certainly also the case with the ancient pigment. Since the color has penetrated into the white ground and paint lines of this type have uneven edges, it can be assumed that the painters of the time used an aqueous solution of copper sulfate which was available to them as the mineral chalcanthite from the Laurion mines. On contact with the potash-containing white ground a basic copper carbonate was precipitated, which dissociated during firing and was finally reduced to elemental copper. It was apparently protected against reoxidation by surface sintering of the kaolinite particles.

One may well ask why the Attic vase painters turned to this somewhat exceptional pigment when they could have produced a red much more simply and cheaply from iron oxide pigments. The probable answer is that, when they began to work with copper compounds, they first intended to enrich the polychrome palette with blues and greens. Instead, they obtained a red after the firing, which may at first have been a disappointment. Such reconstruction of the events is indicated by the finding of sherds on which the copper-red has been overpainted by Egyptian Blue after the firing. The painter wanted to correct a color that had gone wrong and used Egyptian Blue for this purpose[34] because it was

well known to him as a cold-spreadable pigment used in wall paintings.

There remains only the question why the copper-red technique was retained at all after such disappointment. The reason is that copper red gives a more beautiful and brighter shade of color than an iron oxide pigment. Thus, it appears to have remained in use for some decades around the turn of the 5th to the 4th century B.C.

Apart from the case just mentioned, blues, and still more greens, are seldom encountered on ancient ceramics. The most frequent use of blue painting was made in Egypt during the 18th dynasty. The pigment used there was identified by some authors as Egyptian Blue (cf. Ref. [24]). However, more recent investigations of ceramics from Thebes and Tell el Amarna yielded cobalt aluminate as the pigment phase[24, 36]. Its composition indicates a highly developed technique[24]. This blue coloring agent was only rediscovered three thousand years later ("Thenard's Blue"). The blue color residues on the white ground of Attic lekythoi proved to be Egyptian Blue, the green ones are copper hydroxychloride, which was previously known in ancient times only as a pigment in wall paintings[37]. All these pigments were clearly applied *after* the firing, sometimes with gypsum and sometimes with an organic bonding agent, the artist taking less account of experience in ceramics than of those in wall painting.

Thus, although there were other and more easily accessible blue and green pigments (azurite, malachite), the Attic lekythos-painters remained true to traditions that were more than a thousand years old. This example clearly shows again what has repeatedly been found in other connections, namely that technical tradition played a large part in ancient times, and that it was retained for long periods of time and over considerable distances.

7. Concluding Remarks

About 200 ceramic fragments were available for the investigations described above, a number that is not large if we consider that reliable statements about material from such a large area and covering a time span of almost 6 millenia require extensive statistical material. It is, however, large when judged by the experimental effort involved in the analyses, and particularly in view of the difficulties in obtaining specimens. It may be that some of the results will have to be revised or modified if it should become possible to expand the statistical basis appreciably at a later date. That it was possible at all to expand the coverage so far is due to the understanding assistance of many colleagues and Institutions in Germany and elsewhere.

We are particularly indebted to Prof. Buchholz of Giessen, who stood by the work also as archaelogical mentor, Prof. Marinatos of Athens (deceased), Prof. Dehn and Dr. Pingel of Marburg, who placed the rich material from the collection at the Prehistorical Seminar of the University at our disposal, Prof. Hauptmann, Prof. Nissen, and Frau Prof. Dr. Nagel-Strommenger of Berlin, who made it possible to study the Iranian and Iraqi ceramics. We are also grateful for valuable support from Dr. Alexiou of Heraklion, Dr. Beckel of Würzburg, Dr. Borheim of Marburg, Dr. Bracker of Cologne, Prof. Dohrn of Cologne, Frau Dr. Grunwald of Bonn, Dr. Hepding of Darmstadt, Prof. Himmelmann of Bonn, Prof. Kaiser of Cairo, Frau Dr. Lambert of Athens, Prof. Levi of Athens and Rome, Prof. Mellaart of London, Prof. Milojčič of Heidelberg, Prof. W. Müller of Munich, Frau Dr. Philippaki of Athens, Prof. Sakellarakis of Athens, Prof. Schiering of Mannheim, Frau Prof. Simon of Würzburg, Dr. Thimme of Karlsruhe and Prof. Walter of Innsbruck.

The Deutsche Forschungsgemeinschaft and recently the Stiftung Volkswagenwerk aided the work by research grants. Bayer AG Leverkusen provided support by way of apparatus. Finally, we thank K. Sehrig, P. Zajons, B. Reinfandt, and L. Hänig for their collaboration.

Received: March 10, 1975 [A 74 IE]
German version: Angew. Chem. 87, 639 (1975)
Translated by Express Translation Service, London

[1] *Ch. F. Binns* and *A. D. Fraser*, Am. J. Archaeol. *33*, 1 (1929).
[2] *Th. Schumann*, Ber. Dtsch. Keram. Ges. *23*, 408 (1942).
[3] *F. Oberlies* and *N. Köppen*, Ber. Dtsch. Keram. Ges. *31*, 287 (1954).
[4] *F. Oberlies* and *N. Köppen*, Ber. Dtsch. Keram. Ges. *39*, 19 (1962).
[5] *F. Oberlies*, Naturwissenschaften *55*, 277 (1968).
[6] *M. Farnsworth* and *H. Wisely*, Am. J. Archaeol. *62*, 165 (1958).
[7] *M. Farnsworth* and *I. Simmons*, Am. J. Archaeol. *67*, 389 (1963).
[8] *J. V. Noble*, Am. J. Archaeol. *64*, 307 (1960).
[9] *U. Hofmann*, Angew. Chem. *74*, 397 (1962); Angew. Chem. internat. Edit. *1*, 341 (1962).
[10] *U. Hofmann* and *R. Theisen*, Z. Anorg. Allg. Chem. *341*, 207 (1965).
[11] *U. Hofmann*, *R. Theisen*, and *Y. Yetmen*, Ber. Dtsch. Keram. Ges. *43*, 607 (1966).
[12] *U. Hofmann*, Naturwissenschaften *53*, 218 (1966).
[13] *M. K. Pavićević*, Ber. Dtsch. Keram. Ges. *51*, 61 (1974).
[14] *A. Winter*, Techn. Beitr. Archäol., I. Röm. German. Zentralmuseum Mainz (1959).
[15] *A. Winter*, Mitt. Dtsch. Archäol. Inst., Athen. Abt., *83*, 315 (1968).
[16] *W. Noll*, *R. Holm*, and *L. Born*, Naturwissenschaften *58*, 615 (1971).
[17] *W. Noll*, *R. Holm*, and *L. Born*, Naturwissenschaften *59*, 270 (1972).
[18] *W. Noll*, *R. Holm*, and *L. Born*, Naturwissenschaften *59*, 511 (1972).
[19] *W. Noll*, *R. Holm*, and *L. Born*, Jahrb. Staatl. Kunstsammlungen Baden-Württemberg *10*, 103 (1973).
[20] *W. Noll*, *R. Holm*, and *L. Born*, Ber. Dtsch. Keram. Ges. *50*, 328 (1973).
[21] *W. Noll*, *R. Holm*, and *L. Born*, N. Jahrb. Min. Abh. *122*, 119 (1974).
[22] *W. Noll*, *L. Born*, and *R. Holm*, Naturwissenschaften *61*, 361 (1974).
[23] *W. Noll*, *L. Born*, and *R. Holm*, Naturwissenschaften *62*, 87 (1975).
[24] *W. Noll* and *K. Hangst*, N. Jahrb. Min. Mh., 1975, 209.
[25] *J. Ohnsorge* and *R. Holm:* Rasterelektronenmikroskopie. Thieme, Stuttgart 1973.
[26] *L. Reimer* and *G. Pfefferkorn:* Rasterelektronenmikroskopie. Springer, Berlin 1973.
[27] *F. R. Matson* in *R. H. Brill:* Science and Archaeology. M. I. T. Press, Cambridge, Mass. 1971, p. 65.
[28] *H. Salmang* and *H. Scholze:* Die Keramik. Physikalische und chemische Grundlagen, 5. Aufl. Springer, Berlin 1968, p. 282ff.
[29] *G. Delcroix* and *J. L. Huot*. Les Fours dits "de potier" dans l'orient ancien, in: "Syria", Vol. XLIX, Paris 1972, p. 35ff.; see also *Ch. Singer*, *E. J. Holmyard*, and *A. R. Hall:* A History of Technology, 3rd Edit. Clarendon Press, Oxford 1956, pp. 391—397.
[30] *G. Gattow* and *O. Glemser*, Z. Anorg. Allg. Chem. *309*, 20, 121 (1961).
[31] *A. Muan* and *S. Somiya*, Am. J. Sci. *260*, 230 (1962).
[32] *H. Schmalzried*, private communication 1974.
[33] *F. Schachermeyer:* Die ältesten Kulturen Griechenlands. Kohlhammer, Stuttgart 1955, p. 53.
[34] *W. T. Chase* in *R. H. Brill:* Science and Archaeology. M. I. T. Press, Cambridge, Mass. 1971, p. 80.
[35] *H. J. Schwing*, Berliner Jahrb. Vor- und Frühgeschichte *6*, 179 (1966).
[36] *J. Riederer*, Archaeometry *16*, 102 (1974).
[37] *W. Noll* and *K. Hangst*, N. Jahrb. Min. Mh. *1975*, in press.

Chemical Nickel Plating

By Hans Niederprüm[*]

Metal layers can be deposited from aqueous solutions not only by electric current as in electroplating but also by strong reducing agents. Chemical deposition of nickel on metallic and nonmetallic substrates, together with the long-known silvering of glass, are the most widespread examples. This remarkable reaction has recently found a variety of industrial applications mainly in the preparation of corrosion-resistant, hard, and wear-resistant protective layers, in the metallizing of plastics, and in electronics.

1. Introduction

The chemical deposition of nickel from aqueous solution by strong reducing agents without the use of electric current was discovered[1] (or rather rediscovered[2]) by *Brenner* and *Riddell* some 30 years ago and has since acquired considerable industrial importance[3]. The field of metallization by chemical means has developed into an independent branch of surface technology which continues to attract new scientific and industrial interest[4-8].

Chemically produced metal layers are characterized in many cases by special chemical, physical, technological, and mechanical properties and, especially for engineering plating, extend the classical electrolytic metallization processes. Furthermore, semiconductors and insulators can be metallized after suitable pretreatment and are then amenable to further processing by conventional electrolytic methods, especially in the electroplating of plastics and in the electronics industry for the production of printed circuits[9, 10]. Chemically deposited layers are independent of geometric shape and can thus be formed with equal characteristics in inaccessible places. Hence metal parts of complicated shape—tubes, hollow bodies, drillholes, *etc.*—can be easily metallized in this way, while electroplating of such articles can be performed only with considerable effort (*e.g.* with the aid of shaped anodes) or not at all[11].

Industrially interesting possibilities going beyond the field of electroplating of plastics, are also offered by a combination of chemical and electrolytic metallization processes, *e.g.* for hard chromium plating of complicated pieces that have already been nickel plated by nonelectrolytic means. Thus, pressure cylinders can be protected against corrosion even in the ducts; owing to insufficient penetration, this cannot be achieved by chrome plating alone, which is nevertheless still necessary for the actual pressure surfaces. Finally, repair of nickel plating, *e.g.* of worn-out injection molds, is of importance.

Since reducing agents are more expensive than external current, chemical processes of metal deposition are employed only when the specific properties of the layer justify the higher costs or when electrolytic processes cannot be used (as in the case of nonconductors). For articles of intricate shape the costs of molds and of the processing technique play a large role in addition to the costs of the actual metal deposition, so that in such cases thick (hard) nickel plating by chemical means is no more expensive than hard chromium plating from an electrolytic bath.

[*] Dr. H. Niederprüm
Bayer AG, Sparte AC
509 Leverkusen (Germany)

Fewer metals can be deposited chemically, of course, than by electrolysis since no chemical reducing agent is so variable as electric current. However, two- or three-component alloys containing, *e.g.*, phosphorus or boron can be obtained by means of special reducing agents but not electrolytically. The most widely used and furthest developed chemical techniques are those for chemical nickel plating, and for the long known silver plating of glass. Second place is taken by electroless deposition of copper (cf. [12-14]), which is of importance mainly for the production of printed circuits. Baths for the electroless deposition of the precious metals (gold, silver, palladium, platinum) or of tin, iron, or cobalt, or of alloys of these metals[15-17], are not yet used industrially on a large scale[18, 19]. The development of further or improved processes will be easier when new reducing agents become available[15, 20-22].

2. Principles of the Chemical Deposition of Metals

As is well known, in electrolytic deposition of metals the metal ions are reduced to the metal at the cathode. This function of the cathode as an electron donor is assumed in the nonelectrolytic processes by a reducing agent which is oxidized in solution and/or on the surface of the object to be metallized. For thermodynamic reasons the redox potential of the redox pair used must be more negative than that of the metal/metal-ion pair. However, the potential difference may not be too great, for then, as in crystallization from supersaturated solutions, the nucleation rate avalanches and the bath decomposes. The strong reducing agents sodium hypophosphite and sodium tetrahydridoborate are thus suitable for the deposition of nickel or cobalt; for the deposition of copper, which is higher up in the electrochemical series, the less active formaldehyde is used, but only in alkaline solution since its reducing power is insufficient in acids (Table 1).

Table 1. Standard potentials of some reducing agents in aqueous solutions of activity 1; gases at 1 bar (potential differences against a standard hydrogen electrode at 25 °C). For comparison: standard potentials of nickel and copper.

$H_2PO_2^- + 3OH^-$	→	$HPO_3^{2-} + 2H_2O + 2e^-$; $E_0 = -1.57$ V
$H_3PO_2 + H_2O$	→	$H_3PO_3 + 2H^+ + 2e^-$; $E_0 = -0.40$ V
$HCHO + 3OH^-$	→	$HCOO^- + 2H_2O + 2e^-$; $E_0 = -1.11$ V
$HCHO + H_2O$	→	$HCOOH + 2H^+ + 2e^-$; $E_0 = 0.056$ V
$BH_4^- + 8OH^-$	→	$H_2BO_3^- + 5H_2O + 8e^-$; $E_0 = -1.24$ V
$BH_4^- + 3H_2O$	→	$H_3BO_3 + 7H^+ + 8e^-$; $E_0 = -0.48$ V
$[Ni_s]$	→	$Ni^{2+} + 2e^-$; $E_0 = -0.25$ V
$[Cu_s]$	→	$Cu^{2+} + 2e^-$; $E_0 = 0.345$ V

In view of the redox potentials of redox pairs used for the metallization reaction it should not be possible to prepare aqueous baths consisting of a metal salt and a reducing agent that would be sufficiently stable for practical purposes, because the redox reaction should be spontaneous with attendant deposition of the metal, *i.e.* decomposition of the bath. Inhibition of reaction[23] is, however, very frequently observed ("irreversible redox systems") and it is this phenomenon which ultimately permits reductive deposition of metals; with no such inhibition the standard potentials (in water) of the reducing agents commonly used would lead to spontaneous decomposition with evolution of hydrogen.

Although thermodynamically unstable, the baths used for reductive metallization possess sufficient kinetic stability under certain conditions owing to the activation energy needed for decomposition. Energy in the form of heat may be applied to overcome the inhibition of the reaction, and the baths are thus often used at elevated temperatures (up to 95 °C). Equilibration can also be accelerated by catalysts; such catalysts for the reductive deposition of metals include many metals known as hydrogenation or dehydrogenation catalysts, *e.g.* palladium, silver, nickel, iron, or platinum. Thus, if a catalytically active object that may itself be a metal or provided with metal nuclei is dipped into the metastable aqueous solution of the metal salt and reducing agent then, after a short induction period, the redox reaction sets in at the surface of the object and reduced metal is deposited there. Since the new surface also acts as a catalyst the process does not come to a standstill until equilibrium has been established. Chemical deposition of metals is thus a heterogeneous, quasi-autocatalytic reaction that occurs only at the surface of the object to be metallized.

In many cases, however, the inhibition of decomposition of the reducing agent is counteracted by the catalytically active surface, and chemical deposition of metal is thus usually accompanied by considerable evolution of hydrogen. This is detrimental to the economics of the process, and as a result the reduction yields are usually below 50 %. Since the metal salt/water/reducing agent systems are very sensitive to impurities, which can easily be entrained during practical operation and may act as catalytic seeds, stabilizers (inhibitors) are added. These stabilizers may be metal salts of, *e.g.* lead, thallium, cadmium, zinc, bismuth, or molybdenum, or organic sulfur compounds containing sulfur in oxidation state 2+ (*e.g.* thiourea, mercaptopropionic acid) which are known to be capable of deactivating catalysts used for the hydrogenation of organic compounds; arsenic compounds, sulfides, cyanides, thiocyanates, and selenium derivatives also act in this way. The concentration of such substances is critical, since at higher concentrations the surface of the object to be metallized is also inactivated and deposition of the metal finally comes to a halt. The choice of the stabilizer and its concentration can generally be determined only empirically.

Baths for chemical metallizing also contain complexing agents, buffers, accelerators, acids or bases for control of pH, and wetting agents. The complexing agents may be, for example, alkali metal salts of organic acids (tartaric, citric, glycolic, lactic, succinic, or malonic acid) or amino compounds (ethylenediamine, ethylenediaminetetraacetic acid); along with their buffer action, they have the task of converting the metal salts into chelate complexes so as to prevent precipitation of metal hydroxides or sparingly soluble salts, and of maintaining a low metal-ion concentration. Acetate, borax, or an ammonium compound is often also added as a buffer to maintain constancy of the bath pH, which shifts into the acid region as deposition of the metal progresses.

The rates of reductive metallization reactions are determined mainly by four parameters: the concentrations of the metal ions and the reducing agent, the pH, and the temperature. The concentration of the metal ions and the pH are controlled by the additions to the bath; at a given temperature, given surface-to-volume ratio, and a given stabilizer content, the rate of deposition is a function of the content of the reducing agent. A prerequisite is suffient stirring of the bath or movement of the articles, so that sufficient bath solution is in contact with the surface being metallized. For several reasons (stability of the bath, rate of diffusion, movement of the bath solution) the content of the reducing agent cannot be increased indefinitely. The rate of deposition is usually 20—30 µm/h, which corresponds to a current density of 2—3 A/dm^2 in electrolytic processes.

Nevertheless, on closer consideration it will be seen that the rate of the autocatalytic metallization reactions are influenced by even further factors (cf. [24, 25]) that will not, however, be considered here.

Little is yet known about the mechanism of nonelectrolytic deposition of metals, and especially about the initial processes, as also in the electrolytic technique in the case of electrocrystallization[26, 27–32]. Attempts to follow the rate of the metal deposition continuously by suitable measuring devices, to set up relevant parameters that influence the rate by means of specific coupling factors[33], and also to determine the optimal particle size and covering density of the catalytically active metallic seeds that act as initiators[34, 35] are of practical interest.

3. Reducing Agents

The most important reducing agents used in industrial baths for chemical metallization are sodium hypophosphite, formaldehyde, sodium tetrahydridoborate and dimethylamine- or diethylamine-borane. Some of these materials are listed in Table 1, together with their redox potentials at pH 1 and pH 14 calculated from thermodynamic data[36–38]. These show that sodium hypophosphite and sodium tetrahydridoborate are powerful reducing agents in both alkaline and acidic solutions, while formaldehyde will only work in alkaline solution[39].

Consideration of the standard potentials in relation to the suitability of reducing agents for metal deposition is, however, only of qualitative value. This is because on the one hand, owing to proton transfers, the potentials corresponding to the Nernst equation are strongly dependent on the pH, and secondly, because these potentials are influenced by the formation and decomposition of complexes which determine the concentrations (activities) of the reacting ions. Finally the standard potentials are not in general identical with the formal, directly measured, potentials owing to the inhibition discussed above, which is observed particularly when gases or strong complexes are formed.

The reduction capacity of a reducing agent is of more practical importance since, in contrast to the situation in electrolytic processes, oxidation products (*e.g.* phosphite, borate, or formate) are formed in this method and can become

enriched in the bath with a consequent unfavorable influence on the rate, the stability of the bath, and the properties of the coating. This disadvantageous feature of chemical metallization is increased by the fact that the metals deposited must be replaced later as salts (enrichment of anions), an operation that is not necessary in electrolytic processes since dissolution of the anode provides the metal supplement[40]; however, this additional disadvantage becomes less important with decreasing redox equivalent weight. Table 2 shows the number of reduction equivalents supplied per unit weight for some reducing agents. Hydrazine could be considered ideal from this point of view, since only nitrogen and water are formed on its oxidation in either alkaline or acid solution:

$$N_2H_4 + 4OH^- \rightarrow N_2 + 4H_2O + 4e^-;\ E_0 = -1.16\,V$$
$$N_2H_5^+ \rightarrow N_2 + 5H^+ + 4e^-;\ E_0 = -0.23\,V$$

Table 2. Reducing agents for chemical nickel plating.

Formula	Mol. wt.	No. of electrons donated	Redox equivalent weight
N_2H_4	32.05	4	≈ 8
HCHO	30.03	2	≈15
$NaBH_4$	37.84	8	≈ 4.7
$(CH_3)_2NH \cdot BH_3$	58.92	6	≈ 9.8
$(C_2H_5)_2NH \cdot BH_3$	86.98	6	≈14.5
$NaH_2PO_2 \cdot H_2O$	106.01	2	≈44

However, no usable nickel coating can be produced by hydrazine. The reduction capacities of hydridoborates (especially $NaBH_4$) and of formaldehyde are favorable.

Whereas formaldehyde and sodium hypophosphite have long been prepared on an industrial scale, it is only recently that sodium tetrahydridoborate and its derivatives have become accessible on a large scale. In the borosilicate process[41] borax, quartz, sodium, and hydrogen are allowed to react at 450—500 °C:

$$(Na_2B_4O_7 + 7SiO_2) + 16Na + 8H_2 \rightarrow 4NaBH_4 + 7Na_2SiO_3$$

The resulting mixture is extracted under pressure with liquid ammonia, whereupon $NaBH_4$ is obtained in pure form as a white, slightly hygroscopic salt. The boric ester process[42, 43] starts from trimethyl borate, which is treated with sodium hydride generated *in situ* in a mineral oil suspension at 250—270 °C:

$$4NaH + B(OCH_3)_3 \rightarrow NaBH_4 + 3NaOCH_3$$

The mixture is hydrolyzed with water, and the aqueous phase is extracted with isopropylamine.

Amine-borane adducts are prepared industrially by the reaction of the corresponding ammonium chlorides with $NaBH_4$ in a water/solvent mixture[20]:

$$NaBH_4 + R_2NH \cdot HCl \rightarrow R_2NH \cdot BH_3 + NaCl + H_2$$

Owing to its ready solubility in water, dimethylamine-borane is more suitable than the homologous ethyl compound for inclusion in electroless baths; when the latter compound is used, a lower alcohol must be added to assist dissolution. It can be used not only in the preparation of thin conducting coatings but also of thicker nickel layers, *e.g.* on plastics or aluminum, the latter type having a laminar layer structure. Over $NaBH_4$, which can be used only in strongly alkaline solutions, the amine-borane adducts have the advantage of greater resistance to hydrolysis, so that the reducing baths can also be operated under neutral or weakly acidic conditions. Sodium hypophosphite has similar properties.

4. Nickel Plating Baths

4.1. Baths Based on Sodium Hypophosphite

Chemical deposition of nickel on metallic and nonmetallic substrates by means of hypophosphite is the oldest and best-studied process for electroless nickel plating. Acid baths (pH 4—6, $T > 90$ °C) are used mainly for thick nickel plating of steel, cast iron, copper, aluminum, titanium, beryllium, and some alloys; alkaline baths (pH = 7—10, $T = 25$—50 °C) are used in metallizing plastics and other nonconducting materials[44].

On the basis of the classical investigations by *Brenner et al.*[1], who had already developed acid and alkaline (ammoniacal) types of baths, *Gutzeit* introduced the process into American industry at the beginning of the fifties[45, 46]. In the USSR mainly *Gorbunova* and *Nikiforova* interested themselves in this method[47]. In West Germany the first plant came into operation in 1966[48]. With a pump capacity of 8 m^3/h (meanwhile increased to 27 m^3/h[49]) a maximum of 9.6 kg of nickel could be deposited per hour, *i.e.* about 45 m^2 of surface could be covered per hour to a thickness of 25 µm. Some chemically nickel plated articles are shown in Figure 1.

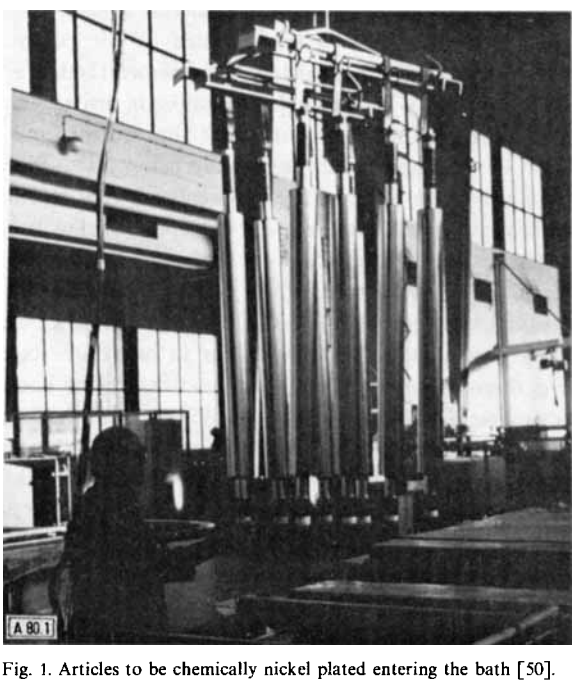


Fig. 1. Articles to be chemically nickel plated entering the bath [50].

Today, besides the Kanigen process[45] there are a number of other industrial processes, both acidic and alkaline, making use of hypophosphite baths. The processes differ not only in the deposition conditions, the method of operation (continuous or batchwise), and the fields of application (thick nickel plating or the formation of conducting films on plastics),

but also mainly in the types and amounts of complexing agents, accelerators, and stabilizers added to the baths.

The basic composition is generally 10—30 g/l of nickel chloride or sulfate and 10—50 g/l of sodium hypophosphite. More recent work concerns also the deposition of ternary and quaternary Ni-Cu(Sn)-P layers[51, 52], and the preparation of especially abrasion-resistant nickel dispersion layers incorporating silicon carbide[53]. The overall redox reaction leading to the deposition of nickel is:

$$H_2PO_2^- + Ni^{2+} + H_2O \rightarrow Ni + H_2PO_3^- + 2H^+$$
$$H_2PO_2^- + H_2O \rightarrow H_2PO_3^- + H_2$$

The reduction of nickel ions is accompanied by decomposition of the hypophosphite with evolution of hydrogen. The latter reaction is presumably the reason why the chemically deposited Ni layers contain varying amounts of phosphorus (2—15%), the exact amount depending on the pH, temperature, concentration of hypophosphite and phosphite, layer thickness, and other factors. Acid hypophosphite baths used industrially give coatings containing 7—10% of P, alkaline baths about 3%. The strongest effect on the layer composition is exerted by the pH: from an acid nickel chloride bath at 94 °C containing glycolic acid, succinic acid, and fluoride ions, the deposited layers contain 2.2, 3.5, 8.9, 11.4, or 14.1% of phosphorus at pH 5.8, 5.0, 4.5, 4.0, and 3.0 respectively[54].

The equations given above show only the initial and the final state. Possible intermediate stages, *e.g.* formation of atomic hydrogen, hydride ions, phosphane, colloidal nickel hydroxide species, *etc.* have been postulated in various publications[55], but there is still no unified theory confirmed by experiment. What is certain is that from industrial baths about 1 mol of nickel is deposited per 3 mol of hypophosphite; the reduction yield, based on the nickel, is 36—38%. The chemicals consumed in nickel plating—nickel salt, reducing agent, and sodium hydroxide—are continuously replaced by addition to a cooled partial stream of the pumped electrolyte. However, the increasing content of sodium phosphite limits the life of the bath, since nickel phosphite is finally precipitated, whereupon the stability of the bath and the quality of the coating deteriorate (roughness). Since regeneration is generally uneconomic, the bath is discarded after a throughput of about 80 g/l of nickel[56].

4.2. Baths Based on Sodium Tetrahydridoborate

In the last few years certain technical and economic advantages (longer life, simpler procedure and operation of the bath) have led to the industrial introduction of nickel tetrahydridoborate baths for thick or hard nickel plating of metallic or ceramic articles. Development of stable baths was achieved at the end of the 1950's[57]. In West Germany the process was introduced into industry by *Lang et al.* under the trade name of Nibodur[58]. The first technical unit with a bath volume of 3000 l was erected in 1967[59]; the capacity will be increased threefold in 1975. Figure 2 shows an electroless nickel plated article[60], and Figure 3 a nickel plating plant[61].

Because of its sensitivity to hydrolysis, sodium tetrahydridoborate must be used at strongly alkaline pH ($\approx$14). Deposition of nickel occurs approximately according to the following overall equation[62]:

$$10\,NiCl_2 + 8\,NaBH_4 + 17\,NaOH + 3\,H_2O \rightarrow$$
$$Ni_{10}B_3\,(=3\,Ni_3B + Ni) + 5\,NaB(OH)_4 + 20\,NaCl + 17.5\,H_2$$

Independently of the age of the bath, the deposits contain, besides nickel, about 5% of boron as well as degradation products of the stabilizer[63]. Little is known about the

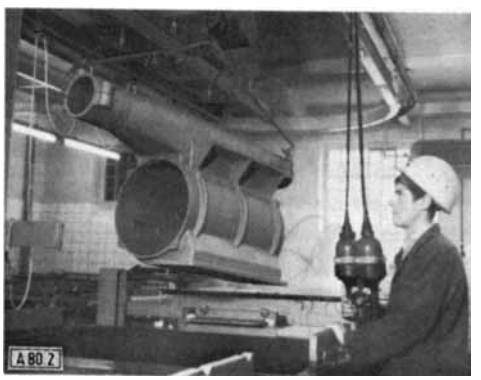


Fig. 2. Chemically nickel plated article on removal from the bath (blower for dust-containing gases) [60].

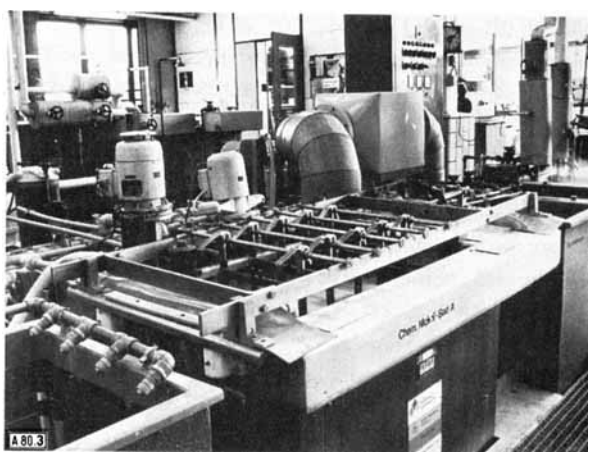


Fig. 3. Nickel plating plant [61].

mechanism of the nickel-boron deposition[64, 65]. According to mass-spectroscopic measurements of the isotopic composition of gaseous hydrogen evolved in the nickel plating in heavy water, the following partial reactions may take place:

1) Reduction to nickel:

$$BH_4^- + 4H_2O \rightarrow B(OH)_4^- + 4H + 4H^+ + 4e^-$$
$$2Ni^{2+} + 4e^- \rightarrow 2Ni$$

$$BH_4^- + 4H_2O + 2Ni^{2+} \rightarrow 2Ni + B(OH)_4^- + 2H_2 + 4H^+$$

2) Reduction to boron:

$$BH_4^- + H^+ \rightarrow BH_3 + H_2 \rightarrow B + 2.5\,H_2$$

3) Hydrolysis of the reducing agent:

$$BH_4^- + 4H_2O \rightarrow B(OH)_4^- + 4H + 4H^+ + 4e^- \rightarrow B(OH)_4^- + 4H_2$$

According to these equations, the H atoms formed by hydrolysis unite to form H_2 molecules which do not take part in the reduction of nickel ions. The observed increase in

the H^+-ion concentration is due only to liberation of protons from the water.

1 kg of $NaBH_4$ precipitates about 2.2 kg of Ni-B alloy from nickel salts; *i.e.* with a layer thickness of 25 µm and a density of 8.25 g/cm³, 10.7 m² of surface can be nickel plated. If the same reduction yield is assumed, about 11.4 kg of $NaH_2PO_2 \cdot H_2O$ would have to be added to a nickel hypophosphite bath for similar results. Thus, even without regeneration, an $NaBH_4$ bath has a considerably longer life. Without an appreciable decrease in the reduction yield or the rate of deposition about 200 g of nickel can be deposited from 1 liter of plating solution[25]. The bath components that are consumed (nickel salt, reducing agent, sodium hydroxide, and stabilizer) are continuously supplemented. After the throughput of the stated amount of nickel the bath can be regenerated in a simple manner: in this process the dissolved borate is converted by lowering of the pH with hydrochloric acid into the sparingly soluble, crystalline sodium tetraborate $Na_2B_4O_7 \cdot 10H_2O$ and is then filtered off together with some precipitated NaCl[66]. A nickel tetrahydridoborate bath can thus be operated for an almost unlimited period—for several years. The initial composition of a continuously operating bath is as follows:

30 g/l $NiCl_2 \cdot 6H_2O$, 50—60 g/l ethylenediamine, 40—50 g/l NaOH, 0.2—0.3 g/l $NaBH_4$, 20—30 mg/l stabilizer. The rate of deposition almost exclusively dependent on the $NaBH_4$ content, is 15—20 µm/h with a surface-to-volume ratio of up to 4 dm²/l. Metal compounds have proved to be the best stabilizers[65, 67, 68], being incorporated in reduced form into the precipitate and conferring on it favorable mechanical properties (low coefficient of friction, high hardness and wear-resistance). In a continuously operated plant[69, 70] the heated plating tank, manufactured from stainless steel, is protected against chemical nickel deposition by anodic polarization[71].

4.3. Baths Based on Amine-Borane

Sodium tetrahydridoborate is unsuitable for baths used to metallize plastics or other temperature- or alkali-sensitive materials. For this field of application, therefore, nickel-amine-borane baths—acid, neutral, and alkaline—have been developed, which operate at 25—65 °C[14]. Dimethylamine- or diethylamine-borane is used as the reducing agent. The following overall equation is the basis of the nickel deposition:

$$3Ni^{2+} + R_2NH \cdot BH_3 + 5OH^- \rightarrow 3Ni + H_3BO_3 + R_2NH_2^+ + 2H_2O$$

Owing to hydrolytic processes and the co-deposition of boron, the reduction yield is in practice only 30—50 %. Among the first steps in the deposition of nickel are assumed to be adsorption and dissociation of the amine-borane on the catalyst surface, *inter alia* with the formation of boron, the particle size of the catalyst being critical[72].

The amine-borane baths described in the patent literature are similar to hypophosphite baths. The preferred complexing agents are glycolic, lactic, citric, and malonic acids[73]. Organic sulfur compounds are generally used as stabilizers. Amine-borane baths have a long life, since they become only slowly enriched with oxidation products; even high concentrations of dialkylamine and boric acid (which form a soluble ammonium borate complex) exert only a slight influence on the deposition of nickel[74]. The technically important point is that under suitable conditions coatings of almost pure nickel can be produced; the boron content of the layer is a function of the pH (the layer contains 1.3, 1.0, or 0.7 % B at pH 7.5, 8, or 8.5 respectively).

5. Properties of Electroless Deposited Nickel Layers

Chemically produced Ni-P and Ni-B coatings on metallic and nonmetallic substrates are characterized by interesting chemical, physical and mechanical-technological properties. As deposited the (metastable) layers are generally amorphous to X-rays: on heat treatment at 250—400 °C an irreversible exothermal change of the structure takes place, with separation of hard nickel phosphides or borides in a softer crystalline matrix of nickel; the principal compounds detected by X-ray crystallography are Ni_3P and Ni_3B[63, 75]. The structure of the layers varies somewhat from case to case; whereas smooth layers with a laminar structure are deposited from hypophosphite and some amine-borane baths, the Ni-B coatings produced from tetrahydridoborate baths exhibit a honeycomb (spherical segment) form of growth that is unfavorable for brightness but presumably favorable for the adhesion of lubricating films in friction processes and for the adhesion of layers subsequently deposited electrolytically.

Thicker nickel coatings on metals resemble electrolytically produced nickel layers in their chemical and corrosion-chemical behavior, but in their technological properties they are more like hard chromium layers. Their most striking property is the great (micro)hardness of 500—700 kg/mm² (Vickers hardness) even in the freshly deposited state; values of 1000—1200 kg/mm² can be achieved by annealing (precipitation hardness)[76]. This is accompanied by good wear properties and stability under friction. Fig. 4 shows how the hardness of an Ni-B layer depends on the heat treatment[77].

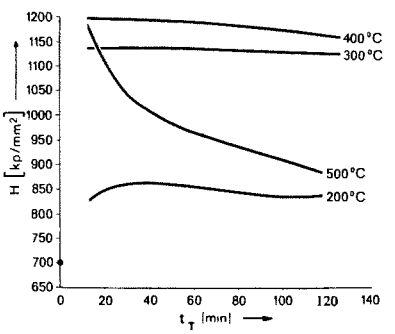


Fig. 4. Relations between the hardness (H) of Ni-B layers and the duration (t_T) and temperature of the heat treatment.

Ni-B layers are only very weakly ferromagnetic, and thus their layer thickness can be measured magnetically, which is not the case for Ni-P layers; depending on their P content, the latter sometimes show appreciable ferromagnetism. Chemically deposited nickel layers are usually stable at high temperatures; above 400 °C, however, diffusion processes begin, involving the ground material, and these can be utilized to produce some desired changes in the properties of the coating/metal combination, *e.g.* for the formation of the extremely hard iron borides (Vickers hardness up to 2000 kg/mm²)[63].

Extensive but partially contradictory investigations have been published on the corrosion resistance of chemically produced nickel layers[78]. In general, as for electrolytically deposited nickel coatings the stability is greater in alkaline than in acid media, and in nonoxidizing than in oxidizing ones. For Ni-B coatings on steel an oxidizing aftertreatment in chromic acid has a favorable effect against uniform corrosion, as also has treatment in air above 600 °C (diffusion of nickel into iron and *vice versa*). Protection against stress corrosion is also conferred by chemically produced nickel layers[79, 80].

Corrosion resistance is very greatly influenced by the type of pretreatment and by having a good-quality surface on the substrate material, and, on the other hand, by the bath composition. Thus, the corrosion resistance (measured by the salt spray test) of Ni-P layers is more dependent on the type of the complexing agent in the bath than on the thickness and P content of the layers, particularly in the alkaline region[81].

For thin nickel coatings used as conducting films on plastics the conductivity, corrosion resistance, and susceptibility to passivation all play an important part. Nickel layers 0.3—0.6 μm in thickness, from amine-borane baths, have only a slight tendency toward passivation and a good conductivity, so that subsequent treatment in an electrolytic copper bath can be applied directly without flash nickel plating[14, 82]. Recent electrochemical investigations have shown that the corrosion potential and the contact corrosion of Ni-B conducting layers are more favorable than those of the usual Ni-P layers[83].

6. Fields of Application

The main area for the application of thicker, hard, nickel layers (usually 10—50 μm, although thicker layers can be produced) is in the protection of metallic and, in special cases, also nonmetallic substrates against friction, wear, and corrosion[84–87]. Here the more expensive rust- and wear-resistant materials can frequently be replaced by simpler, chemically nickel plated materials. In the ceramics industry Ni-B layers have proved their value for vacuum-tight soldered joints[88]. Being as a rule catalytically inactive, ceramic materials are activated before metallization *e.g.* by treatment with a palladium salt solution followed by an amine-borane dip.

In the plating of plastics thin nickel coatings serve as conducting layers for subsequent electrolytic metal deposition. To start the catalytic deposition of nickel the plastic articles—at present over 90% of them are ABS graft polymers—are generally first etched in chromic-sulfuric acid, then activated by solutions containing colloidal palladium or palladium salts and finally metallized[6]. The usual electrolytic layer system consists of 20—25 μm of copper, 10—12 μm of nickel, and 0.8—1.2 μm of (microdiscontinuous) chromium. Already electrolytically metallized plastics are manufactured in many thousand tons per annum, being mainly for decorative but also to an increasing extent for functional purposes, *e.g.* in the automotive industry (internal and external components), in the radio, gramophone, and television industry, for fittings on sanitary ware, and also for electronics, packaging and household goods, as well as for fashion and artistic goods.

Electroless deposited nickel coatings based on amine-boranes are currently attracting particular interest in the electronics industry, for example as a substitute for gold in printed circuits, switches, and semiconductors. Selective activation of, *e.g.* copper circuits on printed circuit boards, can be effected by pretreatment with tetrahydridoborate solutions[89]; this method is also applicable to passive chromium steel with > 12% Cr and to oxide ceramics. In the Sylek process[90] Ni-B layers can be deposited that are as effective as electrolytic gold layers in respect of the ease of soldering, corrosion-resistance, adhesion, and contact- and tear-resistance, while being only one-tenth of the price[91–93]. Similar coatings containing 0.2—0.3% B from nickel/dimethylamine-borane baths (pH 5—10, T = 45—65 °C) are marketed in the USA under the trade name of Niklad[94]. Electroless deposited nickel layers have also been proposed for use to prevent diffusion between copper and gold coatings[95] and by the additive technique for the metallization of the substrate material for printed circuits in the entertainment electronics industry[96].

7. Future Outlook

Metallization processes are gaining in importance owing to the trend towards metal-saving processes initiated by the increasing shortage of raw materials. A cheap, more easily accessible material (steel, aluminum, or plastic) can be protected against corrosive attack or provided with technically valuable properties such as great hardness and wear-resistance by means of relatively thin layers *e.g.* of a nobler metal or a combination of layers, composed for example of copper, nickel, and chromium[97, 98]. In view of the attempts in such directions, chemically produced metallic coatings may have a still more important part to play in the future than at present.

Received: June 13, 1975 [A 80 IE]
German version: Angew. Chem. *87*, 652 (1975)
Translated by Express Translation Service, London

[1] *A. Brenner* and *G. Riddell*, Proc. Am. Electroplat. Soc. *33*, 23 (1946).
[2] *F. A. Roux*, US-Pat. 1207218 (1916).
[3] *A. Brenner* in: Handbuch der Galvanotechnik. Hanser Verlag, München 1966, Vol. 2, pp. 725ff.
[4] *G. G. Gawrilov*: Chemische (stromlose) Vernicklung. E. G. Leuze Verlag, Saulgau/Württ. 1974.
[5] Stromloses Dickvernickeln nach dem Kanigen-, Durni-Coat- und Nibodurverfahren, International Nickel Deutschland GmbH, 1971.
[6] *R. Weiner et al.*: Kunststoffgalvanisierung, E. G. Leuze Verlag, Saulgau/Württ. 1973, pp. 194ff.
[7] *D. W. Baudrand* in: Plating of Plastics, R. Draper Ltd., Teddington/England 1971, pp. 99ff.
[8] *G. Woldt* in: Jahrbuch der Oberflächentechnik. Metallverlag, Berlin 1975, pp. 206ff., and earlier data.
[9] *K. Heymann, W. Riedel*, and *G. Woldt*, Angew. Chem. *82*, 412 (1970); Angew. Chem. internat. Edit. *9*, 425 (1970).
[10] *A. F. Bogenschütz*: Oberflächentechnik und Galvanotechnik in der Elektronik. E. G. Leuze Verlag, Saulgau/Württ. 1974.
[11] *H. Niederprüm*, Proc. "Surface 66". Forsterverlag, Zürich 1967, pp. 186ff.
[12] *F. Pearlstein* and *R. F. Weighman*, Plating *60*, 474 (1973).
[13] Symposium Plating in the Electronics Industry, Indianapolis, USA, Jan. 1973; Met. Finish. J. *1973*, No. 5, p. 135.
[14] *H. Niederprüm* and *H. G. Klein*, Metalloberfläche *24*, 468 (1970).
[15] *F. Pearlstein* and *R. F. Weightman*, Plating *61*, 154 (1974); J. Electrochem. Soc. *121*, 1023 (1974).
[16] *R. Sard et al.*, Plating *58*, 893 (1971).
[17] *Y. Okinaka*, J. Electrochem. Soc. *120*, 739 (1973); *121*, 56 (1974).
[18] *A. F. Bogenschütz* and *U. George*: Legierungsüberzüge und Legierungsbäder. E. G. Leuze Verlag, Saulgau/Württ. 1975.
[19] *H. G. Klein, H. Niederprüm*, and *K. Glaser*, Galvanotechnik *62*, 799 (1971).

[20] *H. Niederprüm* in: Ullmanns Encyklopädie der Technischen Chemie. 4th Edit. Verlag Chemie, Weinheim 1974, Vol. 8, p. 650.
[21] *M. Lelental*, J. Electrochem. Soc. *120*, 1650 (1973).
[22] *H. E. Bellis*, DOS 2211439 (1972).
[23] *F. Seel:* Grundlagen der analytischen Chemie. Verlag Chemie, Weinheim 1970.
[24] *I. Dumesic et al.*, J. Electrochem. Soc. *121*, 1405 (1974).
[25] Galvanotechnik *65*, 912 (1974).
[26] *W. I. Lorenz*, Chem.-Ing.-Tech. *45*, 175 (1973).
[27] *K. Müller*, Metalloberfläche *14*, 65 (1960).
[28] *T. Markovič*, Metalloberfläche *21*, 110 (1967).
[29] *T. Markovič*, Galvanotechnik *59*, 394 (1968).
[30] *F. L. Shippey* and *F. M. Donahue*, Plating *60*, 43, 135 (1973).
[31] *F. M. Donahue* and *C. V. Yu*, Electrochim. Acta *15*, 237 (1970).
[32] *F. M. Donahue*, Proc. Interfinish Basel 1972. Forsterverlag, Zürich 1973, pp. 193 f.
[33] *G. Hermann*, Galvanotechnik *65*, 462 (1974).
[34] *K. Heymann et al.*, Galvanotechnik *62*, 291 (1971).
[35] *I. F. Hamilton* and *P. C. Logel*, J. Catal. *29*, 253 (1973).
[36] Gmelins Handbuch der Anorganischen Chemie. 8th Edit. Verlag Chemie, Weinheim 1965. Vol. P, Part C, p. 99.
[37] *R. T. Sanderson:* Inorganic Chemistry. Reinhold, New York 1967.
[38] *W. H. Stockmayer et al.*, J. Am. Chem. Soc. 77, 1980 (1955).
[39] *W. Lux:* Anorganisch-chemische Experimentierkunst. 3rd Edit. J. A. Barth, Leipzig 1970, p. 320.
[40] Exception: *e.g.* electrolytic chromium plating. Insoluble anodes are used and the metal is added subsequently as CrO_3.
[41] *F. Schubert* and *K. Lang*, Angew. Chem. 72, 994 (1960).
[42] *A. Hajós:* Komplexe Hydride. VEB Deutscher Verlag der Wissenschaften, Berlin 1966.
[43] *E. R. Winiarczyk*, DAS 1218413 (1959).
[44] *K. Parker*, Proc. Interfinish Basel 1972. Forsterverlag, Zürich 1973, p. 202.
[45] General American Transportation Corp., Trade name: Kanigen = *K*atalytic *Ni*ckel *Gen*eration.
[46] Symposium on Electroless Nickel Plating. ASTM Special Technical Publication No. 265 (1959), Philadelphia 3, Pa., USA.
[47] *K. M. Gorbunova* and *A. A. Nikiforova:* Physico-chemical Principles of Nickel Plating. Israel Program for Scientific Translations, Jerusalem 1963.
[48] Galvanotechnik *57*, 3, 3 (1966).
[49] *K. Meyer*, Galvanotechnik *65*, 303 (1974).
[50] Works photograph, Blasberg, Solingen.
[51] *F. W. Hirth* and *H. Speckhardt*, Galvanotechnik *64*, 452 (1973); *65*, 105 (1974).
[52] *G. O. Mallory*, Trans. Inst. Met. Finish. *52*, 156 (1974).
[53] *W. Metzger* and *Th. Florian*, Oberflächentechnik *13*, 91 (1975).
[54] *I. P. Randin* and *H. E. Hintermann*, Plating 72, 665 (1972).
[55] *G. Salvago* and *P. L. Cavalloti*, Plating 72, 665 (1972).
[56] *T. E. Such* and *I. Pitcock*, Plast. Polym. *1974*, No. 8, p. 165.
[57] E. I. Dupont de Nemours & Co; Bayer AG.
[58] *K. Lang*, Metalloberfläche *19*, 8, 133 (1965); Galvanotechnik *56*, 43 (1965).
[59] Die chemische Vernickelung von Metallen (Nibodur). Rundtischgespräch: Galvanotechnik *58*, 546 (1967).
[60] Works photograph, Anke, Essen.
[61] Works photograph, Schlötter, Geislingen.
[62] *H. G. Klein, H. Niederprüm*, and *E. M. Horn*, DFBO-Mitt. *21*, 201 (1970).
[63] *H. G. Klein, H. Niederprüm*, and *E. M. Horn*, Metalloberfläche *25*, 9, 2 (1971); *26*, 1, 15 (1972).
[64] See [4], pp. 131f.
[65] *K. M. Gorbunova et al.*, J. Electrochem. Soc. *120*, 613 (1973).
[66] *H. G. Klein, H. Niederprüm*, and *N. Lönhoff*, DAS 1771004 (1968).
[67] *H. G. Klein* and *E. Zirngiebl*, DBP 1254935 (1960).
[68] *H. E. Bellis*, US-Pat. 3674447 (1969).
[69] *K. Lang* and *H. G. Klein*, DBP 1237399 (1963).
[70] *H. G. Klein et al.*, DOS 1920294 (1969).
[71] *H. G. Klein et al.*, DAS 1521246 (1965); DAS 1277642 (1964).
[72] *M. Lelental*, J. Catal. *32*, 429 (1974).
[73] *H. G. Klein* and *H. Niederprüm;* DAS 1950983 (1969).
[74] *G. G. Mallory*, Plating *58*, 319 (1971).
[75] *F. W. Hirth* and *H. Speckhardt*, Metall *26*, 1012 (1972).
[76] *K. Parker*, Plating *61*, 834 (1974).
[77] *H. Wiegand* and *K. Schwitzgebel*, Metall *21*, 1024 (1967).
[78] See [4], pp. 103f.
[79] *E. M. Horn et al.*, DOS 1621245 (1967); DOS 1771257 (1968).
[80] *W. Bergmann et al.*, Technik *26*, 16 (1971).
[81] *G. O. Mallory*, Plating *61*, 1005 (1974).
[82] *W. Frick*, Oberflächentechnik *50*, 450 (1973).
[83] *H. G. Klein* and *D. Kuron*, Metalloberfläche *28*, 333 (1974).
[84] J. Oberflächentechnik IOT *1970*, No. 12, p. 46.
[85] *R. Hurrle*, Z. Wirtsch. Fertigung *66*, 172 (1971).
[86] *D. W. Baudrand*, Society of Automotive Engineers, Inc., Business Aircraft Meeting, Wichita, Ka., USA, April 1974.
[87] *H. G. Klein*, Sprechsaal Keram., Glas, Email, Silic. *101*, 446 (1968).
[88] Oberfläche *1971*, No. 10, p. 564.
[89] *H. E. Bellis* and *D. E. Booker*, DOS 2439075 (1974).
[90] Sylek 201; E. I. Dupont de Nemours & Co.
[91] *H. E. Bellis*, Plating *62*, 153 (1975).
[92] Blick durch die Wirtschaft, July 31, 1974.
[93] The cost of electrolytic deposition of fine gold in Dec. 1974 was DM 2.90 for $\mu m/dm^2$; cf. Galvanotechnik *66*, 250 (1975).
[94] Allied Kelite, USA.
[95] *I. C. Turn* and *E. L. Owen*, Plating *61*, 1015 (1974).
[96] *N. Lönhoff*, Trans. Inst. Met. Finish. *46*, 194 (1968).
[97] *H. W. Lieber*, Metall *22*, 613 (1974).
[98] *W. Metzger*, Galvanotechnik *66*, 210 (1975).

Zeolites—Their Synthesis, Structure, and Applications

By Friedrich Schwochow and Lothar Puppe[*]

During the last 15 years zeolitic molecular sieves, which should not be confused with the amorphous aluminosilicate ion exchangers, have attained increasing importance as specific adsorbing agents and catalysts. The progress made in all sectors of the zeolite field is perhaps best appreciated from the increase in publications from 34 at the First International Conference on Molecular Sieves held in London in 1967 to 116 at the last Meeting, which was held in Zürich in 1973. The present review provides an introduction to this extensive subject which still provides stimulus to intensive research.

1. Occurrence and Synthesis

1.1. Natural Zeolites

Zeolites are silicate structures containing water, having the general formula:

$$x[(M^{I},M^{II}_{1/2})\cdot AlO_2]\cdot ySiO_2\cdot zH_2O$$

where M^{I} = Li, Na, K, *etc.*
and M^{II} = Mg, Ca, Sr, Ba, *etc.*[1]

They were first described as a mineral group by the Swedish mineralogist *Cronstedt*[2] in 1756 and are found in very diverse quantities in nature, their occurrence ranging from mineralogical rarities (*e.g.* faujasite[3] and offretite[4]) to huge deposits (*e.g.* analcite, erionite, mordenite, and phillipsite[5]). 34 zeolitic minerals are now known, derived for the most part by meta-

[*] Dr. F. Schwochow and Dr. L. Puppe
Bayer AG
509 Leverkusen (Germany)

morphism of silicate materials of volcanic origin[6, 7]. Sedimentary rocks of zeolitic composition arose at high pH under the action of hot alkaline salt solutions, preferentially from volcanic ashes, tuffs, and pumices, some of which today are also of commercial interest as mineable deposits[5, 8, 9]. The industrially valuable zeolites in these rock deposits are in particular, chabazite, erionite, clinoptilolite, and mordenite, which often occur together but also individually in sufficient purity.

In addition, crystallization of zeolites can also be observed in basalt inclusions, where hydrothermal conditions often lead to the formation of particularly beautiful single crystals[10]. Mineable zeolitic minerals are found particularly in the United States[8], but economic utilization of natural zeolites has now also been started in Japan, Italy, Bulgaria, and Yugoslavia[5].

1.2. Synthesis of Zeolites

Systematic study of the preparation and properties of zeolites was introduced in the 1940's mainly by *Barrer* and his school in Britain[11] and in the laboratories of Union Carbide Corporation in the United States[12].

For their preparation one starts with aqueous alkaline reaction mixtures containing "reactive" silicon and aluminum compounds. The reactions that can occur can essentially be divided into three main groups, depending on the source of the SiO_2:

1) Reaction of natural or synthetic glasses with alkali metal hydroxide solutions[13, 14].

2) Reaction of suspensions of solid silicic acid fillers in alkaline metal aluminate solutions.

3) Crystallization of gels obtained by mixing aqueous alkaline silicate and aluminate solutions.

In all three types of reactions the planned crystallization of a desired type of zeolitic framework depends in the first place on maintaining specific ranges of concentration. This is difficult, because at least four of the starting components (*e.g.* SiO_2, Al_2O_3, Na_2O, and H_2O) and very often five (*e.g.* additionally K_2O) must be controlled, and, furthermore, because the synthetic starting mixtures have compositions totally different from that of the crystalline zeolite that is to be prepared.

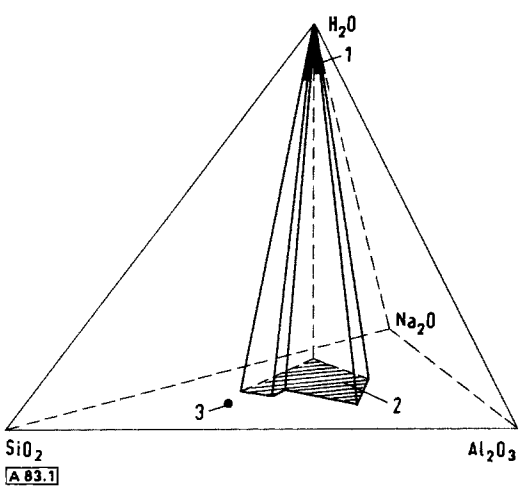


Fig. 1. Schematic representation of relative concentrations for zeolite synthesis in the system SiO_2—Al_2O_3—Na_2O—H_2O. 1, concentration region for zeolite A reaction mixtures; 2, region of relative concentrations necessary for synthesis in the solid diagram; 3, composition of the crystalline (dehydrated) zeolite A.

In Figure 1 the starting concentrations and the composition of the crystalline final product are shown as a four-component tetrahedron for the case of zeolite A.

Conversion of the amorphous reaction mixtures into the crystalline zeolites can generally be achieved at 60 to 100 °C. Only for very SiO_2-rich types such as mordenite is crystallization at higher temperatures essential, *i.e.* in autoclaves.

To understand the course of the reaction one must imagine that in all the above three types of reactions a gel-like alkali metal aluminosilicate is formed first. In the gel phase, before crystallization sets in, rearrangement reactions occur by exchanges between SiO_4 and AlO_4 tetrahedra in the aluminosilicate skeleton[15–17], while simultaneously the liquid phase present together with the gel becomes supersaturated with SiO_2 and Al_2O_3. It is not yet completely clear which SiO_2- and Al_2O_3-containing compound are given up in this process from the gel to the solution as crystallization precursors[18, 19]. However, the formation of seeds that occurs in the liquid phase proceeds preferentially on the inner surface of the gel, so that the seed formation is influenced not only by the concentration and structure of the precursors present in the solution but also by the morphology of the solid phase[20–25].

During the subsequent period of crystal growth the necessary concentrations of SiO_2 and Al_2O_3 are maintained in the solution by gradual dissolution of the gel. Figure 2 shows electron micrographs of the course of crystallization of faujasite beginning with the gel phase and finishing with the final product.

The kinetic course of this reaction is very complex, as has been described principally by *Zhdanov et al.* in their fundamental papers[26–29], but the present state of knowledge does not permit planned building of new structures of a prescribed type. Even when the relative concentrations were kept constant, the particular structure that crystallized depended to a great extent on the nature of the silicate starting material used. Possibilities of control were obtained by the use of especially reactive silicates (*e.g.* $Na_2SiO_3 \cdot 5\,H_2O$)[30], special silicic acid sols, or silicic acid fillers[31, 32]. With less reactive starting materials the gels first had to be "aged" at low temperatures (gel ripening or digestion step)[33–35] before crystallization could be induced at the higher temperatures.

The desired final products are metastable in the liquid phases present. For example, in the system SiO_2—Al_2O_3—Na_2O—H_2O only the industrially insignificant natrolite and analcite are the thermodynamically stable zeolite phases[36].

1.3. Manufacture

The commercial production of "structurally pure" zeolites began as developments from the fundamental work by *Milton* and *Breck*[34, 35, 37–39] in the early 1950's. The aims were cheaper raw materials (industrial water-glasses and calcined kaolins) and higher concentrations of solids in batch processes or shorter reaction times in continuous production, but these ran into problems additional to those described above. Difficulties frequently arose from crystal morphology and particle size distribution of the crystals[40]. The source of the SiO_2, the alkali content, and the intensity of mechanical movement during crystallization exert a considerable influence on the physical properties of the product. Figure 3 shows electron micrographs of two zeolite A preparations synthesized in batches with different alkali contents.

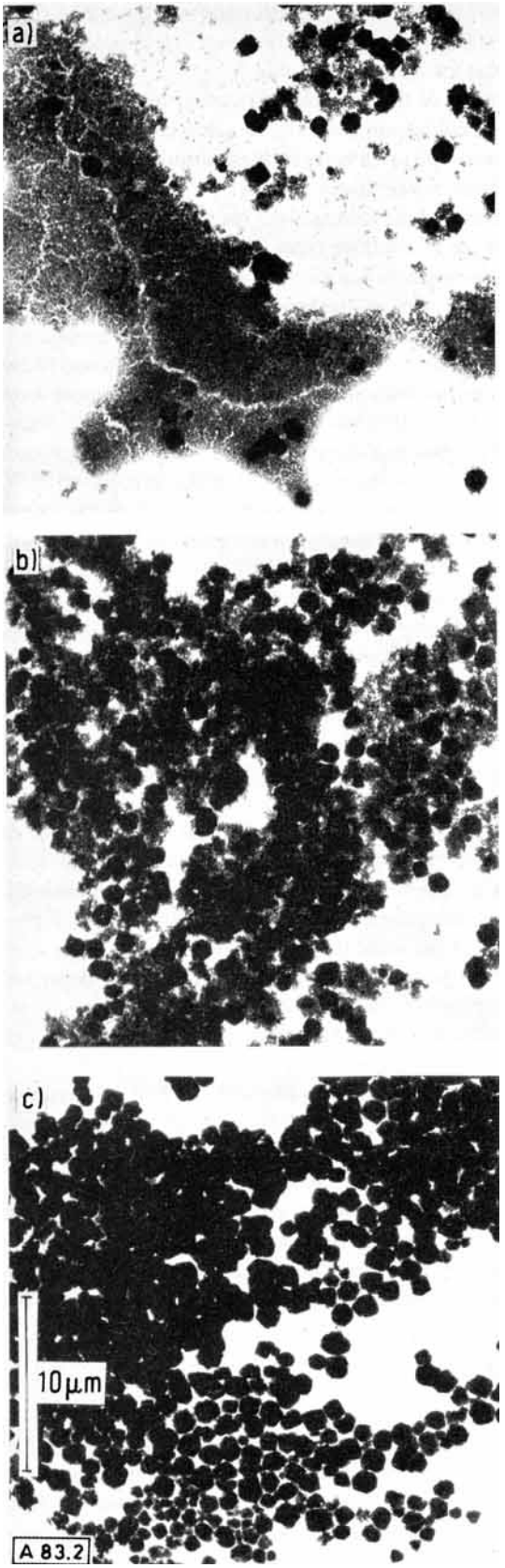


Fig. 2. Electron micrographs showing the course of faujasite crystallization from the gel phase (a) through an intermediate stage (b) to the crystalline end product (c).

With some zeolite structures, however, control of the crystal size is almost impossible. For comparison, Figure 4 shows synthetic erionite which crystallizes only in very thin needles, whereby further working is made more difficult.

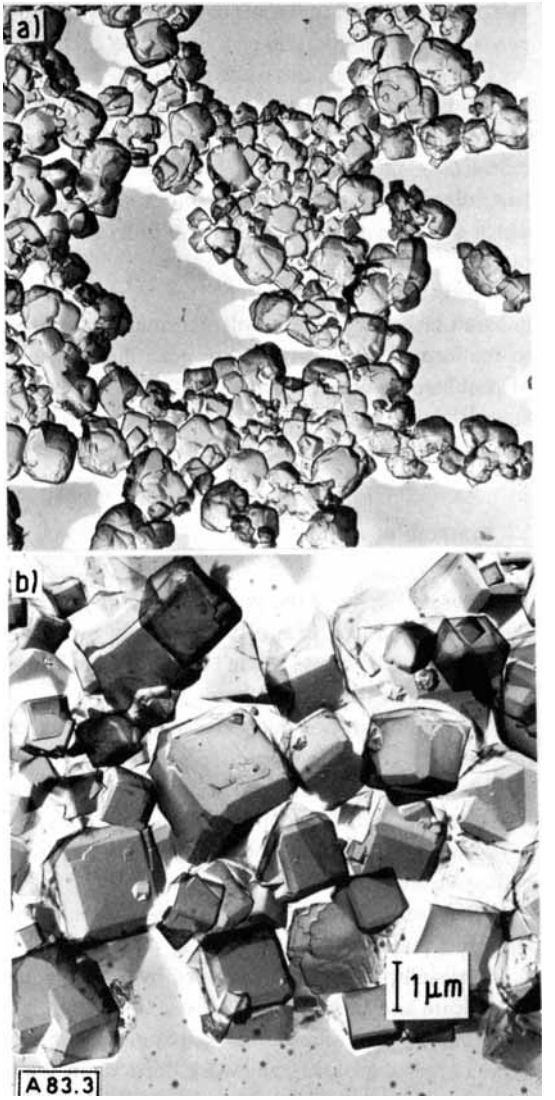


Fig. 3. Electron micrographs (carbon replica) showing crystallization of zeolite A at high (a) and low (b) alkali content.

Only part of the crystalline powder obtained in zeolite synthesis is used as such for adsorption work; most of it is processed further into zeolite paste or granulate (see Section 3.1).

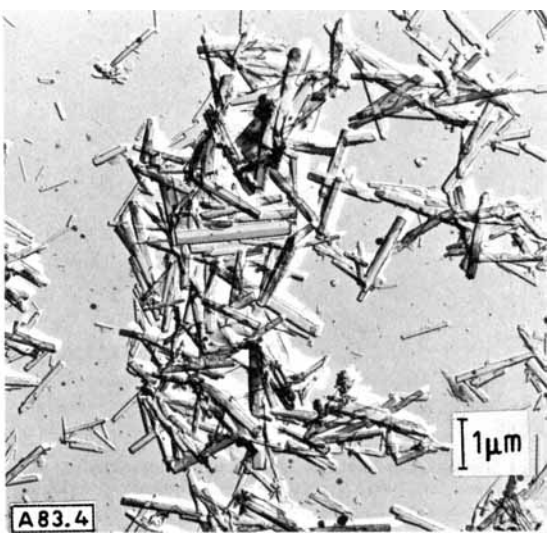


Fig. 4. Electron micrograph (carbon replica) of erionite.

Pellets are prepared with the usual arrangements for granules (*e.g.* with extruders or granule sifters), and binders are added. The latter may be clay materials (kaolins, bentonites, attapulgites) or synthetic binders (water-glass, silicic acid sols, aluminum hydroxide). For example, silica-gel-bound, spherical granulates can also be prepared by a dropping procedure[41, 42]; the granulates resulting in this way can be converted into binder-free material by subsequent transformation of the gel-like SiO_2 binder into zeolite[43]. It is also possible to prepare molecular sieve granulates directly from spheres that consist of amorphous silicic acid[44].

The Na form of the zeolite that is present in most cases after crystallization must still be converted into the cation form required for the particular type of application; in accordance with their main fields of application, modern industrial zeolites contain as cations Na^+, K^+, NH_4^+, Mg^{2+}, Ca^{2+}, Ba^{2+}, or the cations of lanthanoids or of catalytically active transition metals.

2. Structure

2.1. Framework Structures of Zeolites

The principle on which the structures of zeolites are built up can be most easily visualized if we start from a truncated octahedron as the framework-forming unit: if the corners of such a truncated octahedron are occupied alternately by SiO_4 and AlO_4 tetrahedra (the primary building units), one then obtains a fundamental aluminosilicate skeleton composed of four-membered and six-membered rings; this is denoted as a sodalite cage or a β-cage (Fig. 5a). From this polyhedron the important zeolite structures such as those of sodalite, zeolite A, and faujasite can then be constructed.

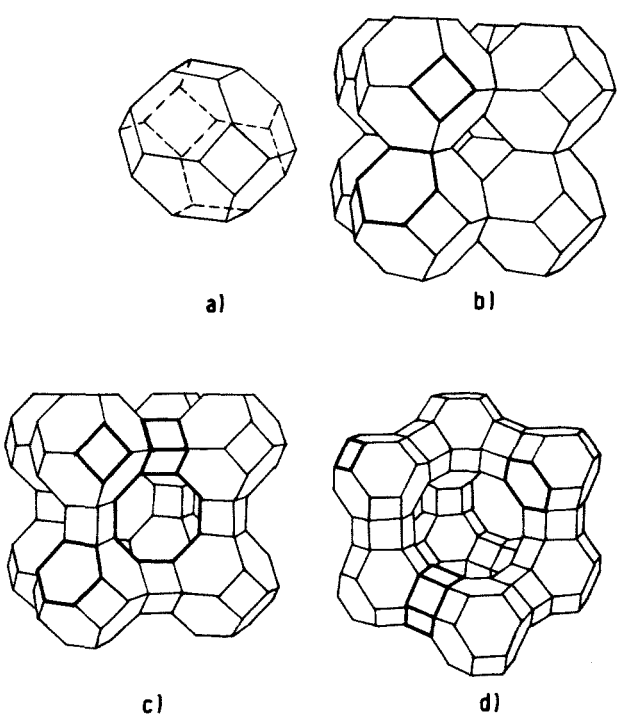


Fig. 5. Formation of important fundamental frameworks from the sodalite cage. a, β-cage; b, sodalite framework; c, zeolite A framework; d, faujasite framework. The essential secondary building units (cf. Fig. 7) are emphasized.

The structure of sodalite[45, 46] is formed by successive series of β-cages where each square face is shared between two cages while every eight β-cages are so arranged in cube-like form that they enclose a ninth β-cage (Fig. 5b). If the square faces of the β-cage are linked to one another to form a cube, then the structure of zeolite A is obtained[47, 48], such that a larger void, termed the α-cage, appears in the interior of each group of eight β-cages (Fig. 5c). Joining up of the building units as hexagonal prisms so as to give a lattice analogous to the diamond structure results in the faujasite structure[48, 49] (Fig. 5d).

The frameworks described in the preceding paragraph have in common the feature that the β-cages enclose a system of identical cavities. The entrances, termed windows or pore openings, to these voids form a three-dimensional sieve with mesh widths between 3 and 10 Å. This fact, which is of the utmost importance for industrial applications, leads to the well known name of "molecular sieves" for the crystalline aluminosilicates. In contrast to other porous materials such as active charcoal, silica gels, and active clays, all of which

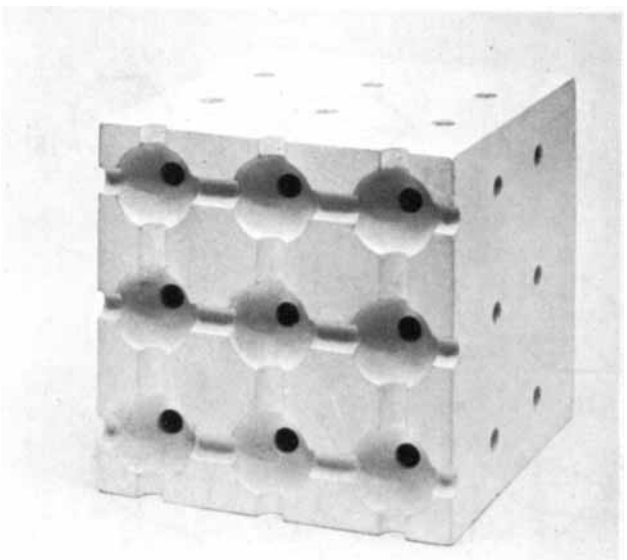


Fig. 6. Model of the pore and channel system in zeolite A.

contain pores of widely varying sizes, the molecular sieve zeolites have strictly specific pore openings of constant cross-section. Figure 6 shows a model of the structure and the channel system of zeolite A.

2.2. Most Important Structural Frameworks

The α- and β-cage building units described in the above examples are unsuitable for describing all possible framework types of zeolites. For complete classification of zeolites—a task that has occupied especially *Barrer*[50, 51], *Meier*[52, 53], and *Breck*[54]—we can start from the eight "secondary building units" (SBU)[52] that are collected in Figure 7.

Figure 8 shows as an example the framework of erionite based upon four- and six-membered rings. The classification of zeolite structures comprises seven groups in accordance with these secondary building units (Table 1).

Table 1. Survey of typical zeolite structures arranged according to the secondary building units (SBU) (cf. Fig. 7).

SBU	Zeolite	Composition of the unit cell	SiO_2/Al_2O_3 [molar]	Pore size [Å]	Refs.
(4)	Analcite	$Na_{16}[(AlO_2)_{16}(SiO_2)_{32}]\cdot 16H_2O$, cubic	3.6—5.8	—	[6, 8]
	Phillipsite	$(Na,K)_{10}[(AlO_2)_{10}(SiO_2)_{22}]\cdot 20H_2O$, orthorhombic	2.6—4.4	4.2—4.4	[8]
(6)	Erionite	$(Ca,Mg,K_2Na_2)_{4.5}[(AlO_2)_9(SiO_2)_{27}]\cdot 27H_2O$, hexagonal	5.8—7.4	3.6—4.8	[8]
	Sodalite	$Na[(AlO_2)_6(SiO_2)_6]\cdot 7.5H_2O$, cubic	2.0	2.6	[83]
(4-4)	Zeolite A	$Na_{12}[(AlO_2)_{12}(SiO_2)_{12}]\cdot 27H_2O$, cubic	2.0—2.5	4.1	[47]
(6-6)	Faujasite	$(Na_2,Ca)_{32}[AlO_2)_{64}(SiO_2)_{128}]\cdot 256H_2O$, cubic	4.2—4.6	7.4	[3]
	Chabazite	$Ca_2[AlO_2)_4(SiO_2)_8]\cdot 13H_2O$, rhombohedral	3.2—6.0	3.7—4.2	[8]
(4-1)	Natrolite	$Na_{16}[(AlO_2)_{16}(SiO_2)_{24}]\cdot 16H_2O$, orthorhombic	2.8—3.2	2.6—3.9	[84]
(5-1)	Mordenite	$Na_8[(AlO_2)_8(SiO_2)_{40}]\cdot 24H_2O$, orthorhombic	8.2—10.0	6.7—7.0	[85]
(4-4-1)	Clinoptilolite	$Na_6[(AlO_2)_6(SiO_2)_{30}]\cdot 24H_2O$, monoclinic	8.5—10.5	?	[8]

As Table 1 shows, various molar SiO_2/Al_2O_3 ratios occur in zeolite structures. The smallest possible SiO_2/Al_2O_3 ratio of 2 (*Löwenstein*'s rule[55]) is found in sodalite and in zeolite A, while mordenite and clinoptilolite with $SiO_2/Al_2O_3 \approx 10$ have markedly silica-rich zeolite structures. The individual structural types also show very great differences in the cross-section of their pore openings. For example, zeolite A belongs to the narrow-pored zeolites whereas faujasite shows wide pores. Several values are given for the pore openings in some of the zeolite structures, since these frameworks contain different channels of varying apertures[50].

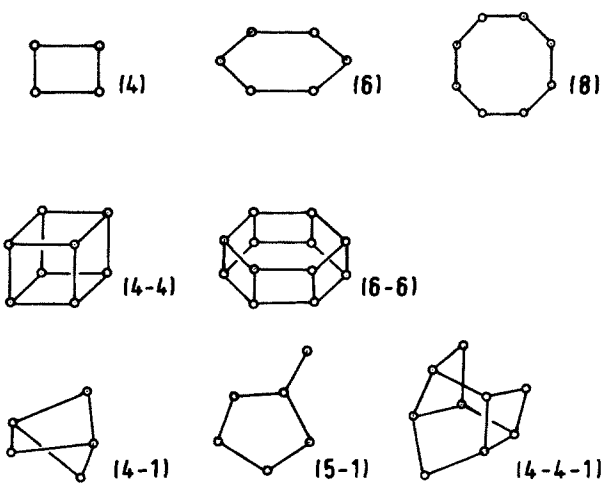


Fig. 7. Secondary building units (SBU) for the construction of zeolites.

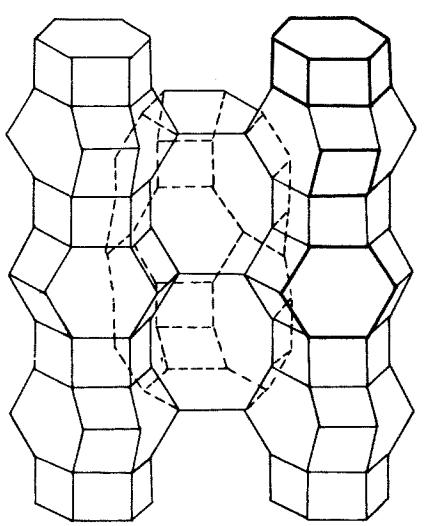


Fig. 8. Construction of the erionite framework (essential secondary building units emphasized).

2.3. Cations in the Zeolite Framework

The preceding description of the zeolite framework has so far taken no account of the fact that the AlO_4 tetrahedra present in the aluminosilicate framework each contribute a negative charge to the structure, and that these negative charges must be balanced by cations. The cations can be characterized from three points of view:

1) As in the amorphous aluminosilicate ion exchangers, the cations are relatively mobile in the anion skeleton and can be replaced by other cations[56–59].

2) The cross-section of the pore openings can be influenced by changing the size of the cations or by replacing univalent cations by ones of higher valence[60], *i.e.* the apertures to the cavities in zeolites can be widened or narrowed by ion exchange, whereby separation of specific molecules becomes possible (the "molecular sieve effect").

3) Since a change in the cationic occupation is always accompanied by alterations in the charge distribution within the zeolite cavities, the nature and the position of the cations affect the adsorptive behavior and especially the catalytic activity of the zeolite[61–64].

The position of the cations in the framework has been intensely studied and clarified for only a few types such as the faujasite structure[49, 65, 66]. Figure 9 gives the main positions of the cations in this structure: position I lies within the hexagonal prisms, position II is raised slightly above the plane of the six-ring window, and position III is within the large cavity but in the neighborhood of the four-membered ring[49].

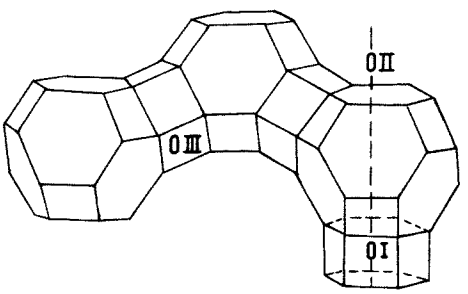


Fig. 9. Principal positions of cations in the faujasite structure (for explanations see text).

It is because the adsorptive and catalytic properties depend on the precise position and mobility of the cations that structural investigations currently in progress are increasingly concentrated on the arrangement of the cations[66-69].

2.4. Variability of the Structures

In a number of zeolites distinguished by considerable industrial importance the AlO_4 tetrahedra may be replaced by SiO_4 tetrahedra without altering the framework of the anionic skeleton; in other words, the SiO_2/Al_2O_3 ratio can be varied within a certain range. Both the zeolite A structure and the faujasite structure illustrate this possibility, in that species of the same structure can be prepared with different SiO_2 contents: the zeolite type ZK 4[70] can be considered as a SiO_2-rich zeolite A. In the faujasite types there is a general differentiation between the synthetic types of zeolite X with $SiO_2/Al_2O_3 = 2$ to 3 and those of zeolite Y with $SiO_2/Al_2O_3 = 3$ to 6[71].

Part of the aluminum can also be removed from the synthesized aluminosilicate anion skeleton by subsequent treatment. For example, by treatment of mordenite with mineral acids extremely SiO_2-rich species can be prepared in which, however, the basic zeolitic framework remains unchanged[72].

Aluminum may be removed not only by extraction with acids but also by complexing agents[73], and still further possibilities of structural modification are provided by decationization processes[74, 75]. In this last way "cation-free" molecular sieves can be prepared that are used especially for catalytic reactions in petrochemistry; for this purpose the ammonium form of the zeolite is prepared and is then heated. Thermal removal of the ammonia is followed by rearrangement of the lattice whereby cationic aluminum is formed[75].

Simple organic cations such as $(CH_3)_4N^+$, $(CH_3)_2\overset{+}{N}H_2$, $(C_2H_5)_4N^+$ and 1,4-dimethyl-1,4-diazoniabicyclo[2.2.2]octane (DDO) play a significant part in the synthesis of certain zeolite structures. Thus, some of the structures found in nature can be synthesized only by the use of such cations (synthesis of offretite)[76]; conversely, new structure types have been discovered by using such organic cations[76-82] (see also Fig. 10). The most important representatives of such synthetic molecular sieves are collected in Table 2.

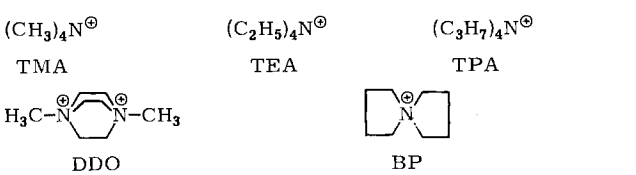


Fig. 10. Important organic cations for syntheses of certain zeolite structures.

3. Applications

3.1. Zeolites as Adsorbents

The water present after the synthesis in the cavities of the framework can be removed from zeolites *e.g.* by heating (activation of the molecular sieve). Any gas or vapor can be taken up into the resulting system of cavities, provided that the molecules are small enough to fit into the adsorption voids[51]. This selective adsorption according to molecular size finds its most important application in the separation of normal from branched-chain paraffins[86-91]. However, it is also possible to separate molecules of equal cross-section: owing to the interaction between the adsorbate and the cations of the molecular sieve, the molecules are retained in the channel system according to their degree of polarity[92-95]. A characteristic feature of adsorption on zeolites is their large adsorption capacity even at partial pressures below 10 torr (see Fig. 11).

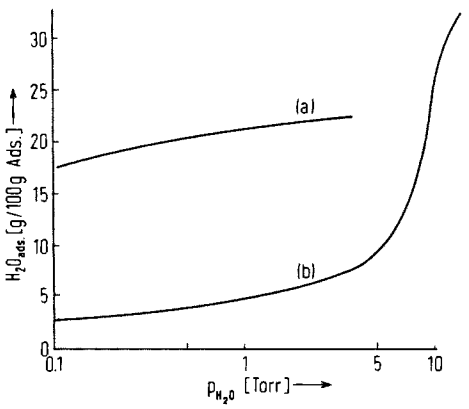


Fig. 11. Adsorption capacity of Na-zeolite A granulate (a) and silica gel (b) for water vapor. Ordinate: H_2O coverage in g H_2P/100 g adsorbent. Abscissa: Partial pressure of water vapor.

Thus, molecular sieves occupy a dominating position as adsorbents in all cases where traces of impurities are to be removed from gases or liquids[96]. For example, in drying residual concentrations corresponding to a dew point below −75 °C can be achieved. Moreover, molecular sieves have a high loading capacity in the lower partial pressure region

Table 2. Survey of some synthetic zeolites containing nitrogenous organic cations.

Designation	org. cation	cryst. time [d]	Compn. of the cryst. zeolite		Refs.
			SiO_2/Al_2O_3 [molar]	Cations in framework	
ZK 4	TMA	1—3	3.2	Na^+, TMA	[70]
Ω	TMA	3	7.3	Na^+, TMA	[76]
Offretite	TMA	4—8	7.7	Na^+, K^+, TMA	[75, 78]
ZSM 8	TEA	6	43	Na^+, TEA	[79]
β	TEA	60	75	Na^+	[80]
ZSM 5	TPA	5—8	31.1	Na^+	[81]
ZK 5	DDO	8	4.7	Na^+, DDO	[77]
LOSOD	BP	20	2	Na^+	[82]

even at temperatures up to *ca.* 100 °C[97, 98]. Adsorption technologists have developed methods suitable for the regeneration of molecular sieves, *e.g.* by raising the temperature, lowering the pressure (pressure-swing process), or flushing with purified gases[99], and these processes are so mild that the capacity of the molecular sieve is not appreciably decreased by a large number of adsorption-desorption cycles.

The most important applications of granulates as adsorbing agents are collected in Table 3.

4) The concentration of activated molecules is approximately 100 times greater in zeolite cavities than in comparable amorphous catalysts.

5) The catalytic activity is increased by the molecular sieve effect, which allows a catalytic transformation of only those molecules that can penetrate the zeolite channel system (selectoforming[112, 113]).

The structural types used at present in commercial catalytic processes are mostly zeolites X or Y, as well as erionite and

Table 3. Survey of principal possibilities for the application of molecular sieves in industrial adsorption processes operating with periodic regeneration.

Fields of application	Purpose of application: Drying	Purification	Separation
Refineries and Petrochemical industry	Paraffins, olefins, acetylenes, reformer circulating gas, hydrocracking gas, solvents, LPG	Sweetening [a] of "liquid petrol gas" and aromatics; removal of CO_2 from olefin-containing gases, purification of synthesis gas	Separation of normal and branched-chain paraffins [86—91] Separation of aromatic cpds. [100, 101]
Technical gases	H_2, N_2, O_2, Ar, He, CO_2 natural gas, input gas for air-separation plants	Sweetening [a] and CO_2 removal from natural gas, removal of hydrocarbons from air, preparation of protective gases	Separation of nitrogen and oxygen [102, 103]
Industrial furnaces	Exogas, cracking gas, reformer gas	Removal of CO_2 and NH_3 from exogas and from ammonia fission gas	

[a] "Sweetening" is the removal of sulfur-containing compounds.

Development of acid-stable zeolites has also made it possible to use aluminosilicates to remove noxious substances such as SO_x and NO_x from exhaust air[104]. Together with the processes that involve adsorption-desorption cycles, mention should be made of three further important applications in which the molecular sieve is not regenerated:

1) Refrigerators and air conditioners include in their cooling system cartridges containing molecular sieve granulates for drying purposes (avoidance of hydrolysis).

2) The space between the panes of double-glazed windows must be kept free from condensation of moisture and solvents; for this purpose molecular sieve granulates are used increasingly as insertions into the double glazing framework[105].

3) In plastics systems based on polyurethane drying of the polyol component is achieved by means of zeolites in powder form or in paste-like slurry in castor oil[106]. In this way evolution of CO_2 can be avoided, which would otherwise lead to the formation of bubbles and thus irregular surfaces.

3.2. Zeolites as Catalysts

In contrast to the classical amorphous catalysts based on SiO_2 and Al_2O_3 the zeolitic catalysts display the following properties[107, 108]:

1) Because of their structure, crystalline aluminosilicates have a defined arrangement of SiO_4 and AlO_4 tetrahedra that can be prepared with complete reproducibility.

2) In many cases the catalytically active centers in the framework can be assigned to the cationic positions (cf. Section 2.3).

3) Catalytically active transition-metal ions, which can be introduced into the framework by ion exchange, can be reduced to the metal *in situ*, extremely high dispersions being thus achieved[109–111].

mordenite which can be applied in the lanthanoid or decationized form or loaded with noble metals[63].

As produced by synthesis, the alkali metal forms of these zeolites are largely inactive as catalysts[63, 114]; after the introduction of, for example, trivalent lanthanoid cations the positive charges added must saturate several separated negative charges in the anionic framework whereby strong electrostatic fields are built up in the interior of the cavities[114] (see Fig. 12).

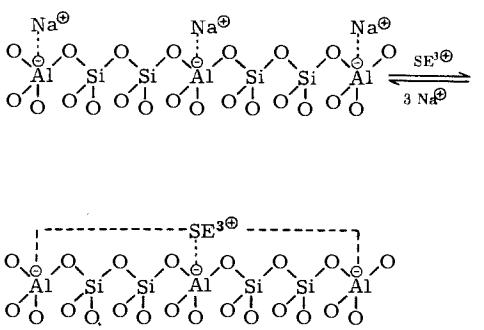


Fig. 12. Replacement of Na^+ ions by trivalent cations of lanthanoids (La^{3+}) in aluminosilicate framework, schematic.

This effect can be strengthened by decreasing the aluminum content[115], for then the negative charges on the AlO_4 tetrahedra in the middle are separated still further from one another. The special activity of lanthanoid-zeolite Y types in catalytic cracking[116] can be explained by assuming polarization of the C—H bonds of the hydrocarbons in the electrostatic field of the zeolite[114]. In decationized zeolites (see Fig. 13) the catalytic activity is caused by the formation of Brönsted and Lewis acid centers, which can be demonstrated in the same way as for amorphous aluminosilicates[115, 117, 118].

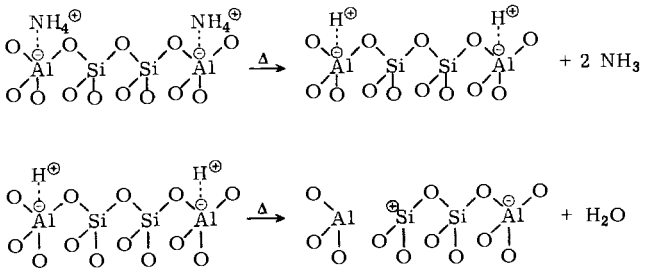


Fig. 13. Decationized zeolites with Brönsted and Lewis acid centers.

Table 4 provides a survey of the most important types of reactions involving zeolitic catalysts in the petrochemical industry.

of the catalytic centers and then to effect a planned synthesis of that structure.

Received: July 2, 1975 [A 83 IE]
German version: Angew. Chem. 87, 659 (1975)
Translated by Express Translation Service, London

[1] *K. F. Fischer* and *W. M. Meier*, Fortschr. Mineral. *42*, 50 (1965).
[2] *A. Cronstedt*, Akad. Handl. Stockholm, 18, 120 (1756).
[3] *G. Bergerhoff, W. H. Baur*, and *W. Nowacki*, Neues Jahrb. Mineral. Mh. *9*, 193 (1958).
[4] *J. M. Bennet* and *J. A. Gard*, Nature *214*, 1005 (1967).
[5] *F. A. Mumpton*, Ind. Miner. (London) *73*, 30 (1973).
[6] *R. L. Hay*, Geol. Soc. Am. Spec. Pap. *85*, 130 (1966).
[7] *K. S. Deffeyes*, J. Sediment. Petrol. *29*, 602 (1959).
[8] *R. A. Sheppard*, Adv. Chem. Ser. *101*, 279 (1971).
[9] *R. A. Munson* and *R. A. Sheppard*, Miner. Sci. Eng. *6*, 19 (1974).
[10] *G. P. L. Walker*, Mineral. Mag. *32*, 503 (1960).

Table 4. Survey of typical fields of application of zeolite catalysts in petrochemistry (decat. = decationized form; La = lanthanoids).

Process	Example	Catalyst type
Cracking	Fission of C_{15+} to C_{5-10} hydrocarbons [116, 119]	Decat. La-zeolite Y
Hydrocracking	Fission of middle and heavy distillates in the presence of hydrogen [120 122]	Ni, Mo, W, Pt, or Pd on zeolite Y
Isomerization	Conversion of C_{4-6}-paraffins into isomers [123, 124]	Pd on decat. zeolite Y
Reforming	Dehydrogenation of saturated, cyclic hydrocarbons to aromatic compounds [125]	Ni and Co on zeolite X
Alkylation	Alkylation of aromatic compounds [126—128]	Ca-Zeolite Y, La-zeolite X or Y, H-zeolite Y
Hydrogenation	Hydrogenation of aromatic compounds [129]	Ni, Co, or Pt on Ca-zeolite X

3.3. Zeolites as Ion Exchangers

In contrast to the amorphous aluminosilicates that find use as inorganic ion exchangers[130], crystalline zeolites have so far been applied only rarely for this purpose. Three examples of their application are worth mentioning:

1) A mixture of Ag and Ba zeolites can desalinate sea-water sufficiently for it to be drinkable, but this application is limited to emergencies because of its high cost[131, 132].

2) Since zeolitic molecular sieves are largely stable to radioactive radiation, they can be used in the atomic energy industry as ion exchangers *e.g.* for the recovery and purification of cesium-137[133].

3) Very recently it has been proposed to use zeolites as water softeners in place of part of the phosphates in detergents[134, 135].

4. Concluding Remarks

The above review of the most important aspects of the field of zeolites would not be complete without mentioning that, for many areas of their application, it has been necessary to modify their structures in order to overcome the relatively low thermal stability that is the main disadvantage of all zeolitic aluminosilicates. Further development will certainly tend increasingly toward combination of the zeolites both with one another and with other adsorbents and catalysts, and will be able to base itself increasingly on knowledge of the relationships between the structure, properties, and types of application. Indeed, it seems that in the near future it should be possible, for a given problem of separation or catalysis, to develop hypotheses about the optimal structure of the channel and pore system or about the arrangement

[11] *R. M. Barrer:* Molecular Sieves. Society of Chemical Industry. London 1968, p. 39.
[12] *D. W. Breck* and *E. M. Flanigen*, Molecular Sieves. Society of Chemical Industry, London 1968, S. 47.
[13] *G. Heinze, F. Schwochow*, and *H. Weber*, DAS 1814488 (1967), Bayer AG.
[14] *R. Aiello, C. Colella*, and *R. Sersale*, Adv. Chem. Ser. *101*, 51 (1971).
[15] *B. Fahlke, W. Wieker*, and *E. Thilo*, Z. Anorg. Allg. Chem. *347*, 82 (1966).
[16] *F. Polak* and *A. Cichocki*, Adv. Chem. Ser. *121*, 209 (1973).
[17] *M. A. Borowiak* and *J. M. Berak*, Rocz. Chem. *48*, 509 (1974).
[18] *B. D. McNicol, G. T. Pott, K. R. Loos*, and *N. Mulder*, Adv. Chem. Ser. *121*, 152 (1973).
[19] *J. L. Guth, Ph. Caullet*, and *R. Wey*, Bull. Soc. Chim. Fr. *1974*, 1758, 2363.
[20] *B. D. McNicol, G. T. Pott*, and *K. R. Loos*, J. Phys. Chem. *76*, 3388 (1972).
[21] *R. Aiello, R. M. Barrer*, and *I. S. Kerr*, Adv. Chem. Ser. *101*, 44 (1971).
[22] *A. Culfaz* and *L. B. Sand*, Adv. Chem. Ser. *121*, 140 (1973).
[23] *G. T. Kerr*, J. Phys. Chem. *70*, 1047 (1966).
[24] *J. Ciric*, J. Colloid Interface Sci. *28*, 315 (1968).
[25] *F. Schwochow* and *G. Heinze*, Adv. Chem. Ser. *101*, 102 (1971).
[26] *S. P. Zhdanov:* Molecular Sieves. Society of Chemical Industry, London 1968, p. 62.
[27] *S. P. Zhdanov*, Adv. Chem. Ser. *101*, 20 (1971).
[28] *S. P. Zhdanov* and *N. N. Buntar:* Synthetic Zeolites. Nauka, Moscow 1962, p. 105.
[29] *S. P. Zhdanov* and *E. N. Egorova:* Chemistry of Zeolites. Nauka, Leningrad 1968.
[30] *T. V. Whittam*, DOS 1567824 (1965), P. Spence & Sons Ltd.
[31] *F. Schwochow, H. Weber*, and *G. Heinze*, DOS 2028163 (1970), Bayer AG.
[32] *G. Heinze, F. Schwochow*, and *H. Weber*, DOS 1812339 (1968), Bayer AG.
[33] *J. G. Gottstine* and *E. H. Westerland*, DAS 1138383 (1961), Union Carbide Corp.
[34] *D. W. Breck*, DAS 1164384 (1960), Union Carbide Corp.
[35] *D. W. Breck*, DAS 1098929 (1959), Union Carbide Corp.
[36] *E. E. Senderov* and *N. I. Khitarov*, Adv. Chem. Ser. *101*, 149 (1971).
[37] *R. M. Milton*, DAS 1038016 (1954), Union Carbide Corp.
[38] *R. M. Milton*, DAS 1038017 (1954), Union Carbide Corp.
[39] *D. W. Breck, E. M. Flanigen, R. W. Milton*, and *T. B. Reed*, 134th Meeting Amer. Chem. Soc., Chicago 1958.
[40] *W. Meise* and *F. F. Schwochow*, Adv. Chem. Ser. *121*, 169 (1973).
[41] *G. Heinze* and *E. Podschus*, DAS 1164995 (1961), Bayer AG.

[42] *G. Heinze* and *E. Podschus*, DAS 1165562 (1961), Bayer AG.
[43] *G. Heinze*, DBP 1203238 (1964), Bayer AG.
[44] *E. Michalko*, DOS 1567894 (1972), United Oil Products.
[45] *L. Pauling*, Z. Kristallogr., Mineral. Petrogr. *74*, 213 (1930).
[46] *J. Loens* and *H. Schulz*, Acta Crystallogr. *23*, 434 (1967).
[47] *T. B. Reed* and *D. W. Breck*, J. Am. Chem. Soc. *78*, 5972 (1956).
[48] *L. Broussard* and *D. P. Shoemaker*, J. Am. Chem. Soc. *82*, 1041 (1960).
[49] *J. V. Smith*, Adv. Chem. Ser. *101*, 171 (1971).
[50] *R. M. Barrer*, Adv. Chem. Ser. *121*, 1 (1973).
[51] *R. M. Barrer*, Brit. Chem. Eng. 7, 267 (1959).
[52] *W. M. Meier:* Molecular Sieves. Society of Chemical Industry, London 1968, p. 10.
[53] *W. M. Meier* and *D. H. Olson*, Adv. Chem. Ser. *101*, 155 (1971).
[54] *D. W. Breck*, Adv. Chem. Ser. *101*, 1 (1971).
[55] *W. Loewenstein*, Am. Mineral. *39*, 92 (1954).
[56] *H. S. Sherry* in *J. A. Marinsky*: Ion Exchange. Marcel Dekker, New York 1969, Vol. 2, p. 89.
[57] *H. S. Sherry*, Adv. Chem. Ser. *101*, 350 (1971).
[58] *F. Wolf* and *H. Furtig*, Kolloid-Z. Z. Polym. *206*, 48 (1965).
[59] *F. Wolf, D. Ceacareanu*, and *K. Pilchowski*, Z. Phys. Chem. (Leipzig) *254*, 96 (1973).
[60] *D. W. Breck, W. G. Eversole, R. M. Milton, T. B. Reed*, and *T. L. Thomas*, J. Am. Chem. Soc. *78*, 5963 (1956).
[61] *D. H. Olson, G. T. Kokotailo*, and *J. F. Charnell*, J. Colloid Interface Sci. *28*, 305 (1968).
[62] *J. Ward*, J. Catal. *10*, 34 (1968).
[63] *P. E. Pickert, J. A. Rabo, E. Dempsey*, and *V. Schomaker*, Proc. 3rd Int. Congr. Catalysis, Amsterdam 1964. Wiley, New York 1965, Vol. 1, p. 714.
[64] *P. Pichat, J. C. Vedrine, P. Gallezot*, and *B. Imelik*, J. Catal. *32*, 190 (1974).
[65] *D. W. Breck*, J. Chem. Educ. *41*, 678 (1964).
[66] *H. Lechert*, Adv. Chem. Ser. *121*, 74 (1973).
[67] *I. E. Maxwell* and *J. J. DeBoer*, J. C. S. Chem. Commun. *1974*, 814.
[68] *K. H. Steinberg, H. Brenner, F. Hofmann, Ch. M. Minachev, R. V. Dmitriev*, and *A. N. Detink*, Z. Anorg. Allg. Chem. *404*, 142 (1974).
[69] *W. Oehme, D. Freude*, and *H. Schmiedel*, Z. Phys. Chem. (Leipzig) *255*, 566 (1974).
[70] *G. T. Kerr*, Inorg. Chem. *5*, 1537 (1966).
[71] *E. Dempsey, G. H. Kuchl*, and *D. H. Olson*, J. Phys. Chem. *73*, 387 (1969).
[72] *M. M. Dubinin, G. M. Fedorova, D. H. Plavnik, L. I. Piguzova*, and *E. N. Prokofeva*, Izv. Akad. Nauk SSSR, Ser. Khim. *11*, 2429 (1968).
[73] *G. T. Kerr*, J. Phys. Chem. *72*, 2594 (1968).
[74] *C. V. McDaniel* and *P. K. Maher:* Molecular Sieves. Society of Chemical Industry, London 1968, p. 186.
[75] *G. T. Kerr*, J. Catal. *15*, 200 (1969).
[76] *R. Aiello* and *R. M. Barrer*, J. Chem. Soc. *A 1970*, 1470.
[77] *G. T. Kerr*, Science *140*, 1412 (1963).
[78] *T. E. Whyte, jr., E. L. Wu, G. T. Kerr*, and *P. B. Venuto*, J. Catal. *20*, 88 (1971).
[79] *C. J. Plank, E. J. Rosinski*, and *M. K. Rubin*, DOS 2049755 (1971), Mobil Oil Corp.
[80] *R. L. Wadlinger, G. T. Kerr*, and *E. J. Rosinski*, US-Pat. 3308069 (1967).
[81] *R. J. Argauer* and *G. R. Landolt*, US-Pat. 3702886 (1972).
[82] *W. Sieber* and *W. M. Meier*, Helv. Chim. Acta *57*, 1533 (1974).
[83] *R. M. Barrer, J. W. Baynham, F. W. Bultitude*, and *W. M. Meier*, J. Chem. Soc. *1959*, 195.
[84] *M. H. Hey* and *F. A. Bannister*, Mineral. Mag. *23*, 243 (1932).
[85] *P. G. Harris* and *G. W. Brindley*, Am. Mineral. *39*, 819 (1954).
[86] *D. B. Broughton* and *A. G. Lickus*, Petr. Refiner *40*, 173 (1961).
[87] *D. B. Broughton*, Chem. Eng. Prog. *64*, 60 (1968).
[88] *W. F. Awery* and *M. N. Y. Lee*, Oil Gas J. *60*, 121 (1962).
[89] *G. J. Griesmer et al.*, Hydrocarbon Process *44*, 147 (1965).
[90] *W. R. Franz et al.*, Petr. Refiner *38*, 125 (1959).
[91] *D. E. Cooper et al.*, Chem. Eng. Prog. *62*, 69 (1966).
[92] *R. M. Barrer* and *B. Coughlan:* Molecular Sieves. Society of Chemical Industry, London 1968, p. 233.
[93] *R. Mitchell*, DAS 1218998 (1954), Union Carbide Corp.
[94] *S. P. Zhdanov, A. V. Kiselev, N. N. Novikova*, and *Yu. A. Eltekov*, Russ. J. Phys. Chem. *39*, 729 (1965).
[95] *A. V. Kiselev, W. N. Semenova*, and *Yu. A. Eltekov*, Kinet. Katal. *8*, 1937 (1967).
[96] *G. E. Hales*, Chem. Eng. Prog. *67*, 49 (1971).
[97] *E. Rabinowitsch*, Z. Phys. Chem. *B 16*, 43 (1932).
[98] *A. Tiselius* and *S. Brohult*, Z. Phys. Chem. *A 168*, 249 (1934).
[99] *E. Ruhl*, Chem.-Ing.-Tech. *43*, 870 (1971).
[100] *D. B. Broughton et al.*, Chem. Eng. Prog. *66*, 70 (1970).
[101] *R. S. Atkins*, Hydrocarbon Process *49*, 132 (1970).
[102] *F. Bayer* and *J. F. Mahler*, Chem. Eng. *77*, 54 (1970).
[103] *J. C. Davis*, Chem. Eng. *79*, 88 (1972).
[104] *W. C. Miller*, Chem. Eng. *80*, 62 (1973).
[105] *G. Heinze* and *G. Ulisch*, DAS 1944912 (1971), Bayer AG.
[106] *H. Gruber* and *H. Weber*, DAS 1928129 (1969), Bayer AG.
[107] *P. B. Venuto* and *R. S. Landis*, Adv. Catal. *18*, 259 (1968).
[108] *Kh. M. Minachev* and *Ya. I. Isakov*, Adv. Chem. Ser. *121*, 451 (1973).
[109] *M. Selenina*, Z. Anorg. Allg. Chem. *387*, 179 (1972).
[110] *V. Penchev, N. Davidova, V. Kanazirev, H. Minchev*, and *Y. Neinska*, Adv. Chem. Ser. *121*, 461 (1973).
[111] *F. Figueras, R. Gomez*, and *M. Primet*, Adv. Chem. Ser. *121*, 480 (1973).
[112] *S. D. Burd* and *J. Marink*, Oil Gas J. *70*, 52 (1972).
[113] *N. Y. Chen, J. Mazink, A. B. Schwartz*, and *P. B. Weisz*, Petrol. Interam. *27*, 42 (1969).
[114] *J. A. Rabo, C. L. Angell, P. H. Kasai*, and *V. Schomaker*, Discuss. Faraday Soc. *41*, 328 (1966).
[115] *J. A. Rabo, P. E. Pickert, D. N. Stamires*, and *J. E. Boyle*, Actes 2nd Congr. Intern. Catalyse, Paris 1960. Editions Technip, Paris 1961, Vol. 2, p. 2055.
[116] *P. B. Weisz* and *J. N. Miale*, J. Catal. *4*, 527 (1965).
[117] *J. B. Uytterhoeven, L. G. Christner*, and *W. K. Hall*, J. Phys. Chem. *69*, 2117 (1965).
[118] *P. B. Venuto, E. L. Wu*, and *J. Cattanach:* Molecular Sieves. Society of Chemical Industry, London 1968, p. 117.
[119] *C. J. Plank, E. J. Rosinski*, and *W. P. Hawthorne*, Ind. Eng. Chem. Prod. Res. Dev. *3*, 165 (1964).
[120] *R. L. Miller*, Chem. Eng. *79*, 60 (1972).
[121] *A. Becher, H. Blume, E. Grasshoff, E. Onderka, J. Welker, W. Weiss, D. Sachse*, and *H. Klotsche*, Chem. Technol. *23*, 666 (1971).
[122] *A. W. Agfonov*, Chem. Technol. *26*, 9 (1974).
[123] *J. A. Rabo, P. E. Pickert*, and *R. L. Mays*, Ind. Eng. Chem. *53*, 733 (1961).
[124] *H. W. Kouwenhoven*, Adv. Chem. Ser. *121*, 529 (1973).
[125] *R. L. Mays, P. E. Pickert, A. P. Bolton*, and *M. A. Lanewala*, Oil Gas J. *63*, 91 (1965).
[126] *P. B. Venuto, L. A. Hamilton, P. S. Landis*, and *J. J. Wise*, J. Catal. *5*, 81 (1966).
[127] *Kh. M. Minachev, Ya. I. Isakov*, and *V. I. Garanin*, Dokl. Akad. Nauk SSSR *165*, 831 (1965).
[128] *Kh. M. Minachev, Ya. I. Isakov*, and *V. I. Garanin*, Neftekhimiya *6*, 63 (1966).
[129] *V. J. Frilette* and *P. B. Weisz*, US-Pat. 3140322 (1964), Mobil Oil Corp.
[130] *R. N. Shreve:* Greensand Bibliography to 1930. US Bur. Mines Bull. *1930*, 328.
[131] *H. Weber* and *E. Podschus*, DAS 1094239 (1958), Bayer AG.
[132] *H. Weber*, DAS 1095259 (1957), Bayer AG.
[133] *L. A. Bray* and *H. T. Fullam*, Adv. Chem. Ser. *101*, 450 (1971).
[134] *M. J. Schwuger, H. Smolka*, and *H. Rostek*, DOS 2412837 (1974), Henkel & Cie.
[135] *P. Berth, G. Jakobi, E. Schmadel, M. J. Schwuger*, and *C. H. Krauch*, Angew. Chem. *87*, 115 (1975); Angew. Chem. internat. Edit. *14*, 94 (1975).

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

1-*tert*-Butyl-3-trimethylsilyl-4,4-dimethyl-2-phospha-1-tetrazene

By *Otto J. Scherer* and *Walter Glässel*[*]

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

Formal replacement of one of the two imine nitrogen atoms in tetrazene derivatives[1] by a phosphorus atom leads to phosphatetrazenes. We have synthesized the first compound of this type:

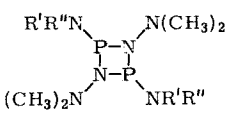
$$(CH_3)_2N{-}NR{-}Li \xrightarrow[-LiCl/-RCl]{+RR'N{-}PCl_2} (CH_3)_2N{-}NR{-}P{=}NR'$$

(1) *(2)*

R = $(CH_3)_3Si$, R' = $(CH_3)_3C$

Evidence opposing the formation of the 2-phospha-2-tetrazene isomer, $(CH_3)_2N{-}N{=}P{-}NRR'$, is provided by the findings: 1) The $^4J_{PH}$ coupling constants of the isolated product lie in the range found for "phosphatriazenes" $RR'N{-}P{=}NR''$ (R = $(CH_3)_3Si$, R' = R'' = $(CH_3)_3C$[2a]; R = R' = $(CH_3)_3Si$, R'' = $(CH_3)_3C$[2b]); 2) Attempts at a directed synthesis of the phospha-2-tetrazene $(CH_3)_2N{-}N{=}P{-}NR'R''$ led to a $(PN)_2$ four-membered ring[3]:

$$(1) \xrightarrow[-LiCl/-RCl]{+R'R''N{-}PCl_2} 1/2$$



(3)

R = $(CH_3)_3Si$
R' = $(CH_3)_3C$, R'' = CH_3

(2): distillable greenish yellow liquid which can be stored for several weeks at room temperature on exclusion of air. In solution the compound can even be exposed to air (open NMR sample tube) for several hours (*ca.* 10 h) without undergoing significant change. ^{1}H-NMR measurements in toluene down to −70 °C revealed no change in the spectrum; thus a phosphatetrazene isomer equilibrium arising by migration of the $(CH_3)_3Si$ group hardly appears likely[4]. ^{31}P-NMR (20 % solution in C_6H_6, 85 % H_3PO_4 as external standard): δ = −321 ppm.

(3): colorless crystals, m. p. 65—67 °C (b. p. 83—85 °C/0.01 torr; yield 25 %), readily soluble in aprotic organic solvents. ^{31}P-NMR: δ = −79.2 ppm. The NMR data indicate that the compound exists solely in one isomeric form (*cis* or *trans*).

Procedure:

A solution of $(CH_3)_3CNHSi(CH_3)_3$ (29.06 g, 200 mmol) in diethyl ether (100 ml) is metalated with *n*-C_4H_9Li-hexane solution (124 ml, 200 mmol). The resulting solution is added dropwise with ice cooling to PCl_3 (26.1 g, 190 mmol) in ether (300 ml), stirred for 1 h at room temperature, and cooled to −78 °C. After addition of $(CH_3)_2N{-}NLi{-}Si(CH_3)_3$ [prepared by metalation of $(CH_3)_2N{-}NH{-}Si(CH_3)_3$] (200 mmol) in ether (100 ml), the mixture is stirred for 12 h, and then evaporated at water pump vacuum. The residue is taken up in pentane (50 ml) and filtered through a G3 frit. Fractional distillation (Vigreux column) affords 9.41 g (21 % based on PCl_3) of *(2)*, b. p. 44—45 °C/0.01 torr.

Received: June 12, 1975 [Z 270 IE]
German version: Angew. Chem. *87*, 667 (1975)

[1] Both 1- and 2-tetrazenes are known. To our knowledge, however, alkyl derivatives exist only in the 2-tetrazene form; cf. *N. Wiberg* and *W. Uhlenbrock*, Chem. Ber. *105*, 63 (1972).

[2] a) *O. J. Scherer* and *N. Kuhn*, Angew. Chem. *86*, 899 (1974); Angew. Chem. internat. Edit. *13*, 811 (1974); and references cited therein; b) J. Organometal. Chem. *82*, C3 (1974).

[3] The product *(3)* could also arise from the non-distillable precursor $(CH_3)_2N{-}NR{-}PCl{-}NR'R''$ by intermolecular elimination of RCl. The assumption of a phospha-2-tetrazene intermediate is, however, supported by the successful quantitative conversion of $R_2N{-}P{=}NR'$ (R = *i*-C_3H_7; R' = $(CH_3)_3C$) into the four-membered ring dimer: *O. J. Scherer* and *W. Glässel*, to be published.

[4] Experience gained with related amine/imine systems [2a] opposes the occurrence of a $(CH_3)_3Si$ shift that is still too fast at −70 °C. The phospha-2-tetrazene, which could be present as *cis* or *trans* isomer, would have to exist exclusively as one of the two isomeric forms. In the case of *(2)*, either the inversion barrier of the imine nitrogen is drastically lowered by the *tert*-butyl group [5a], or the two isomers do not differ in the chemical shift of their proton signals down to −70 °C [5b].

[5] a) Cf. studies on guanidines: *H. Kessler* and *D. Leibfritz*, Tetrahedron *26*, 1805 (1970); b) cf. *N-tert*-butylaziridines: *F. A. L. Anet* and *J. M. Osyang*, J. Am. Chem. Soc. *89*, 352 (1967); *S. J. Brois*, *ibid.* *89*, 4242 (1967).

Synthesis of *tert*-Alkyl-Substituted Glycines[1]

By *Ulrich Schöllkopf* and *Rolf Meyer*[*]

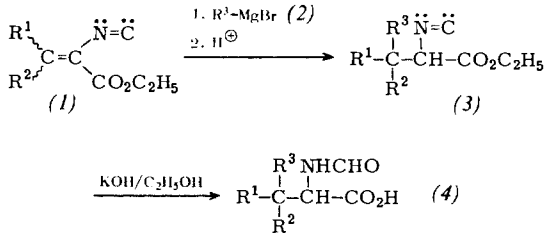
α-Metalated isocyanides[2] have already opened up many novel routes to amino acids[3, 4]. We now wish to report a high-yield synthesis of *tert*-alkyl-substituted glycines [type *(4)*]. These compounds are employed *inter alia* in molecular biology in order to delineate the recognition range of tRNA synthetases[5].

In their synthesis a Grignard reagent *(2)* is added to the β-substituted ethyl α-isocyanoacrylates *(1)*[6]. Hydrolysis yields α-*tert*-alkyl-substituted ethyl α-isocyanoacetates *(3)* which can readily be converted (as is generally the case[4]) into amino acid derivatives *(4)* in good yields. As far as we have yet been able to establish, the yields of the addition

[*] Prof. Dr. O. J. Scherer and Dipl.-Chem. W. Glässel
Fachbereich Chemie der Universität
675 Kaiserslautern, Postfach 3049 (Germany)

[*] Prof. Dr. U. Schöllkopf and Dipl.-Chem. R. Meyer
Organisch-Chemisches Institut der Universität
34 Göttingen, Windausweg 2 (Germany)

step *(1)*→*(3)* with methylmagnesium halide [$R^3=CH_3$ in *(2)*] are unsatisfactory, presumably because this relatively small reagent preferably adds to the ester carbonyl group.



Experimental:

All operations are carried out under nitrogen. A solution of *(1)*[6] (20 mmol) in light petroleum (20 ml) and ether (20 ml) is added dropwise over 30 min to a stirred (magnetic stirrer) solution of *(2)* (40 mmol, prepared *in situ* from alkyl bromide and magnesium) in ether (50 ml) (but not in tetrahydrofuran[7]) at −5 °C. The addition product precipitates as a brown "tar" and should not be dissolved by addition of more solvent since otherwise *(3)* cannot be isolated.

Stirring is continued for 30 min at −5 °C and the mixture is cooled with ice-water prior to addition of glacial acetic acid (40 mmol) in water (50 ml), whereupon the precipitate dissolves. The ethereal phase is separated off, the aqueous phase extracted twice with ether (2 × 50 ml), and the ether extracts dried over sodium sulfate. The solvent is drawn off and the residue distilled. – An effective precision glass stirrer should be used for quantities exceeding 0.1 mol, and the excess of *(2)* should not be greater than 20%.

Table 1. α-*tert*-Alkyl-substituted ethyl α-isocyanoacetates *(3)* [a] and α-*tert*-alkyl-substituted *N*-formylglycines *(4)* [b] prepared.

	R^1	R^2	R^3	*(3)* Yield [%]	*(3)* B. p. [°C/torr]	*(3)* NMR [c]	*(4)* [d] M. p. [°C]	*(4)* [d] NMR [c]
(a)	CH_3	CH_3	C_2H_5	62	58—61/0.3	4.06	180—182	4.24
(b)	CH_3	CH_3	C_6H_5	72	107—110/0.05	4.36	179—180	4.68
(c)	C_2H_5	C_2H_5	C_2H_5	76	82—86/0.4	4.20	171—172	4.65
(d)	C_2H_5	C_2H_5	C_6H_5	79	121—128/0.1	4.37	209—212	5.05
(e)	CH_3	C_6H_5	C_2H_5	73	103—106/0.05	4.48	167—168	5.06
(f)	CH_3	C_6H_5	C_6H_5	87	[e]	4.48	178—181	5.68
(g)	$-(CH_2)_5-$		C_2H_5	71	92—96/0.1	4.31	179—180	4.48
(h)	$-(CH_2)_5-$		C_6H_5	73	133—134/0.1	4.20	222—225	4.48

[a] IR bands at *ca.* 2140 (NC) and 1745 cm^{-1} (CO).
[b] IR bands (KBr) at *ca.* 3320 (NH), 1620 (CH=O), and 1710 cm^{-1} (CO_2H).
[c] ^{1}H-NMR ($CDCl_3$), signal of the CH proton, τ values.
[d] Yield of conversion *(3)*→*(4)* almost quantitative.
[e] Not distillable.

For the conversion *(3)*→*(4)*, compound *(3)* (10 mmol) is refluxed with KOH (0.6 g) in 90% ethanol (20 ml) for 30 min. The solvent is drawn off in a water pump vacuum, the solvent is dissolved in water (15 ml) (if necessary with slight warming), and the solution acidified with 1 ml of conc. hydrochloric acid (to pH 1–2). The *N*-formyl amino acids *(4)*, which often precipitate as oils, can be induced to crystallize in an ice bath. They are filtered off under suction, dissolved in a small volume of ethanol, and water is added dropwise to the hot solution until it remains turbid. The compounds *(4)* precipitate on cooling. Correct elemental analyses were obtained in all cases.

Received: December 3, 1973 [Z 965 IE]
German version: Angew. Chem. 86, 624 (1974)
Publication delayed at authors' request

[1] Syntheses with α-Metalated Isocyanides, Part 26.— Part 25: *U. Schöllkopf* and *P.-H. Porsch*, Chem. Ber. *106*, 3382 (1973).

[2] *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *82*, 842 (1968); Angew. Chem. internat. Edit. 7, 805 (1968).

[3] Cf. [1]; *U. Schöllkopf* and *K. Hantke*, Liebigs Ann. Chem. *1973*, 1571; *D. Hoppe* and *U. Schöllkopf*, *ibid.* *763*, 1 (1972); *U. Schöllkopf*, *F. Gerhart*, *R. Schröder*, and *D. Hoppe*, *ibid.* *766*, 116 (1972); *M. Suzuki*, *T. Iwasaki*, *K. Matsumoto*, and *K. Okumura*, Chem. Ind. (London) *1972*, 687; *1973*, 228; *W. Vaalburg*, *J. Strating*, *M. G. Woldring*, and *H. Wynberg*, Synth. Commun. *2*, 423 (1972).

[4] Cf. *U. Schöllkopf*, *D. Hoppe*, and *R. Jentsch*, Angew. Chem. *83*, 357 (1971); Angew. Chem. internat. Edit. *10*, 331 (1971).

[5] Cf. *H.-J. Prätorius*, Diplomarbeit, Universität Braunschweig 1973.

[6] *U. Schöllkopf*, *R. Harms*, and *D. Hoppe*, Liebigs Ann. Chem. *1973*, 611; route B was preferred.

[7] With Grignard reagents available only in tetrahydrofuran the reaction gives only poor yields.

Chemistry of *cis*-Trioxatris-σ-homobenzene. A Simple Total Synthesis of Streptamine[**]

By *Reinhard Schwesinger* and *Horst Prinzbach*[*]

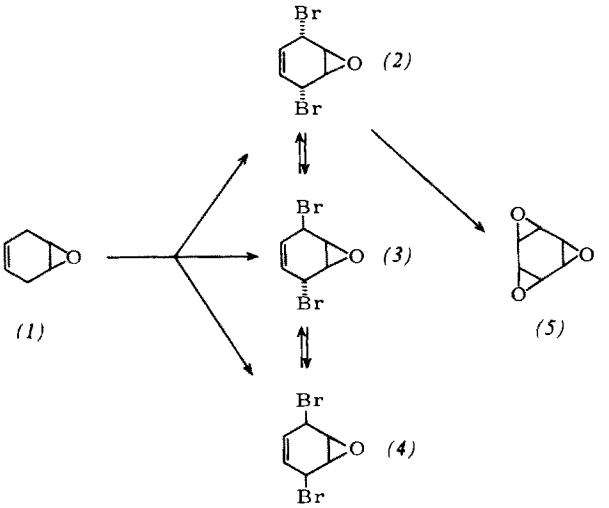
Preparative studies with *cis*-trioxatris-σ-homobenzene (*cis*-"benzene trioxide") *(5)*[1] have so far met with difficulties because radical bromination of the epoxide *(1)* afforded at best only 20% yields of the *exo-cis*-dibromide *(2)*, along with about 26% *trans*-*(3)* and very small amounts of the *endo-cis* products *(4)*. The finding[2] that dibromides *(2)*—*(4)* equilibrate and that the individual equilibrium partners can be isolated in pure form—thus making it possible to isolate *(5)* in increased yields of *ca.* 26% [w.r.t. *(1)*]—has opened up a number of preparatively interesting possibilities[3, 4]. We report here on a simple and productive synthesis of streptamine *(10a)* from *(5)*[5].

Brief reaction of *(5)* with a 5% aqueous solution of hydrazine (molar ratio *ca.* 3:1, 50 °C, 35 min) leads to formation of the previously postulated[6] intermediary epoxyhydrazine adduct *(6a)* [colorless crystals, m.p. *ca.* 235 °C (decomp.); tetracetate *(6b)*, m.p. 179—181 °C] in 97% yield (30% conversion) together with traces of *(11)* (colorless crystals, > *ca.* 220 °C decomp.; tetraacetate *(11b)*, m.p. 57–67 °C). *(6a)* reacts with phthalic anhydride under mild conditions (water, 10 min at 20 °C, 1 min at 60 °C) to give the sparingly soluble

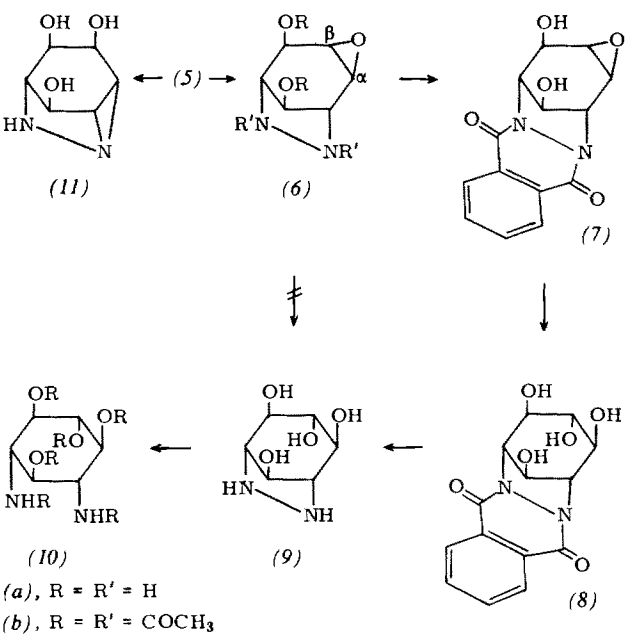
[*] Prof. Dr. H. Prinzbach and Dipl.-Chem. R. Schwesinger
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)

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

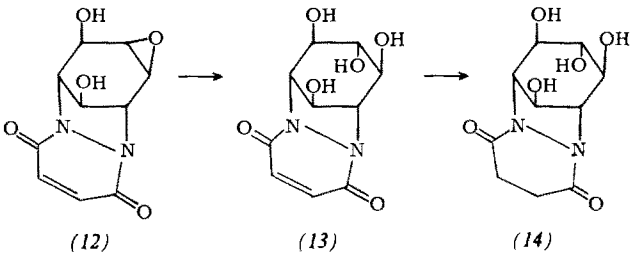
dione *(7)* (colorless crystals, m.p. *ca.* 285 °C (decomp.)). On heating with 20 mol-% phthalic acid in water under pressure (170 °C), *(7)* is hydrolyzed quantitatively to the *scyllo*-tetrol *(8)* (m.p. *ca.* 297 °C (decomp.)). Treatment of *(8)* with 5 M



NaOH (molar ratio 1:6, 90 min, 100 °C) yields the readily soluble hydrazine compound *(9)*[7]; hydrogenolysis of *(9)* over Raney nickel affords streptamine *(10a)*. *(10a)* was precipitated as the sulfate and identified as the hexaacetate *(10b)* by comparison with an authentic sample (melting point, IR, ^{1}H-NMR)[8]. The yield of this preparatively simple synthesis—no intermediate needs to be isolated—amounts to 70—75% referred to *(5)*.



The pressure reaction necessary for the hydrolysis *(7)*→*(8)* can be circumvented by resorting to a slightly different route in which the pyridazinedione *(12)* (faint yellow crystals, m.p. *ca.* 246 °C (decomp.)), obtained by reaction of *(6a)* with maleic anhydride (anhydrous methanol, 0 °C, 10 min) followed by treatment with very dilute sulfuric acid (1 min, 50 °C, 97%), is used in place of *(7)*. On heating for 5 h in 5% sulfuric acid at 100 °C, *(12)* is converted into the tetrol *(13)* (94%, m.p. *ca.* 252 °C (decomp.)), which can be hydrogenated (Raney-Ni, 20 °C, 1 at) to *(14)* (m.p. 218 °C) and then cleaved with aqueous hydrazine to give *(9)*. This route, however, has its disadvantages compared to the reaction sequence *(5)*→*(10)* in than it is necessary to isolate the intermediates *(6)*, *(12)*, and *(13)*.



The obvious direct hydrolysis *(6)*→*(9)* is not attainable; both in alkaline as well as in acid solution, competing reactions are clearly favored.

The structures of the compounds *(6)*—*(14)* are confirmed by elemental analysis and spectral data; the stereochemical details follow, primarily, from the results of ^{1}H-NMR decoupling experiments at 270 and 360 MHz[9].

Received: November 13, 1974 [Z 125 IE]
German version: Angew. Chem. *87*, 625 (1975)
Publication delayed at authors' request

CAS Registry numbers:

(5), 39078-11-0; *(6a)*, 53993-34-3; *(6b)*, 53993-35-4; *(7)*, 53993-36-5; *(8)*, 53993-37-6; *(9)*, 51607-70-6; *(10a)*, 488-52-8; *(10b)*, 7380-63-4; *(11)*, 54020-25-6; *(12)*, 53993-38-7; *(13)*, 53993-39-8; *(14)*, 53993-40-1

[1] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. internat. Edit. *11*, 942 (1972); *E. Vogel*, *H.-J. Altenbach*, and *C. D. Sommerfeld*, Angew. Chem. *84*, 986 (1972); Angew. Chem. internat. Edit. *11*, 939 (1972).

[2] *R. Schwesinger*, Dissertation, Universität Freiburg 1975.

[3] *R. Schwesinger*, *H. Fritz*, and *H. Prinzbach*, Angew. Chem. *85*, 1110 (1973); Angew. Chem. internat. Edit. *12*, 993 (1973); *R. Schwesinger*, *H. Fritz*, and *H. Prinzbach*, Angew. Chem. *85*, 1107 (1973); Angew. Chem. internat. Edit. *12*, 989 (1973); *S. Kagabu* and *H. Prinzbach*, Angew. Chem. *87*, 248 (1975); Angew. Chem. internat. Edit. *14*, 252 (1975); *H. Prinzbach*, *C. Kaiser*, and *H. Fritz*, Angew. Chem. *87*, 249 (1975); Angew. Chem. internat. Edit. *14*, 253 (1975); *H. Prinzbach*, *H.-W. Schneider*, and *R. Schwesinger*, unpublished; *L. Knothe* and *H. Prinzbach*, Tetrahedron Lett., in press.

[4] For the use of *(4)* in the synthesis, *inter alia*, of *trans*-"benzene trioxide" and of *cis*-"benzenediimine" see *R. Keller*, Diplomarbeit, Universität Freiburg 1974; *B. Gallenkamp*, Part of a dissertation, in preparation, Universität Freiburg.

[5] Earlier syntheses: *M. L. Wolfrom*, *S. M. Ohn*, and *W. J. Polglase*, J. Amer. Chem. Soc. *72*, 1724 (1950); *K. Heyns* and *H. Paulsen*, Chem. Ber. *89*, 1152 (1956); *T. Suami* and *S. Ogawa*, Bull. Chem. Soc. Jap. *38*, 2026 (1965); *N. Kurihara*, *T. Kurokawa*, and *M. Nakajima*, Agr. Biol. Chem. *31*, 1166 (1967); *S. Ogawa*, *T. Abe*, *H. Sano*, *K. Kotera*, and *T. Suami*, Bull. Chem. Soc. Jap. *40*, 2405 (1967); *F. W. Lichtenthaler*, *H. Leinert*, and *T. Suami*, Chem. Ber. *100*, 2383 (1967); *T. Suami*, *S. Ogawa*, *H. Uchino*, and *M. Uchida*, Bull. Chem. Soc. Jap. *46*, 3840 (1973).

[6] *R. Schwesinger*, *H. Fritz*, and *H. Prinzbach*, Angew. Chem. *85*, 1111 (1973); Angew. Chem. internat. Edit. *12*, 994 (1973).

[7] *T. Suami*, *S. Ogawa*, *H. Uchino*, and *M. Uchida*, Bull. Chem. Soc. Jap. *46*, 3840 (1973).

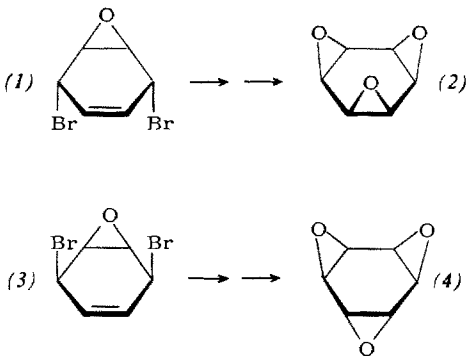
[8] We thank Prof. *F. W. Lichtenthaler* for a sample of streptamine hexaacetate *(10b)*.

[9] We thank Prof. *H. Achenbach* for the MS measurements, Dr. *H. Fritz* for recording the high-field ^{1}H-NMR and ^{13}C-NMR spectra, and Dr. *H. König* for valuable suggestions.

streptamine and (±)-Hyosamine[**]

By *Horst Prinzbach*, *Reinhold Keller*, and *Reinhard Schwesinger*[*]

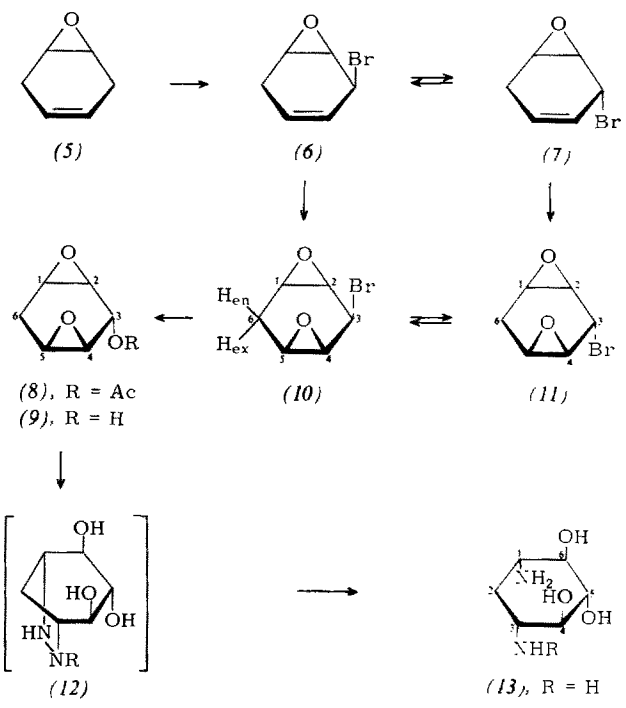
Investigations in connection with the optimization of methods for the synthesis of the dibromoepoxycyclohexenes *(1)* and *(3)*[1]—starting materials for the synthesis of trioxa-tris-σ-homobenzenes ("benzene trioxides") *(2)* and *(4)*—also revealed a preparatively useful entry to the monobromoepoxycyclohexenes *(6)* and *(7)*. These bromides, which are readily accessible from benzene in three steps open up—like *(1)* and *(3)*—a number of most promising applications in the field of inositol-like natural products. We report here on the



simple total synthesis of the antibiotic building units 2-deoxystreptamine *(13)*[2] and (±)-hyosamine *(14)*[2,3]; the syntheses are modelled on the synthesis of streptamine from *(2)*[1] and provide *(13)* and *(14)* in excellent yields.

Reaction of *(5)* with equimolar amounts of *N*-bromosuccinimide in CCl_4 affords a mixture of *(6)* and *(7)* (ratio *(6)*:*(7)* *ca.* 1:9) [total yield of mixture 85—90% for 1 mol amounts; unreacted *(5)* and any dibromides that are formed[1] can largely be removed by distillation or by crystallization from methanol (−50 °C)]. Systematic equilibration experiments in acetonitrile (tetraethylammonium bromide catalyst) and acetone (tetrapropylammonium bromide) for enrichment of the desired *endo*-bromide *(6)* resulted in a ratio of *(6)*:*(7)* of *ca.* 6:4. The following findings were decisive in assessing the value of this synthesis: (i) The bromides *(6)* and *(7)* are quantitatively and stereospecifically oxidized to the *cis*-diepoxides *(10)* and *(11)* on treatment with trifluoroperacetic acid; (ii) *(10)* and *(11)* can—like the allyl bromides *(1)*/*(3)* and *(6)*/*(7)*—equilibrate, the equilibrium in acetonitrile and in acetone being very much more in favor of the desired *endo* product *(10)* (*ca.* 9:1)[4] than in the equilibrium *(6)*/*(7)*. The 1:9 crude mixture *(6)*/*(7)* is therefore oxidized directly to *(10)*/*(11)* (*ca.* 1:9) [*(11)*, colorless crystals, m.p. 110 °C, ^{1}H-NMR ($CDCl_3$, 270 MHz): τ = 5.21 (m, 3-H, $J \approx 1.5$ Hz); 6.59 (dd, 2(4)-H, $J = 4.0$, ≈ 1.5 Hz); 6.80 (m, 1(5)-H); 7.21 (sd, 6_{en}-H, $J = 17.5$ Hz); 7.45 (dt, 6_{ex}-H, $J = 17.5$, 3 Hz)], the endo-bromodiepoxide *(10)* enriched to *ca.* 9:1 by heating (5 h) in acetone/tetrapropylammonium bromide and isolated pure from methanol [*(10)*, colorless crystals, m.p. 142 °C, ^{1}H-NMR ($CDCl_3$, 270 MHz): τ = 5.27 (t, 3-H, $J = 3$ Hz); 6.58 (m, 1(5)-H); 6.64 (t, 2(4)-H, $J = 3$, 4 Hz); 7.19 (dt, 6_{en}-H, $J = 17.5$, 1.5 Hz); the *exo*-acetate *(8)* [colorless crystals (methanol), m.p. 91 °C, ^{1}H-NMR ($CDCl_3$, 270 MHz): τ = 4.46 (m, 3-H, $J \approx 1.5$ Hz); 6.86 (m, 1(5)-H; 6.93 (dd, 2(4)-H, $J = 4$, ≈ 1.5 Hz); 7.25 (sd, 6_{en}-H, $J = 17.3$ Hz); 7.68 (dt, 6_{ex}-H, $J = 17.3$, 3 Hz) was achieved by treatment with tetramethylammonium acetate in acetone solution (56 °C, yield 97%); the equilibration of pure *(10)* with *(11)* is precluded by the rate of the reaction and the low solubility of the tetramethylammonium bromide formed. For synthesis of the pure alcohol *(9)* [colorless crystals (methyl acetate), m.p. 82—84 °C], the acetate *(8)* is hydrolyzed by treatment with ammonia in methanolic solution. Incorporation of the 1,3-*cis* amino-substituents according to the method described by *Suami et al.*[6] is effected by reaction of the acetate of *(8)* with excess hydrazine solution at 50 °C and Raney-Ni hydrogenation of the adduct *(12)*[7] without isolation to deoxystreptamine *(13)* [75—80% w.r.t. *(8)*]. *(13)* is identified as the hydrochloride and as the pentaacetate [^{1}H-NMR (D_6-DMSO, 270 MHz): τ = 2.21 (d, N—H, $J = 9$ Hz); 4.93 (t, 5-H, $J = 10$ Hz); 5.14 (t, 4(6)-H, $J = 10$ Hz); 5.94 (dq, 1(3)-H, $J = 10$, 4.5 Hz); 8.1 (s, OAc); 8.26 (s, NAc); 8.1—8.3 (m, CH_2)] by comparison with authentic samples[8].

(±)-Hyosamine *(14)* is obtained analogously in *ca.* 70% yield from *(9)* and methylhydrazine.



All the new products give correct elemental analyses; the structures have been verified by additional spectroscopic data (IR, ^{13}C-NMR, MS).

Received: May 20, 1975 [Z 249a IE]
German version: Angew. Chem. 87, 626 (1975)

CAS Registry numbers:
(5), 6253-27-6; *(6)*, 55990-87-9; *(7)*, 56084-57-2; *(8)*, 55990-88-0; *(9)*, 55990-89-1; *(10)*, 55990-90-4; *(11)*, 56084-58-3; *(13)*, 2037-48-1; *(14)*, 6216-02-0

[*] Prof. Dr. H. Prinzbach, Dipl.-Chem. R. Keller, and Dipl.-Chem. R. Schwesinger
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *H. Fritz* for the high-field ^{1}H-NMR spectra.

[1] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *87*, 625 (1975); Angew. Chem. internat. Edit. *14*, 630 (1975); *H. Prinzbach*, *R. Keller*, and *R. Schwesinger*, *ibid.* *87*, 627 (1975); Angew. Chem. internat. Edit. *14*, 633 (1975).

[2] The total syntheses from conduritol F developed by *M. Nakajima et al.* (Liebigs Ann. Chem. *689*, 235 (1965)) and from 4,6-dinitropyrogallol

by *D. Dijkstra* (Rec. Trav. Chim. Pays-Bas *87*, 161 (1968)) afford only very low yields.

[3] *T. Suami, S. Ogawa*, and *H. Sano*, Bull. Chem. Soc. Jap. *43*, 1843 (1970); *T. Suami, S. Ogawa, N. Tanno, M. Sugura*, and *K. Rinehart, Jr.*, J. Amer. Chem. Soc. *95*, 8734 (1973).

[4] We have also prepared the formates, alcohols, 4-nitrobenzoates, 4-nitro- and 2,4-dinitrophenolates corresponding to the bromides *(6)* and *(7)*. Only the *endo*-alcohol and *exo*-nitrophenolates are oxidized stereospecifically to the *cis*-1,4-diepoxide analogs of *(10)* and *(11)*. These diepoxides react with hydrazine with simultaneous substitution of the protecting group to give *(12)*. This alternative route to *(13)* is however clearly less productive on a laboratory scale.

[5] Since the mother liquor is reemployed for the equilibration this separation does not incurr any losses.

[6] *T. Suami, S. Ogawa, H. Uchino*, and *M. Uchida*, Bull. Chem. Jap. *46*, 3840 (1973); cf. the most recent published synthesis of 2,5-dideoxystreptamine from *cis*-1,2:4,5-diepoxycyclohexane: *T. Suami, S. Ogawa, H. Uchino*, and *Y. Funaki*, J. Org. Chem. *40*, 456 (1975).

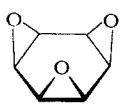
[7] It might be expected that hydrazine attacks preferentially, if not exclusively, at C-1/C-5 in *(8)*/*(9)*. It is currently being investigated whether attack also occurs at C-2/C-4.

[8] We thank Prof. *H. Paulsen* and Prof. *F. W. Lichtenthaler*, respectively, for the samples of deoxystreptamine hydrochloride and deoxystreptamine pentaacetate.

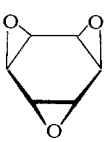
Productive Synthesis of *trans*-Trioxatris-σ-homobenzene (*trans*-"Benzene Trioxide")[**]

By *Horst Prinzbach, Reinhold Keller*, and *Reinhard Schwesinger*[*]

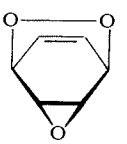
cis-Trioxatris-σ-homobenzene *(1)*, in its capacity as 1,2:3,4:5,6-trisanhydro-*cis*-inositol, has opened up numerous novel syntheses in the field of inositol chemistry[1]. Similar



(1)



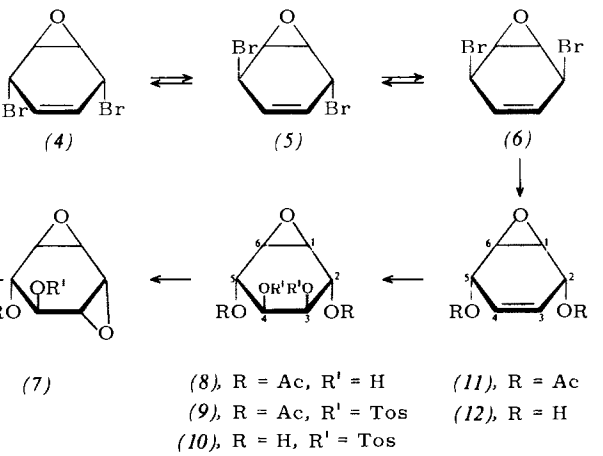
(2)



(3)

applications can be expected from the *trans*-trioxide *(2)* (1,2:3,4:5,6-trisanhydro-*allo*-inositol). However the method recently described in the literature[2] for the synthesis of *(2)*, *i.e.* by thermal rearrangement of the *exo*-peroxide *(3)*, is somewhat demanding and not particularly productive.

We have now discovered a more convenient and advantageous route to *(2)* using the reaction sequence *(6)* → *(7)* → *(2)*[3]. This was made possible by the finding that in the equilibration with the isomers *(4)* and *(5)* on a molar scale, the *endo-cis*-dibromoepoxycyclohexene *(6)* can amount to as much as 40% of the equilibration mixture and can be isolated pure by crystallization from CCl_4 (colorless platelets, m.p. 134—136 °C)[4]. The twofold substitution *(6)* → *(11)* can be accomplished almost quantitatively (97%)—*i.e.* without epimerization or allyl-isomerization—with tetramethylammonium acetate in anhydrous acetone (20 °C, 24 h) [*(11)* colorless crystals, m.p. 80 °C, ^{1}H-NMR ($CDCl_3$): τ = 4.13 (m, 3(4)-H); 4.43 (m, 2(5)-H); 6.66 (m, 1(6)-H); 7.85 (s, CH_3)]. The oxidation with potassium permanganate in $MgSO_4$-buffered aqueous alcoholic solution (pH *ca.* 8) *via* directive action of the epoxide oxygen favors formation of the *endo-cis*-diol *(8)* [^{1}H-NMR ($CDCl_3$/D_6-DMSO): τ = 4.74 (m, 2(5)-H, $J_{2,3}+J_{2,4} \approx 5$ Hz); 5.82 (bd, OH, $J = 5$ Hz);



(4) *(5)* *(6)* *(7)*

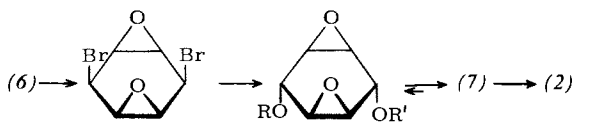
(8), R = Ac, R' = H
(9), R = Ac, R' = Tos
(10), R = H, R' = Tos

(11), R = Ac
(12), R = H

6.24 (st, 3(4)-H); 6.82 (bs, 1(6)-H); 7.86 (s, CH_3)]. At the stage where *(8)* is obtained in 65% yield no *exo*-diol could be detected along with the higher oxidized components.

Both the twofold tosylation *(8)* → *(9)* (tosyl chloride, pyridine; colorless crystals, m.p. 157 °C) and specific hydrolysis of the acetate groups (methanolic NH_3/NH_4Ac solution, 20 °C, TLC check for monoacetate) to give *(10)* [colorless crystals, m.p. 192 °C, ^{1}H-NMR ($CDCl_3$/D_6-DMSO): τ = 4.60 (d, OH, $J = 6$ Hz); 5.28 (m, 3(4)-H, $J_{2,3}+J_{2,4} \approx 5$ Hz); 5.86 (m, 2(5)-H); 6.89 (bs, 1(6)-H); 7.58 (s, CH_3)] proceed in accordance with conventional methods, each giving >90% yields. The cyclization *via (7)* to *(2)*, using monosodium glycolate (THF), as in the synthesis of *(1)*[5], could be achieved in one step (2.2 equiv. base, 20 °C) without detectable (^{1}H-NMR) competing reactions. The product, which was isolated in 80—85% yield, was verified as being *(2)* by mixed melting point and comparison of spectra.

We have also investigated the alternative route *via (13)* to *(16)* so as to circumvent the hydroxylation step *(11)* → *(8)*. Epoxidation of *(6)* with excess trifluoroperacetic acid (1.5 equiv., 0—10 °C) leads, despite the bulky bromine residue, exclusively to the *cis*-diepoxide *(13)* [colorless crystals, m.p. 224 °C, ^{1}H-NMR (D_6-DMSO): τ = 4.97 (m, 3(6)-H); 6.37 (dd, 1(5), 2(4)-H)]. Acetolysis with tetramethylammonium acetate



(13)

(14), R = R' = Ac
(15), R = R' = H
(16), R = H, R' = Tos

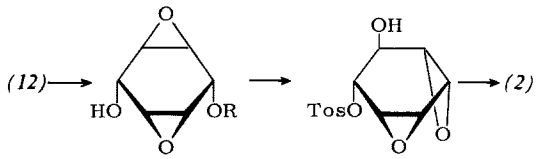
and hydrolysis to the known intermediates *(14)* and *(15)*[6] also proceed without competition[7]. On the other hand, the monotosylation to *(16)* never exceeds more than *ca.* 60%. An additional drawback is that the transformation of *(16)* into *(2)* with potassium *tert*-butoxide/THF *via* epoxide migration to the thermodynamically more stable *(7)*[6] is not free of secondary products (yield *ca.* 50%).

In a further variant the diol *(12)* obtained quantitatively from *(11)* is oxidized with peracetic acid (40%) to the *trans*-diepoxide *(17)*[6], which is then transformed after monotosylation [*(18)*, colorless crystals, 65%, m.p. 109 °C] with CH_3ONa/THF *via (19)*[8] into *(2)* (30%). Although the epoxidation is highly selective (>90%, *i.e.* directive action of the hydroxy groups outshadows that of the epoxide oxygen), the moderate yields obtained in the subsequent steps rule out such a route to *(2)*.

[*] Prof. Dr. H. Prinzbach, Dipl.-Chem. R. Keller, and Dipl.-Chem. R. Schwesinger
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)

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

Both these variants, although not the first choice for the synthesis of *(2)*, are by far the best routes for the synthesis of the dianhydro inositols *(13)*—*(18)*. For example actinamine (*N,N'*-dimethyl-*myo*-inosa-1,3-diamine), a subunit of



(17), R = H
(18), R = Tos

(19)

antibiotics, is obtained in high yield from *(15)* by the method described by *Suami et al.* and proven in our total syntheses of deoxystreptamine and hyosamine[9].

The new compounds *(7)*—*(13)*, *(16)*, and *(18)* have been confirmed by elemental analyses, IR, MS, ^{13}C-NMR, and additional ^{1}H-NMR data.

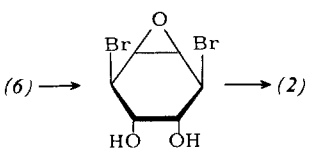
Received: May 20, 1975 [Z 249b IE]
German version: Angew. Chem. *87*, 627 (1975)

CAS Registry numbers:
(2), 39078-13-2; *(5)*, 39573-56-3; *(6)*, 56084-54-9; *(7)*, 50473-94-4; *(8)*, 55990-81-3; *(9)*, 55990--82-4; *(10)*, 55990-83-5; *(11)*, 55990-84-6; *(12)*, 55990-85-7; *(13)*, 56084-55-0; *(16)*, 55990-86-8; *(18)*, 56084-56-1

[1] *H. Prinzbach, C. Kaiser*, and *H. Fritz*, Angew. Chem. *87*, 248 (1975); Angew. Chem. internat. Edit. *14*, 253 (1975); *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *87*, 625 (1975); Angew. Chem. internat. Edit. *14*, 630 (1975); earlier literature cited therein.

[2] *E. Vogel, H.-J. Altenbach*, and *C.-D. Sommerfeld*, Angew. Chem. *84*, 986 (1972); Angew. Chem. internat. Edit. *11*, 939 (1972); *C. H. Foster* and *G. A. Berchtold*, J. Amer. Chem. Soc. *94*, 7939 (1972).

[3] The route corresponding to that for the synthesis of *(1)* from *(4)* is thwarted by the fact that *(6)* can not be hydroxylated uniformly to *(20)*; see, however, the synthesis of *(2)* from *(1)* *via* the 1,2:3,4-dianhydro-*epi*-inositol [8].



(20)

[4] *(6)* is formed together with *(4)* and *(5)* in yields of only *ca.* 1% in the radical bromination of 4,5-epoxycyclohexene (NBS, CCl_4).

[5] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. internat. Edit. *11*, 942 (1972).

[6] *T. Suami, S. Ogawa*, and *S. Oki*, Chem. Lett. *1973*, 901.

[7] Hence, *(14)* is prepared from *(13)*, since diacyl esters of the type *(11)* react with peracids to give complex mixtures.

[8] *H. Prinzbach* and *H.-W. Schneider*, Tetrahedron Lett. *1975*, in press.

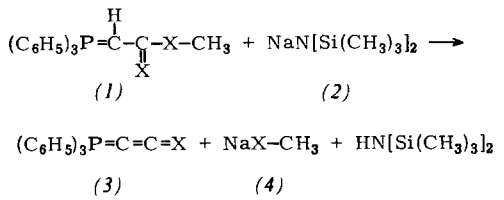
[9] *H. Prinzbach, R. Keller*, and *R. Schwesinger*, Angew. Chem. *87*, 627 (1975); Angew. Chem. internat. Edit. *14* 633 (1975); earlier literature cited therein.

Simple Synthesis of Ketenylidenetriphenylphosphorane and Its Thioanalogs

By *Hans Jürgen Bestmann* and *Dieter Sandmeier*[*]

We recently reported a novel method for the synthesis of imino- and thioketenylidene-triphenylphosphoranes *(3)*, X=N—R and X=S, from 3 moles methylidenetriphenylphosphorane and 1 mole isocyanide or thiophosgene, respectively[1]. The analogous reaction with phosgene, affords only low yields of the expected ketenylidenetriphenylphosphorane *(3)*, X=O.

We have now found a particularly simple synthesis for *(3)*, X=O, namely reaction of the methoxycarbonylmethylenetriphenylphosphorane *(1)*, X=O, with the sodium salt of hexamethyldisilazane *(2)*.



The sodium methoxide *(4)* (X=O) formed on reaction of *(1)* (X=O) with *(2)*, *e.g.* in benzene, precipitates out and after its separation by filtration or centrifugation compound *(3)* (X=O) can be recovered by concentration of the filtrate and precipitation with ether or petroleum ether [yield 80%; m.p. 171—172 °C[2]; ^{31}P-NMR; δ = −5.37 ppm[3]; IR: 2080 cm^{-1} (C=C=O)].

Analogous reaction of the methylthio(thiocarbonyl)methylenetriphenylphosphorane *(1)*, X=S[4], and *(2)* affords the sodium mercaptide *(4)*. X=S, and the thioketenylidenetriphenylphosphorane *(3)*, X=S [yield 76%; m.p. 220—222 °C[5]; ^{31}P-NMR: δ = +8.11 ppm[3], IR: 1950, 2110 cm^{-1} (C=C=S)].

Received: March 24, 1975 [Z 210 IE]
German version: Angew. Chem. *87*, 630 (1975)

CAS Registry numbers:
(1) (X=O), 2605-67-6; *(1)* (X=S), 54985-87-4; *(2)*, 1070-89-9; *(3)* (X=O), 15596-07-3; *(3)* (X=S), 17507-47-0

[1] *H. J. Bestmann* and *G. Schmid*, Angew. Chem. *86*, 479 (1974); Angew. Chem. internat. Edit. *13*, 473 (1974).

[2] *C. N. Matthews* and *G. H. Birum*, Tetrahedron Lett. *1966*, 707: m.p. = 172—173.5 °C.

[3] 100-MHz PFT spectrum. H_3PO_4 as external standard. In footnote [4] of our communication in Angew. Chem. *87*, 35 (1975), Angew. Chem. internat. Edit. *14*, 53 (1975) the external standard should also read H_3PO_4.

[4] *H. J. Bestmann, R. Engler*, and *H. Hartung*, Angew. Chem. *78*, 1100 (1966); Angew. Chem. internat. Edit. *5*, 1040 (1966).

[5] M.p. = 224—226 °C [2].

Mechanism of Electrochemical Pinacolization. The First Asymmetric Synthesis in a Chiral Medium[**]

By *Dieter Seebach* and *Hok An Oei*[*]

Electrochemical reduction of ketones such as acetophenone *(1)* can lead to formation of the alcohol *(3)* and pinacols *(5)*[1]. It is assumed that the alcohol is formed by transfer of two electrons and two protons *in the cathodic double layer*, whereas the pinacols are formed *in the solution* from ketyl *(2)* which escapes from the electrode in the form of radicals *(4)* (depending upon the pH of the solution R is H or the cation of the electrolyte). This mechanism is supported, *inter alia*, by the fact that, a) the ratio of *meso* to *d,l* form in the isolated mixture of pinacols *(5)* is independent of the

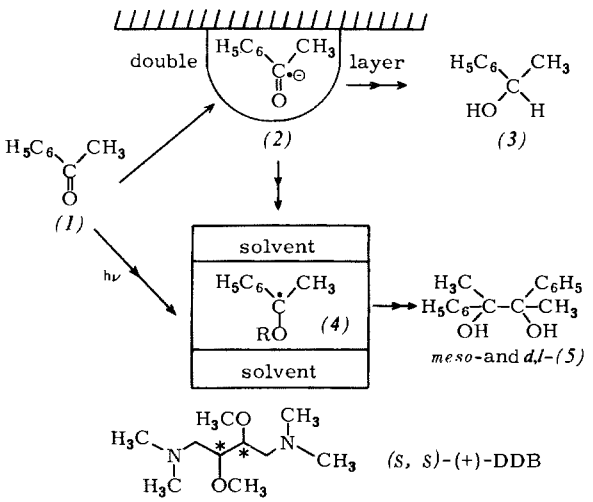
[*] Prof. Dr. H. J. Bestmann [+] and Dipl.-Chem. D. Sandmeier
Institut für Organische Chemie der Universität Erlangen-Nürnberg
852 Erlangen, Henkestr. 42 (Germany)

[+] Author to whom all correspondence should be addressed.

[*] Prof. Dr. D. Seebach and Dipl.-Chem. H.-A. Oei
Institut für Organische Chemie des Fachbereichs 14 der Universität
63 Giessen, Ludwigstrasse 21 (Germany)

[**] We thank Prof. Dr. *D. H. Evans* (University of Wisconsin, Madison, USA) and Dr. *F. Beck* (BASF, Ludwigshafen, Germany) for their help in constructing the electrolysis apparatus. This work was supported by the Deutsche Forschungsgemeinschaft (Projekt Se 158/5), the Fonds der Chemischen Industrie, and the Benkeser Company (Germany).

electrode material[2] and, b) on using a chiral supporting electrolyte optically active *(3)* is formed in the "chiral" double



and of $LiOCH_3$ (Nos. 6 and 7) that is known to be formed at the cathode during electrolysis in methanol actually leads to the optically active pinacol *(5)*. Table 1 shows that this was indeed the case. Electrolysis[6] gave, within the limits of reproducibility, the identical pinacol mixture[7]. No change in this result was observed on variation of the current density by a factor of about 15 (Table 1, Nos. 8—10), while a decrease in DDB content on photolysis, as on electrolysis, is accompanied by the same decrease in the optical yield (cf. No. 6/7 with No. 9/11). A control experiment in which acetone was electrochemically reduced in the presence of inactive acetophenone-pinacol *(5)* regenerated inactive *(5)* with unaltered *meso/d,l* ratio.

The experiments described here are not only a further, stronger indication for the formation of pinacols in the electrochemical reduction of arylalkyl ketones *in the solution*, but, to our knowledge, constitute the first asymmetric electrodimerization in a chiral medium with achiral supporting electrolyte[8].

Received: May 20, 1975 [Z 248 IE]
German version: Angew. Chem. 87, 629 (1975)

Table 1. Formation of 2,3-diphenyl-2,3-butanediol (acetophenone pinacol) *(5)* by photolysis and by electrolysis of acetophenone *(1)* (2g) in (*S,S*)-(+)-DDB-containing medium [4]. (*R,R*)-(+)-*(5)* is formed in excess in each case. Double values denote parallel experiments.

No.	Solvent and salt [g]	*T* [°C]	*(5)* Yield [%] Chem. [a]	Opt. [b]	*meso*/*d,l*
	Photolysis				
1	DDB	25	52	8.3	1.04
	(25)	27	57	8.1	1.14
2	DDB/pentane (40/200)	−72	41	23.5	1.10
3	DDB/CH_3OH	29	44	2.9	0.85
	(25/10)	27	42	3.0	0.93
4	DDB/CH_3OH/LiBr	25	52	3.3	0.50
	(25/10/5)	27	27	3.7	0.55
5	DDB/CH_3OH/LiBr (10/25/5)	29	34	0.2	0.58
6	DDB/CH_3OH/LiBr/$LiOCH_3$	26	24	4.7	0.38
	(25/10/4.3/0.26)	27	31	5.9	0.33
7	DDB/CH_3OH/LiBr/$LiOCH_3$ (10/25/4.3/0.26)	29	29	0.2	0.25
	Electrolysis				
8	DDB/CH_3OH/LiBr	31	91	4.8	0.36
(60 mA)	(25/10/5)	33	88	4.8	0.35
9	DDB/CH_3OH/LiBr	29	84	6.3	0.36
(20 mA)	(25/10/5)	26	93	5.6	0.35
10	DDB/CH_3OH/LiBr	26	97	5.8	0.33
(4 mA)	(25/10/5)	24	95	6.4	0.37
11	DDB/CH_3OH/LiBr				
(20 mA)	(10/25/5)	25	90	0.2	0.26

[a] *meso-* + *d,l*-form.
[b] Referred to *d,l* fraction.

layer that is rich in supporting electrolyte (optical yield up to 8%), whereas *(5)* is isolated[3] in inactive form.

We were able to show some time ago that hydroxy radicals *(4)*, R = H, generated photochemically from acetophenone *(1)* dimerize in the chiral amino-ether DDB to pinacol *(5)*, the *d,l* fraction of which exhibits up to 23% optical activity[4] (Table 1, Nos. 1 and 2). The above theory of electrochemical pinacol formation can therefore be subjected to the following stringent test: electrolysis and photolysis performed under identical conditions must afford the pinacols with the *same* *meso/d,l* ratio, with the *same* optical yields in the *d,l* fraction, and with enrichment of the *same* enantiomer. In the photolysis experiment[5] we first tested whether addition of protic solvent (Table 1, No. 3), of supporting electrolyte (Nos. 4 and 5),

CAS Registry numbers:
(1), 98-86-2; *meso-(5)*, 4217-65-6; *d,l-(5)*, 22985-90-6; (*R,R*)-(+)-*(5)*, 33603-65-5; (*S,S*)-(+)-DDB, 26549-21-3

[1] See *F. Beck:* Elektroorganische Chemie. Verlag Chemie, Weinheim 1974, and literature cited therein.
[2] *J. H. Stocker* and *J. R. H. Jennevein*, J. Org. Chem. *33*, 294, 2145 (1968).
[3] *L. Horner* and *D. Degner*, Tetrahedron Lett. *1968*, 5889; *L. Horner*, Chem. Ing. Tech. *44*, 209 (1972); cf. also *R. N. Gourley, J. Grimshaw*, and *P. G. Millar*, J. Chem. Soc. *C 1970*, 2318.
[4] *D. Seebach* and *H. Daum*, J. Amer. Chem. Soc. *93*, 2795 (1971); *D. Seebach, H. Dörr, B. Bastani*, and *V. Ehrig*, Angew. Chem. *81*, 1002 (1969); Angew. Chem. internat. Edit. *8*, 982 (1969); *H.-A. Oei*, unpublished results, Giessen 1973—1975.
[5] Conditions: Pyrex ampoules containing acetophenone solutions are immersed together with a water-cooled Hanovia-679/A/36 medium-pressure mercury vapor lamp in a cooling bath; reaction TLC-monitored;

and H_2O; finally, chromatography (silica gel, benzene/10% ethyl acetate) without separation of *meso*- and *d,l-(5)*; determination of *meso/d,l* ratio by NMR spectroscopy [*J. H. Stocker*, J. Am. Chem. Soc. *88*, 2878 (1966)].

[6] Conditions: magnetically stirred 15-ml-Hg cathode having an effective surface area of 10 cm^2, 40 ml total volume of solution in the cathode space, 0.5 cm^2 platinum leaf anode, 5 ml anode solution, 1 cm diameter G-3 frit diaphragm, Philips controller PE1527, constant current density of 4–60 mA, 6–80 volt potential, N_2 atmosphere.

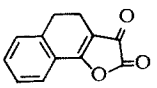
[7] According to NMR analysis of the crude products in the photolyses and electrolyses described here, the alcohol *(3)* is formed in less than 5% yield.

[8] Electroreduction of phenylglyoxylic acid in the presence of alkaloids see: *M. Jubault, E. Raoult*, and *D. Peltier*, Electrochim. Acta *19*, 865 (1974).

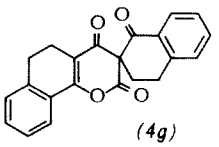
Synthesis and Thermal Decarbonylation of 2,3-Furandiones[1]

By *Shinji Murai, Kiichi Hasegawa*, and *Noboru Sonoda*[*]

We wish to report the first general method for the synthesis of 2,3-furandiones *(2)*, topological isomers of maleic anhydride, and their subsequent thermal decomposition *via* α-oxoketenes *(3)* to 3*H*-pyran-2,4-diones *(4)* (Table 1). Hitherto only three compounds of type *(2)* have been known[2].

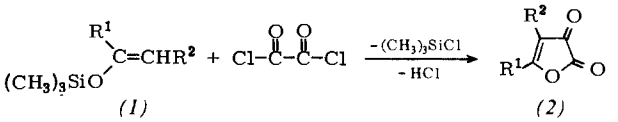


(2g)



(4g)

Addition of oxalyl chloride to a solution of alkenyloxysilanes



(1) *(2)*

(1)[3] in dry ether at room temperature gave *(2)* in good yields. Furandiones *(2)* are all yellow in color having $UV_{max}^{CH_3CN}$ at 354—392 nm (ε = 10000—19000). Three intense IR absorption bands, 1832—1815, 1743—1713, and 1613—1588 cm^{-1}, have been observed. The highest frequency band can reasonably be attributed to the lactone carbonyl of *(2)*. The latter two bands would be those of enone moieties. Interestingly, mass spectra of all of 2,3-furandiones showed a base peak at $m/e = [M-28]^+$ indicating predominant loss of carbon monoxide from molecular ions.

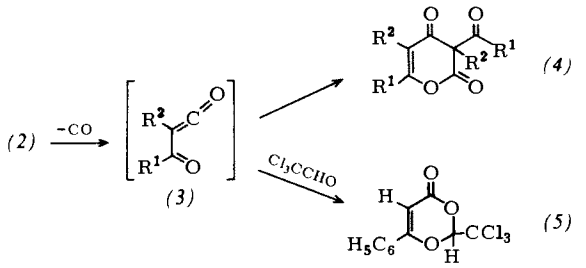
The facile loss of carbon monoxide has also been shown by thermal decomposition of *(2)*. Smooth evolution of carbon monoxide was observed and pyrandiones *(4)* were obtained in high yields when *(2)* were heated without solvent at their respective melting points for 30 minutes. IR data (Table 1) show that the compounds *(4)* which have $R^2 = H$ are virtually completely enolized and have 4-hydroxy-2-pyrone structures. Cheletropic fragmentation of *(2)* gives in addition to carbon monoxide, an α-oxoketene *(3)*, which then undergoes [4π + 2π] cyclodimerization to afford the pyrandiones *(4)*. Such an intermediate from *(2a)* has been trapped by chloral as 1,3-dioxin-4-one *(5)*[5,6].

Table 1. Yield and physical properties of the furandiones *(2a)*—*(2g)* and pyrandiones *(4a)*—*(4g)*.

			(2)		*(4)*		
	R^1	R^2	M.p. [°C] [a] B.p. [°C/torr]	Yield [%] [b]	M.p. [°C] [a]	IR (nujol) [cm^{-1}]	Yield [%]
a	C_6H_5	H	130—132 [c]	85	167.5—168 [d]	1742 [4] 1625 1545	95
b	*p*-$CH_3C_6H_4$	H	130—131 [c]	80	199—200	1739 1620 1541	90
c	*p*-$CH_3OC_6H_4$	H	133—134 [c]	78	194—195	1740 1621 1541	88
d	*p*-BrC_6H_4	H	145—146 [c]	83	268—269	1745 1624 1538	86
e	C_6H_5	CH_3	107.5—109.5	64	130—131	1760 1702 1674 1623	83
f	$C(CH_3)_3$	H	50.5—52 73—75/2	32	95—96	1768 1650 1555	83
g	see above		118—119.5 [c]	76	108—109	1772 1678 1657 1630	84

[a] Purification: *(2a)* by sublimation at 100 °C/0.2 torr; *(2b)*—*(2d)* and *(2g)* by recrystallization from acetonitrile; *(2e)*, *(4a)* and *(4g)* by recrystallization from benzene/hexane, *(2f)* by distillation, *(4b)*—*(4f)* by recrystallization from methanol. Recrystallization of compounds *(2)* should be carried out very quickly.
[b] Based on oxalyl chloride used.
[c] Decomposition at melting point.
[d] Lit. M.p. 171 °C [4].

[*] Dr. S. Murai, K. Hasegawa, and Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)



5-Phenyl-2,3-furandione (2a)

To a stirred solution of α-trimethylsiloxystyrene *(1a)*[3] (9.6 g, 50 mmol) in 50 ml of anhydrous ether was added oxalyl chloride (3.2 g, 25 mmol) over a period of one hour at 25 °C. After 5 h, the mixture containing a yellow precipitate was concentrated *in vacuo* to leave a yellow solid which was washed with dry ether to give *(2a)*; yield 3.7 g (85 %).—For furandiones which are soluble in ether, the concentrated reaction mixture was washed with hexane [in the case of *(2e)*] or directly distilled [in the case of *(2f)*]. Procedures for purification of *(2)* are given in footnote [a] of Table 1.

3-Benzoyl-6-phenyl-3H-pyran-2,4-dione (4a)

Compound *(2a)* (500 mg) was heated (no solvent) at 120 °C for 2 h under reduced pressure (30 torr). The resulting solid was washed successively with hexane and methanol to give *(4a)*; yield 400 mg (93 %).

6-Phenyl-2-trichloromethyl-1,3-dioxin-4-one (5)

A suspension of *(2a)* (1.04 g, 6 mmol, partially soluble) in 10 ml of xylene was added very slowly (over 5 h) to a solution of chloral (2.76 g, 18 mmol) in xylene (10 ml) at 80 °C. Evaporation of the solvent gave a solid which was washed with ether to leave a colorless compound *(5)*; yield 1.25 g (71%), m.p. 196.5 °C (decomp.); IR (nujol): 1714 and 1613 cm^{-1}.

Received: April 2, 1975 [Z 251 IE]
revised: May 13, 1975
German version: Angew. Chem. 87, 668 (1975)

CAS Registry numbers:
(1a), 13735-81-4; *(1b)*, 54731-27-0; *(1c)*, 55991-65-6; *(1d)*, 55991-66-7; *(1e)*, 37471-46-8; *(1f)*, 17510-46-2; *(1g)*, 38858-72-9; *(2a)*, 55991-67-8; *(2b)*, 55991-68-9; *(2c)*, 55991-69-0; *(2d)*, 55991-70-3; *(2e)*, 55991-71-4; *(2f)*, 55991-72-5; *(2g)*, 55991-73-6; *(4a)*, 602-98-2; *(4b)* 55991-74-7; *(4c)*, 55991-75-8; *(4d)*, 55991-76-9; *(4e)*, 55991-77-0; *(4f)*, 55991-78-1; *(4g)*, 55991-79-2; *(5)*, 55991-80-5; oxalyl chloride, 7937-8

[1] Synthesis *via* Silyl Alkenyl Ethers, Part VIII.—Part VII: *K. Mizuno, H. Okamoto, C. Pac, H. Sakurai, S. Murai,* and *N. Sonoda,* Chem. Lett. *1975*, 237.

[2] a) *W. J. Horton, C. E. Hummel,* and *H. W. Johnson,* J. Amer. Chem. Soc. 75, 944 (1953); b) *K. Heusler, J. Kebrle, G. Meystre, H. Ueberwasser, P. Wieland, G. Anner,* and *A. Wettstein,* Helv. Chim. Acta *42*, 2043 (1959); c) *E. Ziegler, G. Kollenz,* and *H. Igel,* Monatsh. Chem. *102*, 1769 (1971); d) *E. Ziegler, G. Kollenz,* and *W. Ott,* Synthesis *1973*, 679; e) *G. Kollenz, E. Ziegler,* and *W. Ott,* Org. Prep. Proced. Int. *5*, 261 (1973).

[3] *H. O. House, L. J. Czuba, M. Gall,* and *H. D. Olmstead,* J. Org. Chem. *34*, 2342 (1969).

[4] *K. Balenovic,* Rec. Trav. Chim. Pays-Bas 67, 282 (1948).

[5] Chloral has been used as an efficient reagent to trap α-oxoketenes: a) *H. Stetter* and *K. Kiehs,* Chem. Ber. *98*, 1181, 2099 (1965); b) *G. Jäger, ibid. 105*, 137 (1972).

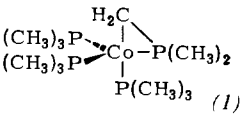
[6] *Ziegler* has reported recently an α-oxoketene generated by thermal decomposition of 4-benzoyl-5-phenyl-2,3-furandione [2d, 2e].

The Dimethylphosphinomethanide Ion, $(CH_3)_2PCH_2^{\ominus}$: A Novel Ligand for Transition Metals

By *H. H. Karsch, H.-F. Klein,* and *Hubert Schmidbaur*[*]

Phosphorus ylides of the type $(CH_3)_3PCH_2$ and $(CH_3)_2P(CH_2)_2^{\ominus}$ represent novel ligand systems which form unusually stable metal-carbon σ-bonds[1]. It now turns out that complexes with the dimethylphosphinomethanide ligand $(CH_3)_2PCH_2^{\ominus}$ can also be obtained from metal halides and phosphorus ylides.

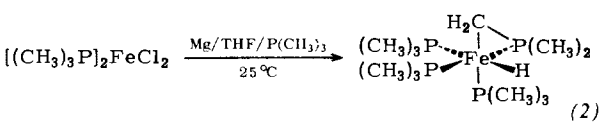
Thus, reaction of $[(CH_3)_3P]_3CoCl$[2, 3] with $(CH_3)_3PCH_2$[4] leads to the formation of the dark red compound *(1)* along with a series of by-products[5]. *(1)* is extremely sensitive to



(1)

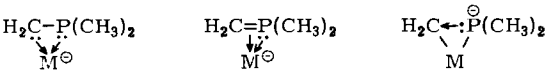
air, sublimable in a vacuum at 80 °C/0.1 torr, and is readily soluble in nonpolar solvents such as benzene and pentane (dec. temp. *ca.* 85 °C). From the ^{1}H-NMR spectrum (selective decoupling), which remains unaltered down to −80 °C, as from the ^{31}P-NMR spectrum, a fluctional structure can be concluded in which an assignment of the three phosphane ligands to definite positions is—in contrast to the case of $CH_3Co[P(CH_3)_3]_4$[3]—not possible[6].

In the search for further examples of this structural type we found that trimethylphosphane itself undergoes oxidative addition with C—H cleavage in the presence of coordinatively unsaturated, but electron-rich metal atoms. Thus in the case of iron, for example, a complex $[(CH_3)_3P]_5Fe$ analogous to the known $[(CH_3O)_3P]_5Fe$[7] could not be obtained for steric reasons; the reduction method leads only to a product having the *empirical* formula $[(CH_3)_3P]_4Fe$, to which the structure *(2)* was ascribed (yield 95%): The IR spectrum of *(2)* shows,



(2)

similarly to that of $[(CH_3)_3P]_4FeH_2$[8], an intense broad band at 1835 cm^{-1}, which is assigned to the ν(FeH) vibration; the rest of the spectrum resembles that of *(1)*. The remaining structural units of the orange-yellow solid, which, like *(1)* is sublimable at 70 °C/0.1 torr (dec. temp. 80 °C), could be established from the NMR spectra. The solutions in benzene, toluene, as well as other solvents tend to undergo decomposition[9]. It would appear that the bonding in *(1)* and *(2)* is best explained by the following resonance formulas:



In fact the reactions of *(2)* conform to an equilibrium of the type

$$[(CH_3)_3P]_3(H)[CH_2P(CH_3)_2]Fe \rightleftharpoons [(CH_3)_3P]_4Fe$$

(the isomer could not be detected spectroscopially). The catalytic activity of this system is at present under investigation.

[*] Prof. Dr. H. Schmidbaur, Dr. H. H. Karsch, and Univ.-Doz. Dr. H.-F. Klein
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

In its reactions *(1)* shows the expected polarization $\overset{\delta+}{Co}—\overset{\delta-}{C}$:

(1) + $[(CH_3)_3PH]Cl \longrightarrow [(CH_3)_3P]_3CoCl + 2\ (CH_3)_3P$

In the meantime, complex *(2)* has also been prepared by another research group[10]. The observations made by this other group led to the same structural propositions[11].

Received: April 28, 1975 [Z 257 IE]
German version: Angew. Chem. *87*, 630 (1975)

CAS Registry numbers:
(1), 55853-14-0; *(2)*, 55853-15-1; $[(CH_3)_3P]_3CoCl$, 26305-75-9; $(CH_3)_3PCH_2$, 14580-91-7; $[(CH_3)_3P]_2FeCl_2$, 55853-16-2; $(CH_3)_3P$, 594-09-2; $[(CH_3)_3PH]Cl$, 55903-13-4.

[1] *H. Schmidbaur*, Acc. Chem. Res. *8*, 62 (1975).
[2] *H. H. Karsch* and *H.-F. Klein*, Inorg. Chem. *14*, 473 (1975).
[3] *H. H. Karsch* and *H.-F. Klein*, Chem. Ber. *108*, 944 (1975).
[4] *H. Schmidbaur* and *W. Tronich*, Chem. Ber. *101*, 595 (1968).
[5] *H. H. Karsch*, *H.-F. Klein*, *C. G. Kreiter*, and *H. Schmidbaur*, Chem. Ber. *107*, 3692 (1974); *H. H. Karsch*, Dissertation, Universität Würzburg 1974.
[6] ^{1}H-NMR (benzene, 30 °C, TMS int.): $\delta CH_3P_A = 1.31$ ppm, d, $^2J(P_AH) = 9.6$ Hz; $\delta CH_3P_B = 1.16$, virtual t, $A_nXX'A'_n$, $N = 4.5$ $\delta CH_2 = -0.54$, dq, $^2J(P_AH) = 1.8$, $^3J(P_BH) = 9.2$. ^{31}P-NMR (toluene, −80 °C, H_3PO_4 ext.): $\delta P_A = +30$, q; $\delta P_B = -12.2$, d; $^2J(P_AP_B) = 13$; $\{^1H\}$.
[7] *E. L. Muetterties* and *J. W. Rathke*, J. C. S. Chem. Comm. *1974*, 850.
[8] *H.-F. Klein*, Angew. Chem. *82*, 885 (1970); Angew. Chem. internat. Edit. *9*, 903 (1970).
[9] ^{1}H-NMR (toluene, −30 °C, TMS int.): $\delta CH_3P_{A-D} = 1.27$, m superposition of signals, 33 H. $\delta CH_2 = -1.03$, m, 2H. $\delta FeH = -14.7$, ddt. $^2_{cis}J(P_{A,D}H) = 63.2$; $^2_{cis}J(P_BH) = 75.4$; $^2_{trans}J(P_CH) = 27.0$. (Selective $\{^{31}P\}$ yields ad and aq structure, respectively.) ^{31}P-NMR (toluene, −40 °C, H_3PO_4 ext.): $\delta P_A = -27.6$, dt (br), $^2_{cis}J(P_{B,C}P_A) = 40$; $^2_{trans}J(P_DP_A) = 11$. $\delta P_B = -20.0$, q, $^2_{cis}J(P_{A,C,D}P_B) = 32$. $\delta P_C = +19$, q; $^2_{cis}J(P_{A,B,D}P_C) = 36$. $\delta P_D = -33.4$, td (br); $^2_{cis}J(P_{B,C}P_D) = 33.6$; $^2_{trans}J(P_DP_A) = 11$.
[10] *E. L. Muetterties*, personal communication.
[11] During these investigations X-ray proof has been obtained for formation of an M—P—C three-membered ring of the kind considered in this communication (M = Pt): *N. Bresciani*, *M. Calligaris*, *P. Delise*, *G. Nardin*, and *L. Randaccio*, J. Am. Chem. Soc. *96*, 5642 (1974).

Selenium-Catalyzed Formation of Sulfate and Sulfur from Sulfite[**]

By *Max Schmidt* and *Heinz-Peter Kopp*[*]

Despite numerous laboratory experiments and a considerable amount of expense and effort in pilot- and full-scale plants the present state of affairs regarding the desulfurization of flue gases—particularly in coal-fired power plant—is still far from satisfactory[2]. Apart from the "non-regenerative" processes, in which solid alkaline earth oxides or (more often) aqueous slurries of the corresponding hydroxides are employed and "solve" the problem of SO_2-containing gas, only by introducing the new problem of enormous volumes of solid or sludge wastes, interest is at present strongly focused on a "product producing" process, whose variants have become known as the "Wellman-Lord" process. In principle the sulfur dioxide is "washed out" of the flue gas by alkaline alkali-metal sulfite solutions in accordance with Eq. (1) at the lowest possible temperature; it is then recovered at the highest possible temperature from the resulting hydrogen sulfite solution with regeneration of "washing liquor" (and, ideally, converted into elemental sulfur). This process has one great industrial and economic disadvantage: the large quantities of sulfur(IV) compounds introduced into the system partially change their oxidation state, which necessitates not only continual addition of bases, but also causes considerable effluent problems (disposal of unusable washing liquor) and drainage problems (stoppages due to deposition of salts and sulfur). The very complicated disproportionation reactions of sulfite to thermodynamically more stable products have various causes. We have studied one of these in detail.

$$SO_3^{2-} + SO_2 + H_2O \underset{\Delta}{\rightleftharpoons} 2HSO_3^- \rightleftharpoons S_2O_3^{2-} + H_2O \quad (1)$$

It was already known as long ago as 1888[3] that elementary selenium promotes disproportionation of sulfite under weakly acidic conditions. Although this phenomena was later the subject of many investigations (final "conclusions" were reached as long ago as 1929, although they are no longer tenable)[4], strangely enough it was not taken into consideration in the development of the Wellman-Lord process.

Selenium, which is present along with metal sulfides in coal, is usually carried over in the flue gas and extracted into the washing liquor, where it concentrates. Its effect on the course of desulfurization and naturally also from an economic aspect, can be prohibitive. Operators are therefore urgently warned not to install such plants if the fuel contains traces of selenium.

One experiment, typical of a whole series of investigations carried out on this problem, will now be outlined and explained with the aid of, partly simplified, summation equations [(2) to (8)].

A solution of $K_2S_2O_5$ (45 g) in oxygen-free water (200 ml) is treated with elemental selenium (with amounts of selenium between 50 mg and 8 g reaction takes place immediately; the intensity of the intermediary colors depends markedly on the amount of selenium). The mixture, whose pH is controlled continuously, is heated to boiling under reflux. Between 20 °C and 100 °C the pH increases within *ca.* 60 min from 3.90 to a maximum of 5.05 (liberation of SO_2) with concomitant increase in concentration of SO_3^{2-} ions. This leads to dissolution of the elemental selenium in a series of redox equilibria according to the summation equation

$$SO_3^{2-} + Se_x \rightleftharpoons Se_xSO_3^{2-} \quad (2)$$

The previously undescribed green selenanemonosulfonic acids corresponding to the sulfanemonosulfonic acids are thereby formed[5]. Selenopolythionates such as $SeS_2O_6^{2-}$ (recognized by a gradual change in color from green to yellow) are formed in a series of complicated equilibrium reactions. This is accompanied by a drop in pH, *e.g.* according to[6]

$$2\,SeS_2O_6^{2-} + H_2O \rightarrow Se_2S_2O_6^{2-} + HSO_3^- + SO_4^{2-} + H^+ \quad (3)$$

The shift to the right in the equilibria summarized in Eq. (2) consumes sulfite more rapidly than it is formed in the equilibrium according to Eq. (3) or to

$$x\,SeSO_3^{2-} + x\,H^+ \rightarrow Se_x + x\,HSO_3^- \quad (4)$$

Finally, with continuously decreasing pH, all the selenium goes into solution, essentially in the form of selenopolythionates. The reaction

$$Se_2S_2O_6^{2-} + SO_3^{2-} \rightarrow SeSO_3^{2-} + SeS_2O_6^{2-} \quad (5)$$

can only play a role until no more sulfite is formed in accordance with Eq. (3) or (4). The pH thus decreases in *ca.* 2 h to 3.70. The reaction mixture now changes drastically within 1—2 min; it becomes colorless, froths (development of SO_2

[*] Prof. Dr. M. Schmidt and Dr. H.-P. Kopp
Institut für Anorganische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

[**] Chemistry of Flue Gas Desulfurization, Part 2.—Part 1: see Ref. [1].

and H_2S) and first selenium and then sulfur are precipitated in elemental form. The pH decreases to 3.15 (100 °C) and 2.05 (20 °C). On cooling, considerable amounts of $KHSO_4$ and K_2SO_4 also precipitate out. This second reaction step can be explained in terms of a number of rapid reactions.

Obviously in the pH range quoted selenotrithionate is no longer stable and decomposes to sulfite, sulfur dioxide and selenium, in agreement with the older literature. In a series of concurrent reactions the selenium reacts with excess sulfite—*via* the extremely short-lived intermediary selenosulfate ion—according to

$$SeSO_3^{2-} + SO_3^{2-} \rightarrow SeO_3^{2-} + S_2O_3^{2-} \quad (6)$$
$$HSeO_3^- + 3HSO_3^- \rightarrow SeS_2O_6^{2-} + SO_4^{2-} + 2H_2O \quad (7)$$

to give thiosulfate and selenotrithionate, whereby the latter immediately decomposes at this pH. These reactions proceed rapidly until transformation of disulfite is complete. The marked frothing due to evolution of SO_2 during decomposition of selenotrithionate provides supporting evidence for the above mentioned reaction scheme. A smaller increase in pH value of about 0.05—0.10 units at this stage can be explained in terms of secondary reactions of the SO_2-saturated solution. Furthermore, it can be shown by taking samples during the reaction that thiosulfate is present in the solution only within a small pH range of 3.68 ± 0.05. It is also clear why selenium separates out first and then sulfur. With decreasing sulfite concentration the selenium is no longer dissolved and precipitates out. Complete consumption of sulfite ions leads the reaction into a pH range where the thiosulfate is also unstable. It decomposes, partly with formation of hydrogen sulfide and sulfate ions and partly *via* further redox reactions in the usual way into sulfur and sulfite, which gives up sulfur dioxide under acid conditions. The major products of the selenium catalyzed conversion of disulfite are therefore elemental sulfur and sulfate. The low pH at the end of the reaction prevents formation of sulfite and thiosulfate. Relatively small amounts of tetrathionate and dithionate, which are formed in secondary reactions, are stable under such conditions.

The selenium employed can be recovered in elemental form in almost 100% yield. Approximately 80% of the sulfur employed (as $K_2S_2O_5$) disproportionates according to

$$H_2O + 3S_2O_3^{2-} \xrightarrow{Se} 2/xS_x + 4SO_4^{2-} + 2H^+ \quad (8)$$

The remainder escapes as gaseous SO_2 and H_2S or is present as $S_2O_6^{2-}$ and $S_4O_6^{2-}$ in the "spent washing liquor". (The reactions described above start at concentrations of *ca.* 8 g $K_2S_2O_5$/200 ml water, though this is almost always widely overstepped in practice.)

Hence, in the designing of flue gas desulfurization plants care must be taken to ensure that as low a concentration as possible of sulfur(IV) compounds are introduced into the washing liquors used in the system.

Received: May 23, 1975 [Z 260 IE]
German version: Angew. Chem. 87, 631 (1975)

CAS Registry numbers:
$S_2O_3^{2-}$, 23134-05-6; Se, 7782-49-2; SO_2, 7446-09-5; SO_3^{2-}, 14265-45-3

[1] *M. Schmidt*, Int. J. Sulfur Chem. b7, 11 (1972).
[2] Cf. *e.g.* Proc. Flue Gas Desulfurization Symp. 1973, EPA-650/2-73-038 (1154 pages); Systemanalyse Entschwefelungsverfahren (work carried out under contract with the German Federal Government) VGB-Techn. Ver. Grosskraftwerksbetreiber e. V. Essen, Nov. 1974 (1018 pages).
[3] *H. Debus*, Liebigs Ann. Chem. *244*, 76 (1888).
[4] *F. Forster* and *E. Haufe*, Z. Anorg. Allg. Chem. *177*, 17 (1929).
[5] *M. Schmidt*, Z. Anorg. Allg. Chem. *289*, 158 (1957).
[6] *V. Zelionkaite*, *J. Janitckis*, and *J. Suliakiene*, Khim. Khim. Tekhnol. *3*, 93 (1963); Chem. Abstr. *59*, 10787 (1963).

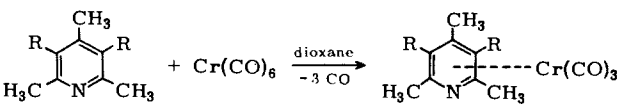
Tricarbonyl-(penta- and 2,4,6-tri-methylpyridine)chromium(0)—True Pyridine π-Complexes[1]

By *Hans-Gernot Biedermann*, *Karl Öfele*, *Nikolaus Schuhbauer*, and *Jakub Tajtelbaum*[*]

As early as 1973 *Timms* reported the synthesis of a π-pyridinetris(trifluorophosphane)chromium complex by cocondensation of chromium atoms, trifluorophosphane and pyridine[2]. No detailed account has yet been published about this product, which is formed in very small yield alongside the σ-bound species.

We have found, for the first time, that pyridine π-complexes can be prepared by treating pyridine derivatives with metal carbonyls without simultaneous formation of pyridine σ-complexes.

On reaction of pentamethylpyridine *(1)* or 2,4,6-trimethylpyridine *(2)* with $Cr(CO)_6$ in boiling dioxane we obtained, respectively, tricarbonyl(pentamethylpyridine)chromium(0) *(3)* and tricarbonyl-(2,4,6-trimethylpyridine)chromium(0) *(4)* as yellow compounds that are stable thermally and against air.



(1), R = CH_3 *(3)*, R = CH_3
(2), R = H *(4)*, R = H

Their composition and structure are proved by elemental analysis, osmometric molecular weight determination and spectroscopic investigations. The η^6-coordination of the pyridine ligands to the metal could be proved for *(3)* by X-ray structure analysis[3].

The IR spectra of the two complexes in *n*-hexane show three carbonyl bands of approximately equal intensity at 1972, 1908 and 1891 cm^{-1} in the case of *(3)* and at 1984, 1923 and 1910 cm^{-1} in the case of *(4)*, which is the typical picture for a symmetry-distorted $Cr(CO)_3$ group[4]. The strong bands $\nu_{C=C,C=N}$ of *(2)* at 1610 and 1570 cm^{-1} and for *(1)* at 1578 cm^{-1} have completely disappeared on complex formation; instead there appears a new, weak, broad band at 1630 cm^{-1} for both complexes. In the ^{1}H-NMR spectrum the complexes *(3)* and *(4)* in C_6D_6, compared with the free ligands, show the upfield shift of the methyl and ring-proton signals—the latter are shifted from 6.63 to 4.25 ppm—that is characteristic of π-bonded aromatic compounds. In the mass spectra of *(3)* and *(4)* the fragments produced by successive loss of CO can be recognized alongside the molecular, ligand and chromium ions.

Experimental:

Since pentamethylpyridine prepared by the method of *Karrer et al.*[5] (hydrogenation catalyst described by *Busch et al.*[6]) occurs mainly as semihydrate, an ethereal solution of the product was treated with small portions of $LiAlH_4$ until no further gas evolution was observable. After filtration, the solvent was evaporated and the residue fractionated.—2,4,6-Trimethylpyridine was dried over BaO and distilled.

For preparation of the complexes *(3)* and *(4)*, with protection by N_2 and with use of dried N_2-saturated solvent, we used a small flask with a Liebig condenser in which was

[*] Priv.-Doz. Dr. H.-G. Biedermann, Dr. K. Öfele, N. Schuhbauer, and Dipl.-Chem. J. Tajtelbaum
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

solution the $Cr(CO)_6$ that sublimes during the reaction. In this way 1.4 g (6.4 mmol) of sublimed $Cr(CO)_6$ and 1.8 g (12.1 mmol) of *(1)* in 10 ml of dioxane were heated for about 36 h at the b. p. The unconsumed $Cr(CO)_6$ was then removed from the cooled yellowish-brown solution by filtration, the dioxane was evaporated at *ca.* 40 °C and the oily residue was covered with pentane, whereupon a yellow crystalline precipitate of *(3)* was formed. This was collected on a frit, washed with pentane and sublimed in a high vacuum at *ca.* 75—80 °C. M.p. 112 °C (dec.); yield *ca.* 30%. The 2,4,6-trimethylpyridine complex *(4)* was prepared analogously. M.p. 122 °C (dec.); yield *ca.* 20%.

Received: May 23, 1975 [Z 261 IE]
German version: Angew. Chem. 87, 634 (1975)

CAS Registry numbers:
(3), 55853-25-3; *(4)*, 55853-04-8; $Cr(CO)_6$, 13007-92-6

[1] Transition-metal π-Complexes with Unsaturated and Aromatic Heterocycles, Part. 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Parts 1 and 2: *K. Öfele* and *E. Dotzauer*, J. Organometal. Chem. *42*, C87 (1972); *K. Öfele, A. Wurzinger*, and *W. Kalbfus, ibid. 69*, 279 (1974).

[2] *P. L. Timms*, 6th Int. Conf. Organometal. Chem., Massachusetts, Abstr. Pap. P8 (1973); Angew. Chem. *87*, 295 (1975); Angew. Chem. internat. Edit. *14*, 273 (1975).

[3] *G. Huttner* and *H. Lorenz*, unpublished work.

[4] *R. D. Fischer*, Dissertation, Universität München 1961.

[5] *P. Karrer* and *S. Mainoni*, Helv. Chim. Acta *34*, 2151 (1951).

[6] *M. Busch* and *H. Stöve*, Chem. Ber. *49*, 1063 (1916).

Reaction of Transition Metal Carbonyl Halides with $AgAsF_6$ in Liquid SO_2: A Key Reaction for the Preparation of Novel Complex Cations

By *Rüdiger Mews*[*]

We recently reported[1] the synthesis of $[Re(CO)_5NSF_3]^+AsF_6^-$ according to

$$Re(CO)_5Br + AgAsF_6 \xrightarrow{NSF_3} [Re(CO)_5NSF_3]^+AsF_6^- + AgBr$$

As intermediate of this reaction we postulated the coordinatively unsaturated cation $Re(CO)_5^+$, which functions as a Lewis acid and adds the base NSF_3.

We have now succeeded in preparing sulfur dioxide complexes *via* a similarly simple route

$$M(CO)_5Br + AgAsF_6 \xrightarrow{SO_2} [M(CO)_5SO_2]^+AsF_6^- + AgBr$$

(1a), M = Mn
(1b), M = Re

Compounds *(1)* have been characterized by their IR spectra and elemental analysis. The CO stretching vibrations are shifted to longer wavelengths because of the positive charge on the central atom. Compared with neutral complexes the same applies for the bands of the SO_2 ligands. On account of this positive charge the ligand is bound only by the donor action of a lone pair of electrons; it can be concluded from the position of the SO vibrations that there is hardly any back bonding. The SO bands of *(1)* appear in the same region as those of F_5Sb—OSO[2a]; however, cationic Ru—SO_2 complexes are already known whose SO bands also lie in this region. Hence, bonding of the SO_2 ligands *via* the sulfur is also probable in the case of *(1)*.

[*] Dr. R. Mews
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstrasse 4 (Germany)

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

temperature, the more stable *(1b)* at 40–50 °C:

$$(1) \underset{\text{liq. } SO_2}{\overset{HV}{\rightleftharpoons}} M(CO)_5F\cdot AsF_5 + SO_2$$

(2a), M = Mn
(2b), M = Re

The reaction is reversible. Compounds *(2)* dissolve quantitatively in liquid SO_2 with regeneration of *(1)*.

From the IR spectra it can be concluded that compounds *(2)* have a bridged $(CO)_5M\cdot F\cdot AsF_5$ structure (as is also present in $Re(CO)_5F\cdot ReF_5$[3]). The CO region contains the three bands to be expected for C_{4v} symmetry, the values for *(2a)* fitting neatly into the series $Mn(CO)_5X\cdot AlX_3$ (X = Cl, Br, I)[4].

Thus the adducts *(2)* are to be regarded as carbonyl fluorides. Only a few members of this class of compounds have previously been described, and they are more difficult to prepare than the above mentioned species. In the case of rhenium only $Re(CO)_5F\cdot ReF_5$[3] and $Re(CO)_5F$ can be regarded as confirmed[5], whereas manganese carbonyl fluorides were previously unknown.

Our investigations show that SO_2 is only weakly bound in *(1)*. When ligands D having more strongly pronounced donor properties are added to solutions of *(1)* the corresponding $[M(CO)_5D]^+$ salts can be isolated:

$$[M(CO)_5SO_2]^+AsF_6^- + D \rightarrow [M(CO)_5D]^+AsF_6^- + SO_2$$

We have so far prepared derivatives with D = NSF_3, N_4S_4, $PF_2N(CH_3)_2$, OH_2, CH_3OH, and $OC(CH_3)_2$ in this way[6]. Attempts are presently being made to extend the reaction to other ligands (the higher homologs As, Sb, Se, Te) and to other transition metals.

Experimental:

Equimolar amounts of $M(CO)_5Br$ and $AgAsF_6$ are stirred in SO_2 (about 10 mmol in 5 ml solution) for 20 h at room temperature. Precipitated AgBr is filtered off and solvent is removed from the filtrate by evaporation at normal pressure. The pure compounds *(1a)* (brownish yellow) and *(1b)* (pale yellow) remain behind. Whereas in the case of *(1a)* elemental analysis always gave an SO_2 content < 1 (the increase in weight during the synthesis however corresponded to the given formula), in the case of *(1b)* an exact analysis was obtained.

In dynamic vacuum *(1a)* loses SO_2 quantitatively within 36 h; quantitative loss of SO_2 from *(1b)* occurs within 20 h at 40–50 °C. Yellow *(2a)* (dec. above 107 °C) and colorless *(2b)* (dec. above 175 °C) are formed, respectively[7].

Received: May 26, 1975 [Z 262 IE]
German version: Angew. Chem. 87, 669 (1975)

CAS Registry numbers:
(1a), 55853-06-0; *(1b)*, 55853-08-2; *(2a)*, 55853-09-3; *(2b)*, 55853-10-6

[1] *R. Mews* and *O. Glemser*, Angew. Chem. *87*, 208 (1975); Angew. Chem. internat. Edit. *14*, 186 (1975).

[2] a) *J. W. Moore, H. W. Baird*, and *H. B. Miller*, J. Am. Chem. Soc. *90*, 1358 (1968); b) *L. H. Vogt Jr., L. Katz*, and *S. E. Wiberley*, Inorg. Chem. *4*, 1157 (1965).

[3] *D. M. Bruce, J. H. Holloway*, and *D. R. Russell*, J. C. S. Chem. Commun. *1973*, 321.

[4] *M. Pankowski, B. Demerseman, G. Bouquet*, and *M. Bigorgne*, J. Organometal. Chem. *35*, 155 (1972).

[5] *T. A. O'Donnell, K. A. Phillips*, and *A. B. Waugh*, Inorg. Chem. *12*, 1435 (1973).

[6] *C. S. Liu, R. Froböse, R. Mews*, and *O. Glemser*, to be published.

[7] IR spectra (Nujol mulls): *(1a)*, 2167 vw, 2061 vs, 2040 s (ν_{CO}); 1311/1305 s, 1119 cm^{-1} m (ν_{SO_2}).—*(1b)*, 2177 w, 2059 vs, 2025 s (ν_{CO}); 1313/1307 s, 1114 cm^{-1} m (ν_{SO_2}).—*(2a)*, 2167 vw, 2075 vs, 2040 s (ν_{CO}); 725 vs, 710 m, 676 cm^{-1} m (ν_{AsF}).—*(2b)*, 2175 vw, 2059 vs, 2019 s (ν_{CO}); 730 s, 712 m, 675 cm^{-1} m (ν_{AsF}).

Theoretical Investigation of Carbenium Ion Stabilization by Trifluoroacetic Acid

By *Joseph J. Dannenberg*[*]

Potential surfaces based on INDO molecular orbital calculations suggest that trifluoracetic acid can stabilize carbenium ions by means of interactions between the CF_3 group and the cation.

Numerous reports describing the unique behavior of trifluoroacetic acid (TFA) and related solvents as solvolytic agents have recently appeared. Such solvents tend to accelerate solvolyses without being very nucleophilic[1]. While solvolysis of cyclohexyl tosylate proceeds with inversion of configuration in acetic and formic acids, solvolysis in TFA does not[2]. Internal return is reported to be unusually facile in TFA[3]. The aryl-assisted pathways (k_Δ) are much more accelerated than the solvent-assisted pathways (k_s) for the solvolyses of species such as 1-methyl-2-phenylethyl tosylate[4]. The 1-methylpropyl cation is reported to be symmetrically hydrogen-bridged in TFA[5].

Much of the behavior mentioned above can be rationalized in terms of a TFA solvent molecule that is bidentate in its capacity to stabilize (solvate) carbenium ions, but has only one nucleophilic site. Thus TFA might stabilize a cation through interaction with either its $-CF_3$ or —COOH end; however, only the —COOH end can be nucleophilic[6].

To investigate this hypothesis, we have performed INDO molecular orbital calculations[7] on the approaches of a 1-methylethyl cation and both the $-CF_3$ and —COOH ends of TFA molecule. For comparison, similar calculations were performed where a molecule of acetic (AcOH) is substituted for TFA. The standard Pople molecular geometries[8] were used.

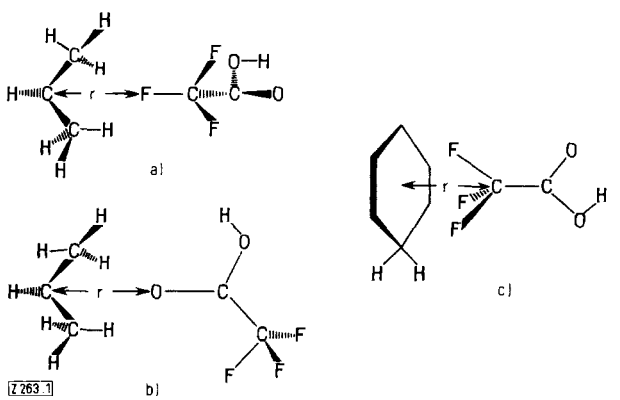


Fig. 1. Orientations of cation-solvent interactions. a) 1-Methylethyl cation and $-CF_3$ end of TFA (for interaction with AcOH, the fluorines are simply replaced by hydrogens); b) 1-methylethyl cation and —COOH end of TFA; c) benzenium ion and TFA. The C—C bond in TFA is colinear with the center of the ring. The benzenium ion is assumed to have the standard benzene geometry except at the protonated (C^1) site where the H—C^1—H angle is taken to be 109.47° and is bisected by the plane of the ring. r = distance.

The TFA (AcOH) was made to approach the cation so that either a C—F (C—H) or C=O bond was coaxial with the formally vacant p-orbital of the cationic site (Fig. 1a and 1b). As can be seen from Fig. 2a, the —COOH end of TFA stabilizes the cation more than the $-CF_3$ end at short distances (as expected for a nucleophilic interaction that leads to bond formation); at intermediate and long distances the converse is true. In the case of AcOH (Fig. 2b), the —COOH end stabilizes the cation more than the $-CH_3$ end at all distances investigated. The calculations suggest that interaction of a carbenium ion with the $-CF_3$ end of TFA might be kinetically favored. A carbenium ion solvated in this way could not be attacked by the solvent without a geometric reorganization involving partial desolvation (*i.e.* activation).

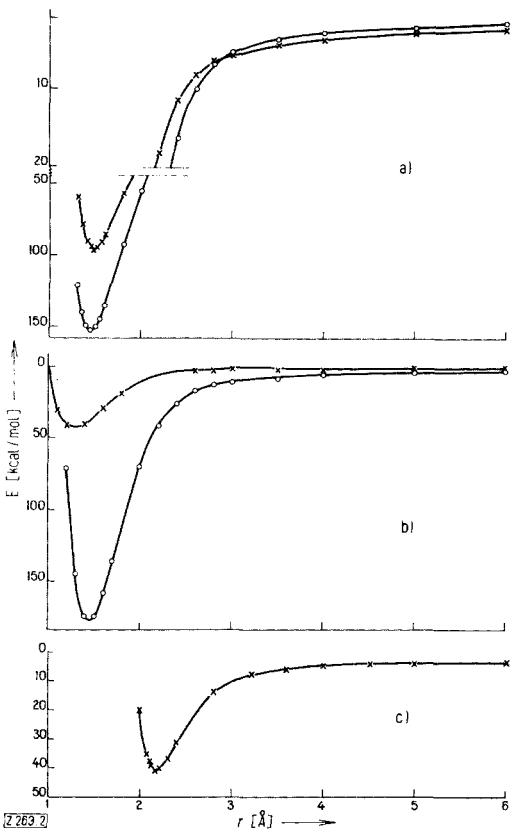


Fig. 2. Potential curves for solvent-cation interactions. r = distance. a) 1-methylethyl cation and TFA. ×—×: $C^{\oplus}$—F distance (see Fig. 1a). o—o: $C^{\oplus}$—O distance (see Fig. 1b); b) 1-methylethyl cation and AcOH. ×—×: $C^{\oplus}$—H distance, o—o: C^{∞}—O distance; c) benzenium ion and TFA. ×—×: distance between C^2 and the plane of the ring (see Fig. 1c).

Unlike the approach of an isolated cation and solvent molecule in a vacuum, the overall dissociation/solvation process clearly must have an activation energy. It is not unreasonable to suppose that this activation energy might be lower for the $-CF_3$ approach by the approximate difference in energy between the two types of interaction at TFA-cation distances that correspond to those in the solvated transition-states for dissociation[9]. The sum of the van der Waals radii for methylene and fluorine (3.35 Å) and methylene and oxygen (3.40 Å) might serve as crude estimates of these distances.

There is, of course, much more to the solvation of a heterolytic dissociation reaction than the interaction of the carbenium ion with an individual solvent molecule. In particular, solvation of the anion and changes in the liquid structure of the bulk solvent must be very important. For this reason, we hesitate to draw conclusions from the relative magnitudes of the stabilizations of 1-methylethyl cation by TFA and AcOH. However in the case of a comparison of cation stabilization by interaction with different orientations of *the same*

[*] Prof. Dr. J. J. Dannenberg
Centre de Mécanique Ondulatoire Appliquée CNRS
Université de Paris VI
23, Rue du Maroc
F-75019 Paris (France)
Permanent address:
Department of Chemistry, Hunter College of the City University of New York, N. Y. 10021 (USA)

solvent, the factors mentioned above should remain relatively constant.

Once we accept the idea that stabilization of carbenium ion by the $-CF_3$ end of TFA might be the kinetically favored process, and that an activation might be necessary before a nucleophilic (bond forming) interaction with the —COOH end is possible, then most of the experimental observations mentioned above can be rationalized. The low nucleophilicity of TFA might be due to interaction of the cation with the formally inert $-CF_3$ group. This leads to increased probability of internal return by the leaving group and the absence of inversion on the trifluoroacetalysis product.

The interaction of the $-CF_3$ end of TFA with the benzenium cations is particularly unique. As the distances between the fluorine atoms in TFA (2.22 Å) is very similar to the C^2—C^4 and C^2—C^6 distances (2.41 Å) in our model for the benzenium ion, each of the three most positively charged carbons (C^2, C^4, C^6) can specifically interact with a particular fluorine atom (see Fig. 1c and 2c). Since the bridged ion (and the transition-state leading to it) for the k_Δ process in the solvolysis of 1-methyl-2-phenylethyl tosylate should have a charge distribution in its benzene ring similar to that of the benzenium ion, TFA might preferentially solvate the transition-state, causing the observed k_Δ/k_s[4].

Received: May 26, 1975 [Z 263 IE]
German version: Angew. Chem. 87, 632 (1975)

CAS Registry numbers:
1-Methylethyl cation, 19252-53-0; benzenium ion, 17333-73-2; TFA, 76-05-1.

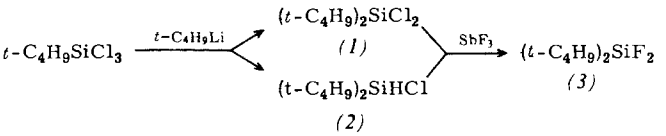
[1] *J. E. Nordlander* and *W. J. Kelly*, J. Am. Chem. Soc. *91*, 996 (1969); *T. W. Bentley, F. L. Schadt*, and *P. v. R. Schleyer*, *ibid. 94*, 992 (1972); literature cited therein.
[2] *J. B. Lambert* and *G. J. Putz*, J. Am. Chem. Soc. *95*, 6313 (1973); *J. B. Lambert, G. J. Putz*, and *C. E. Mixan*, *ibid. 94*, 5132 (1972).
[3] *V. J. Shiner, Jr., R. D. Fischer*, and *W. Dowd*, J. Am. Chem. Soc. *91*, 7748 (1969).
[4] *A. F. Diaz* and *S. Winstein*, J. Am. Chem. Soc. *91*, 4300 (1969); *F. L. Schadt* and *P. v. R. Schleyer*, *ibid. 95*, 7860 (1973); *P. v. R. Schleyer* and *C. J. Lancelot*, *ibid. 91*, 4297 (1969).
[5] *J. J. Dannenberg, D. H. Weinwurzel, K. Dill*, and *B. J. Golberg*, Tetrahedron Lett. *1972*, 1241; *J. J. Dannenberg, B. J. Goldberg, J. K. Barton, D. H. Weinwurzel, K. Dill*, and *M. O. Longas*, unpublished.
[6] For the purpose of the discussion, we define a nucleophile as an agent that can form a *stable chemical bond* with a carbenium ion.
[7] *P. A. Dobosh*, Programm 141, Quantum Chemistry Program Exchange, University of Indiana, Bloomington, Indiana.
[8] *J. A. Pople* and *M. S. Gordon*, J. Am. Chem. Soc. *89*, 4253 (1967).
[9] The semiempirical methods used are approximate. Our conclusions are, therefore, qualitative. Thus, the importance lies in the crossing of the curves in Fig. 2a, and not in the exact energy difference in them or in the exact cation-solvent distance at which they cross.

Synthesis of Tri-*tert*-butylsilanes[1]

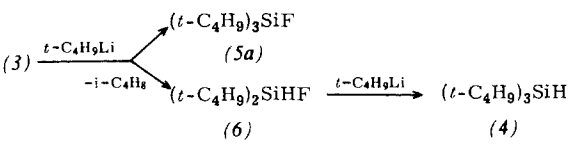
By *Manfred Weidenbruch* and *Walter Peter*[*]

Because of their unusual steric and electronic makeup tri-*tert*-butylsilanes may be considered as potential starting compounds for generation of the still unknown long-lived organosilyl radicals[2] or for the demonstration of silicenium ions[3]. Although mono- and di-*tert*-butylsilanes have been known for almost thirty years from the work of *Sommer et al.*[4, 5], all attempts to synthesize the tri-substituted derivatives have so far remained unsuccessful.

We have now found that reaction of *tert*-butyltrichlorosilane[4] with *tert*-butyllithium in heptane leads not only to di-*tert*-butyldichlorosilane *(1)*[5] but also to varying amounts of di-*tert*-butylchlorosilane *(2)* and isobutene. On heating with antimony trifluoride both compounds *(1)* and *(2)* afford the di-*tert*-butyldifluorosilane *(3)*. This reaction, which proceeds with co-formation of antimony and hydrogen fluoride, immediately provides a simple method for the conversion of Si—H into Si—F bonds which, in view of the accessibility and availability of the fluorinating agent, appears more advantageous than the usual methods.

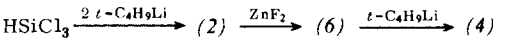


We succeeded in synthesizing the first tri-*tert*-butylsilanes[6] by further reaction of *tert*-butyllithium with *(3)*:

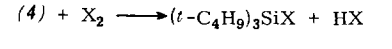


The main product is not the fluorosilane *(5a)*, but the hydrosilane *(4)*, the product pattern being almost independent of the molar ratio of the reactants. This finding and the observed generation of isobutene only at the beginning of the reaction would suggest that the slow transalkylation leading to *(5a)* is accompanied by the formation of intermediary di-*tert*-butylfluorosilane *(6)*, which then undergoes further rapid reaction to the tri-*tert*-butylsilane *(4)*.

Despite good yields of *(4)* and *(5a)* the given reaction sequence is uneconomical as regards organolithium components and involves painstaking separation steps. An alternative method, which circumvents these difficulties and which at the same time exploits the increased reactivity of hydrosilanes, is provided by a synthetic route starting from trichlorosilane. While two reaction steps and temperatures around 70 °C are necessary for the formation of *(1)* from $SiCl_4$, reaction of $HSiCl_3$ with *tert*-butyllithium yields the disubstitution product *(2)* directly without the use of heat. On treatment with zinc fluoride compound *(2)* is fluorinated smoothly to *(6)*, which reacts more rapidly than *(3)* with further *tert*-butyllithium to give pure *(4)*.



The electron pressure of the nine β methyl groups on the Si—H bond in *(4)* manifests itself not only in ν(SiH), which, being 2078 cm^{-1}, proves to be the lowest value recorded so far for all organomonosilanes, but also in the behavior towards electrophiles. Despite steric hindrance, reaction with halogens leads to spontaneous formation of the corresponding tri-*tert*-butylhalosilanes *(5b)*—*(5d)*.



(5b), X = Cl; -30 °C
(5c), X = Br; -30 °C
(5d), X = I; 60 °C

The constitution of the tri-*tert*-butylsilanes is confirmed by elemental analysis, mass spectra, and ^{1}H-NMR spectra.

[*] Prof. Dr. M. Weidenbruch and Dr. W. Peter
Institut für Anorganische Chemie der Technischen Hochschule
51 Aachen, Templergraben 55 (Germany)

Table 1. Prepared di- and tri-*tert*-butylsilanes.

Compound	M. p. [°C]	B. p. [°C/torr]	^{1}H-NMR ($CDCl_3$) δ [ppm]
tBu_2SiHCl *(2)*		168	1.08 (s, CH_3) 4.23 (s, SiH)
tBu_2SiHF *(6)*		129.5	1.05 (s, CH_3) 4.17 (d, SiH) [a]
tBu_2SiF_2 *(3)*		129	1.06
tBu_3SiH *(4)*	33—34	145/100	1.11 (s, CH_3) 3.37 (s, SiH)
tBu_3SiCl *(5b)*	116—118		1.19
tBu_3SiBr *(5c)*	165—168		1.20
tBu_3SiI *(5d)*	221		1.24

[a] J_{HF} = 48 Hz.

Tri-tert-butylsilane (4):

A solution of *tert*-butyllithium (0.15 mol) in pentane (120 ml) is added under argon to *(6)* (21 g, 0.13 mol) and the pentane slowly distilled off after addition of heptane (120 ml). The stirred reaction mixture is heated under reflux for 100 h. After separation of the heptane all products volatile at 70 °C/0.5 torr are removed from the precipitated LiF. Fractional distillation (split-tube column)[*] affords 18 g (70%) *(4)*, b. p. 145 °C/100 torr, which solidifies as colorless crystals, m. p. 33—34 °C.

Analogous reaction of *(3)* (20 g, 0.11 mol) and *tert*-butyllithium (0.22 mol) affords 17 g of a 4:1 mixture of *(4)* and *(5a)*, from which 12 g of pure *(4)* can be isolated.

[*] "Spaltrohr" column, Fischer, Labor- und Verfahrenstechnik, Bonn-Bad Godesberg.

Received: May 27, 1975 [Z 264 IE]
German version: Angew. Chem. 87, 670 (1975)

CAS Registry numbers:
(1), 18395-90-9; *(2)*, 56310-18-0; *(3)*, 558-63-4; *(4)*, 18159-55-2; *(5a)*, 56348-27-7; *(5b)*, 56348-24-4; *(5c)*, 56348-25-5; *(5d)*, 56348-26-6; *(6)*, 56348-23-3

[1] Silicon compounds with strong intramolecular steric interactions, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Presented to the Chemiedozenten Tagung, Düsseldorf, April 8, 1975.—Part 2: *M. Weidenbruch W. Schiffer, G. Hägele*, and *W. Peters*, J. Organometal. Chem. *90*, 145 (1975).

[2] *G. D. Mendenhall, D. Griller*, and *K. U. Ingold*, Chem. Br. *10*, 248 (1974).

[3] Review: *R. J. P. Corriu* and *M. Henner*, J. Organometal. Chem. *74*, 1 (1974).

[4] *L. J. Tyler, L. H. Sommer*, and *F. C. Whitmore*, J. Am. Chem. Soc. *69*, 981 (1947).

[5] *L. J. Tyler, L. H. Sommer*, and *F. C. Whitmore*, J. Am. Chem. Soc. *70*, 2876 (1948).

[6] *Note added in proof* (8. 8. 75): Tri-*tert*-butylsilane *(4)* was also isolated from the reaction of t-$C_4H_9SiCl_3$ with t-C_4H_9Li in approximately 10% yield; *E. M. Dexheimer* and *L. Spialter*, Tetrahedron Lett. *1975*, 1771.

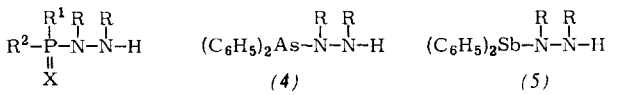
Addition of P—H, As—H, and Sb—H Groups to an N=N Double Bond[1]

By *Karl-Heinz Linke* and *Wilfried Brandt*[*]

Addition of element-hydrogen groups to nitrogen-nitrogen double bonds enables element-substituted hydrazines to be synthesized[2]:

For E = an element of the fifth main group such reactions have been previously recorded only for nitrogen[3] and in one case phosphorus (addition of diethyl hydrogen phosphite to diethyl azodicarboxylate)[4].

We have now succeeded in adding also the P—H group of diphenylphosphinous acid, diphenylthiophinous acid and methyl hydrogen phenylphosphonite, the As—H group of diphenylarsane and the Sb—H group of diphenylstibane to the N=N double bond of the azo ester to produce substituted hydrazines *(1)* to *(5)*:



(4) *(5)*

(1), $R^1 = R^2 = C_6H_5$, X = O

(2), $R^1 = R^2 = C_6H_5$, X = S

(3), $R^1 = C_6H_5$, $R^2 = OCH_3$, X = O

R = $CO_2C_2H_5$

The starting materials were allowed to react in the molar ratio 1:1 in benzene, methylene chloride or diethyl ether at room temperature, the solution of the azo ester being dropped into the solution of the phosphorus, arsenic or antimony compound in order to avoid redox reactions since the azo ester can also act as oxidant. The sensitivity of the arsane and stibane and of the As- and Sb-substituted hydrazines to oxygen and moisture demanded inert conditions in a closed apparatus. Reaction of the stibane must additionally be effected in the dark because of its sensitivity to light. The addition of methyl hydrogen phenylphosphonite occurred only on basic catalysis by its sodium salt, heating of the solution appreciably accelerating the reaction. In all the cases a polar reaction mechanism is probably involved.

The products *(1)* to *(4)* can be isolated as colorless crystalline compounds and characterized by their IR and mass spectra as well as by elemental analysis; they are readily soluble in the usual organic polar solvents. The compound *(5)* was identified only by its mass spectrum since so far it has been possible to obtain it only in admixture with the by-products tetraphenyldistibane and diethyl 1,2-hydrazinedicarboxylate.

(1): yield 92.2%; small rods from methylene chloride/light petroleum; m. p. 176—178 °C. *(2)*: yield 97%; bunches of crystals from methylene chloride/light petroleum; m. p. 107—108 °C. *(3)*: yield 77.5%; scaly crystals from methylene chloride/light petroleum, m. p. 108—110 °C. *(4)*: yield 96.5%; finecrystalline, m. p. 73—76 °C.

Received: May 28, 1975 [Z 265 IE]
German version: Angew. Chem. 87, 671 (1975)

CAS Registry numbers:
(1), 55905-00-5; *(2)*, 55905-01-6; *(3)*, 55905-02-7; *(4)*, 55905-03-8; *(5)*, 55905-04-9; diethyl azodicarboxylate, 1972-28-7; diphenylphosphinous acid, 24630-80-6; diphenylthiophosphinous acid, 55905-05-0; methyl hydrogen phenylphosphonite, 7162-15-4; diphenylarsane, 829-83-4; diphenylstibane, 5865-81-6.

[*] Prof. Dr. K.-H. Linke and Dipl.-Chem. W. Brandt
Institut für Anorganische Chemie der Universität
5 Köln 41, Greinstrasse 6 (Germany)

[1] Part 50 of Chemistry of Hydrazine and its Derivatives. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 49: *K.-H. Linke* and *H. J. Kalker*, Chem. Ber., in press.

[2] *K.-H. Linke* and *H. J. Göhausen*, Chem. Ber. *106*, 3438 (1973); *K.-H. Linke, W. Brandt*, and *H. J. Göhausen*, ibid. *106*, 707 (1973).

[3] *O. Diels* and *M. Paquin*, Ber. Deut. Chem. Ges. *46*, 2000 (1913); *K.-H. Linke* and *H. J, Göhausen*, Chem. Ber. *104*, 301 (1971).

[4] *D. C. Morrison*, J. Org. Chem. *23*, 1072 (1958).

Anion Structure of Ammonium Decamolybdate $(NH_4)_8Mo_{10}O_{34}$

By *Joachim Fuchs, Hans Hartl, Wolf-Dietrich Hunnius,* and *Soroush Mahjour*[*]

Thermal decomposition (110 °C) of ammonium heptamolybdate, $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, affords $2(NH_4)_2O\cdot 5MoO_3$[1]. This product proved identical with an ammonium polymolybdate that crystallized during several days at *ca.* 80 °C as colorless prisms from concentrated aqueous ammonium heptamolybdate solutions to which some ammonia had been added[2].

For determination of the structure, the intensities of 3356 reflections were measured on a Siemens four-circle diffractometer with $Cu_{K\alpha}$ radiation. The triclinic, centrosymmetrical cell with the lattice parameters $a = 10.996 \pm 0.002$, $b = 10.921 \pm 0.002$, $c = 7.775 \pm 0.002$ Å, $\alpha = 79.71 \pm 0.08$, $\beta = 99.25 \pm 0.08$, $\gamma = 107.13 \pm 0.08°$, contains five crystallographically independent molybdenum atoms whose positions were determined by Patterson methods. The coordinates of the oxygen and nitrogen atoms were obtained by a difference Fourier synthesis. The atomic parameters (except for H) were refined to an R value of 5.1 % (anisotropic temperature factors, corrections for absorption and extinction).

Because of the very slow dissolution of the compound in water (with destruction of the structure) a high-polymeric anion structure was suspected. However, it was found that isolated decamolybdate ions, $Mo_{10}O_{34}^{8-}$, were present in which one Mo_8O_{28} unit built up of edge-bridged MoO_6 octahedra was connected at corners to two MoO_4 tetrahedra (Fig. 1).

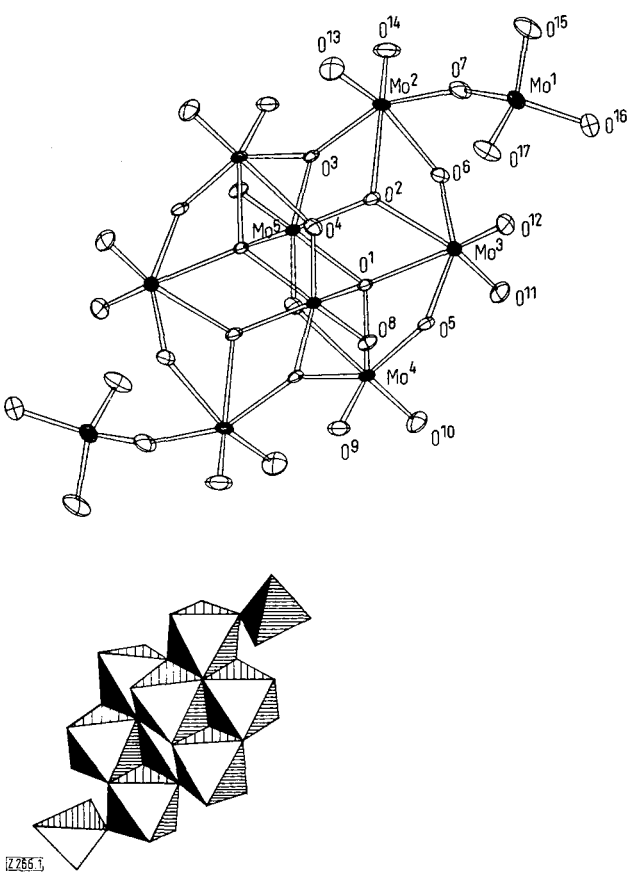


Fig. 1. Structure of the decamolybdate ion $Mo_{10}O_{34}^{8-}$.

Thus the first discrete isopolyanion becomes known which contains both octahedral and tetrahedral units. The Mo_8O_{28} group has the same structure as the fundamental unit of the ammonium polyoctamolybdate, $(NH_4)_6Mo_8O_{27}\cdot 4H_2O$[3], and the $K_2Mo_4O_{13}$ obtainable from melts[4].

The Mo—Mo distances within the octameric unit amount to 3.292 Å (3.256–3.387), whilst the distance of Mo(2) from the tetrahedrally coordinated Mo(1) is 3.700 Å. The Mo—O bond lengths to the terminal O atoms are 1.669–1.750 Å (mean 1.725) and to the bridging O atoms 1.714–2.402 Å (1.978); those to the three-fold coordinated oxygen atoms O(2) and O(3) are 1.869–2.390 Å (2.104) and to the four-fold coordinated O(1) are 1.973–2.441 (2.196). The standard deviations for the Mo—Mo distances are <0.001 Å and for the Mo—O bonds <0.01 Å. The O—Mo—O bond angles at the tetrahedrally coordinated Mo(1) lie between 104.6 and 112.7°. The anions are bonded in the crystal through NH_4^+ by a system of hydrogen bridges (shortest N—O distance 2.72 Å).

Received: June 9, 1975 [Z 266 IE]
German version: Angew. Chem. *87*, 634 (1975)

CAS Registry numbers:
$(NH_4)_8Mo_{10}O_{34}$, 11 089 320.

[1] *E. J. Rode* and *V. N. Tverdokhledov*, Zh. Neorg. Khim. *3*, 2343 (1958); *E. Ma*, Bull. Chem. Soc. Jap. *37*, 171, 648 (1974); *A. B. Kiss, P. Gado, I. Asztalos,* and *A. J. Hegedüs*, Acta Chim. Acad. Sci. Hung. *66*, 235 (1970).

[2] *W.-D. Hunnius*, Z. Naturforsch. *30b*, 63 (1975).

[3] *I. Böschen, B. Buss, B. Krebs,* and *O. Glemser*, Angew. Chem. *85*, 409 (1973); Angew. Chem. internat. Edit. *12*, 409 (1973); *I. Böschen, B. Buss,* and *B. Krebs*, Acta Crystallogr. *B 30*, 48 (1974).

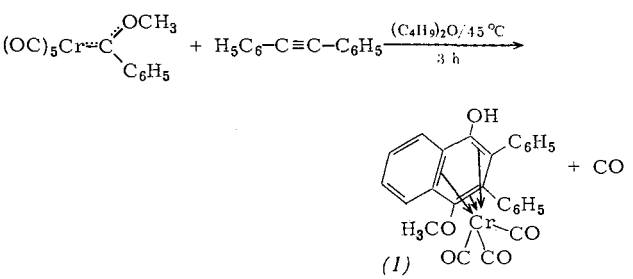
[4] *B. M. Gatehouse* and *P. Leverett*, Chem. Commun. *1970*, 740; J. Chem. Soc. *A 1971*, 2107.

Synthesis of the Naphthol Skeleton from Pentacarbonyl-[methoxy(phenyl)carbene]chromium(0) and Tolan

By *Karl Heinz Dötz*[*]

The [2+1] cycloaddition of carbenes to alkenes and alkynes is already well-known as a preparatively useful reaction[1]. The reaction with alkenes also takes place in the case of carbenes coordinated to a metal carbonyl fragment[2]. However, this type of complex, $(CO)_5M[C(OR)R']$ (*e.g.* M = Cr, R = alkyl, R' = aryl)[3], exhibits a surprisingly different behavior towards alkynes.

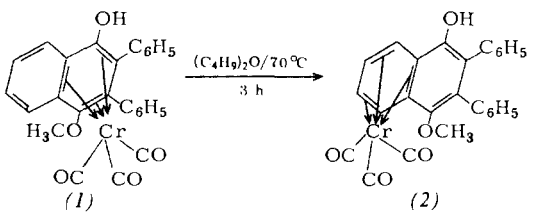
In the reaction of pentacarbonyl[methoxy(phenyl)carbene]chromium(0) with tolan a red product can be isolated, which, on the basis of elemental analysis and mass spectroscopically determined molecular weight, can be assigned the empirical formula $C_{26}H_{18}CrO_5$. Spectroscopic data and the oxidative degradation leading to 2,3-diphenyl-1,4-naphthoquinone on reaction with nitric acid in glacial acetic acid characterize this compound as tricarbonyl(2,3-diphenyl-4-methoxy-1-naphthol)chromium(0) *(1)*.



[*] Prof. Dr. J. Fuchs, Prof. Dr. H. Hartl, Dr. W.-D. Hunnius, and Dipl.-Chem. S. Mahjour
Institut für Anorganische Chemie FB21-WE1 der Freien Universität 1 Berlin 33, Fabeckstrasse 34—36 (Germany)

[*] Dr. K. H. Dötz
Anorganisch-chemisches Institut der Technischen Universität 8 München 2, Arcisstrasse 21 (Germany)

The manner in which the new ligand is coordinated to the metal can be determined indirectly by ^{1}H-NMR spectroscopy. Of the four aromatic rings capable of participating in π complex formation only the persubstituted naphthalene moiety does not bear any hydrogen atoms. From the absence of a characteristic high field shift for protons of a benzene ring coordinated to $(CO)_3Cr$ it follows that the reaction product has the structure *(1)*. This is supported by the observation that when *(1)* is warmed in solution it is completely transformed into the isomer *(2)*, which can also be isolated as the main product in the cyclization reaction under these conditions. The ^{1}H-NMR spectrum of *(2)* shows resonances that can be assigned to the protons forming a pseudo AA'BB' system of the naphthalene moiety bound to the metal.



The IR spectrum (in CS_2) of *(1)* shows three bands in the ν(CO) region at 1953 vs, 1887 vs and 1869 vs cm^{-1}, as would be expected for tricarbonylchromium(0) complexes of condensed aromatics[4]. The same bands of the isomer *(2)* appear at 1963 vs, 1896 vs, and 1885 vs cm^{-1}. Hence a higher donor-acceptor ratio can be ascribed to the naphthol ligands in *(1)*.

Two possible reaction routes come under discussion for the unexpected formation of complex *(1)*:

1. On decomposition of the carbene complex the carbene and a carbon monoxide ligand afford free methoxy(phenyl)ketene[5]. This reacts, as has been described for reactions of diphenylketene with arylalkynes[6], with tolan to give the naphthol derivative which finally binds to the metal.

2. Synthesis of the naphthol skeleton is effected in the coordination sphere of the metal—possibly after substitution of a CO ligand by the alkyne.

Inconsistent with the first possibility is the finding that 2,3-diphenyl-4-methoxy-1-naphthol, which can be obtained by cleavage under CO pressure in ethereal solution, does not coordinate to the metal under the conditions of the cyclization reaction, in the presence of neither hexacarbonylchromium(0) nor pentacarbonyl[methoxy(phenyl)carbene]chromium(0).

The second alternative, on the other hand, makes it quite understandable that the isomer *(1)* is formed exclusively under kinetically controlled conditions; for, in this compound the metal is located almost centrally above the completely substituted naphthalene ring made up of carbene, carbonyl, and alkyne components. Participation of the metal in the reaction is also supported by the observation that no product corresponding to compound *(1)* or *(2)* could be obtained *under the same conditions* from the homologous tungsten-carbene complex and tolan.

Experimental:

A solution of $(CO)_5Cr[C(OCH_3)C_6H_5]$[7] (0.58 g, 1.86 mmol) and tolan (0.33 g, 1.86 mmol) in di-*n*-butyl ether (6 ml) is stirred for 3 h at 45 °C. A red product separates out, further precipitation of which is promoted by addition of pentane (5 ml). After cooling the suspension to −20 °C the precipitate is collected on a G 3 frit and purified chromatographically on silica gel (Merck, Act. 2—3) at −20 °C. A red zone is formed, from which, after elution with methylene chloride/pentane (1 : 1), removal of solvent from eluant, and recrystallization of the resulting residue from methylene chloride/pentane (1 : 5), brick-red crystals of *(1)* can be obtained. Yield 0.53 g (62 %).

Received: June 11, 1975 [Z 267 IE]
German version: Angew. Chem. 87, 672 (1975)

CAS Registry numbers:
(1), 55904-96-6; *(2)*, 55904-97-7; pentacarbonyl[methoxy(phenyl)carbene]-chromium(0), 27436-93-7; tolan, 501-65-5

[1] *W. Kirmse:* Carbene Chemistry, 2nd Ed. Academic Press, New York 1971.
[2] *K. H. Dötz*, Naturwissenschaften, in press.
[3] *E. O. Fischer*, Angew. Chem. *86*, 651 (1974).
[4] *R. D. Fischer*, Chem. Ber. *93*, 165 (1960).
[5] Cf. *B. Dorrer* and *E. O. Fischer*, Chem. Ber. *107*, 2683 (1974).
[6] *L. I. Smith* and *H. H. Hoehn*, J. Am. Chem. Soc. *63*, 1181 (1941); and literature cited therein.
[7] *E. O. Fischer, B. Heckl, K. H. Dötz, J. Müller*, and *H. Werner*, J. Organometal. Chem. *16*, P 29 (1969).

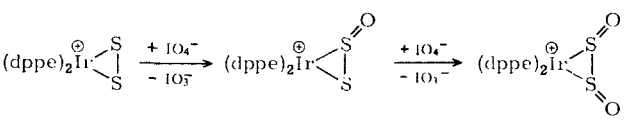
Disulfur Monoxide as Complex Ligand[**]

By *Günter Schmid* and *Günter Ritter*[*]

After the complexation of sulfur monoxide, SO, and disulfur dioxide, S_2O_2[1], we have now succeeded in isolating a complex containing disulfur monoxide, S_2O, as ligand. Although free S_2O is relatively long-lived compared to SO and S_2O_2, which have a lifetime of only milliseconds, the monomer is stable only in the gas phase at ≈1 torr; on condensation it decomposes with formation of SO_2 and polysulfur oxides[2]. The structure and bonding of the molecule have already been described[3].

We have been able to synthesize the first S_2O complex $[(dppe)_2Ir(S_2O)]Cl$ *(1)* [dppe = $(C_6H_5)_2P-(CH_2)_2-P(C_6H_5)_2$] *via* two different routes, one based on the same principle as for the synthesis of the structurally confirmed S_2O_2 complex $[(dppe)_2Ir(S_2O_2)]Cl$ *(2)*[1] the other on its own chemical properties.

(2) is formed on oxidation of the sulfur complex $[(dppe)_2Ir(S_2)]Cl$[4] with IO_4^-[1]. The assumption that this reaction proceeds in two steps has now been proven by the isolation of the S_2O complex:



In order to avoid further oxidation to the S_2O_2 complex, $[(dppe)_2Ir(S_2)]Cl$ is treated with an equimolar quantity of $NaIO_4$, leading initially *via* anion exchange to the $[(dppe)_2Ir(S_2)]IO_4$ complex, from which the cationic S_2O complex and IO_3 are formed in solution by intramolecular redox reaction. Addition of $BaCl_2$ yields $Ba(IO_3)_2$ and *(1)*.

The second synthetic route is based on the reactivity of the S_2O_2 complex *(2)*, which *e.g.* on treatment with excess triphenylphosphane undergoes decomposition to $[(dppe)_2Ir]Cl$ with formation of $(C_6H_5)_3P=O$ and $(C_6H_5)_3P=S$[1]. This reaction must also proceed stepwise for the directed partial deoxygenation to afford the S_2O complex *(1)*.

[*] Prof. Dr. G. Schmid and Dr. G. Ritter
Fachbereich Chemie der Universität
355 Marburg/Lahn, Lahnberge (Germany)

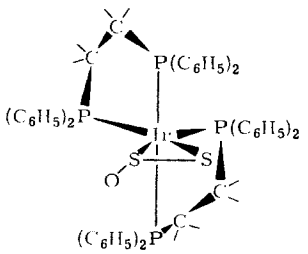
[**] The complex chemistry of lower sulfur oxides, Part 3.—Part 2: Ref. [1].

Indeed such a reduction of *(2)* leads smoothly to the same product as the partial oxidation of the corresponding S_2 complex.

$$[(dppe)_2Ir(S_2O_2)]Cl + (C_6H_5)_3P \longrightarrow$$
(2)

$$(C_6H_5)_3PO + [(dppe)_2Ir(S_2O)]Cl$$
(1)

The new complex *(1)*, a yellow crystalline compound which is very stable to air, shows only one SO band at 1043 cm^{-1} in the IR spectrum. In all probability the molecular structure of the S_2O complex is as shown below, *i.e.* similar to that of *(2)*, whose structure has already been confirmed by X-ray analysis[1].



The iridium is coordinated to four P and two S atoms in a distorted octahedral structure. As in the S_2O_2 complex *(2)* an S—S single bond is also present, while the S—O bond, according to the IR spectrum, exhibits double bond character.

Experimental:

Method 1: To a solution of $[(dppe)_2Ir(S_2)]Cl$ (0.425 g, 0.37 mmol) in CH_3OH (70 ml) is added $NaIO_4$ (0.08 g, 0.37 mmol), also dissolved in methanol. 0.38 g (0.3 mmol) of the $[(dppe)_2Ir(S_2)]IO_4$ thus prepared is dissolved in 30 ml methanol/1 ml H_2O and the resulting solution stirred for 24 h at room temperature. $BaCl_2$ (0.10 g, 0.4 mmol) is added to the solution and precipitated $Ba(IO_3)_2$ is filtered off. The filtrate is evaporated to dryness and the resulting residue extracted with toluene (60 ml) and methanol (10 ml). Concentration of the extract affords 0.25 g (70 %) of crude product, which still contains some IO_3^-. Double recrystallization from toluene/methylene chloride yields analytically pure *(1)*.

Method 2: A mixture of *(2)* (0.411 g, 0.367 mmol) and $P(C_6H_5)_3$ (0.193 g, 0.73 mmol) in toluene (50 ml) and CH_2Cl_2 (15 ml) is heated under reflux for 1 h. Concentration of the ocher yellow solution affords 0.277 g (68 %) of *(1)*, which after recrystallization from toluene/methylene chloride is analytically (C, H, Cl, O, S) and spectroscopically identical with the product prepared by Method 1.

Received: June 11, 1975 [Z 268 IE]
German version: Angew. Chem. 87, 673 (1975)

CAS Registry numbers
(1), 56391-52-7; *(2)*, 56391-51-6; $P(C_6H_5)_3$, 603-35-0; $[(dppe)_2Ir(S_2)]Cl$, 31603-13-1; $NaIO_4$, 7790-28-5

[1] *G. Schmid* and *G. Ritter*, Chem. Ber., in press.
[2] *W. Genz* and *P. W. Schenk*, Z. Anorg. Allg. Chem. *379*, 300 (1970).
[3] *E. Tiemann, J. Hoeft, F. J. Lovas*, and *D. R. Johnson*, J. Chem. Phys. *60*, 5000 (1974); *H. Bock, B. Solouki, P. Rosmus*, and *R. Steudel*, Angew. Chem. *85*, 987 (1973); Angew. Chem. internat. Edit. *12*, 933 (1973); literature cited therein.
[4] *A. P. Ginsberg* and *W. E. Lindell*, Chem. Commun. *1971*, 232.

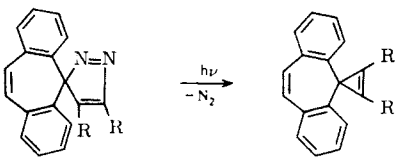
[2π,6π]-Spirenes. Synthesis of the First Member of a New Class of Compounds[**]

By *Heinz Dürr* and *Bernd Weiss*[*]

Dedicated to Professor Eugen Müller on the occasion of his 70th birthday

Hitherto only members of the series of preparatively and theoretically interesting [2π,4π]-, [4π,4π]-, and [4π,6π]-spirenes have been synthesized. Derivatives of the [2π,6π]-spirene type *(2)* were unknown[1] or only postulated as unisolable intermediates[2].

We have now succeeded in the first synthesis of a [2π,6π]-spirene stabilized by benzo groups. Photolysis of the also unknown diaza-[4π,6π]-spirene *(1)* seemed to offer a route for this purpose[1].



(1a), (1b) *(2a)*

(a), R–R = $-(CH_2)_6-$
(b), R = CO_2CH_3

1,3-Dipolar cycloaddition of 5-diazodibenzo[*a,d*]cycloheptene to cyclooctyne proceeded smoothly, affording an 80 % yield of *(1a)* as colorless needles [m.p. 183—184 °C (dec.)]. An analogous reaction with dimethyl acetylenedicarboxylate led to *(1b)* (53 % yield; m.p. 150 °C) whose structure was proved by X-ray analysis[3]. Irradiation of *(1a)* in benzene with a high-pressure Hg lamp (Pyrex filter) and subsequent working up of the photolysate by column chromatography afforded spiro[5*H*-dibenzo[*a,d*]cycloheptene-5,1'-2,3,4,5,6,7-hexahydro-1*H*-cyclopropacyclooctene] *(2a)*, m.p. 130—131 °C, in 10 % yield. Photolysis of *(1b)* did not give a [2π,6π]-spirene.

Experimental:

500 mg of *(1a)* (1.53 mmol) were dissolved in anhydrous benzene (150 ml) and irradiated (high-pressure Hg lamp, GW_v filter) for 6 h, during which 18 ml (52 %) of nitrogen were evolved and the solution assumed a pale yellow color. By column chromatography on silica gel with CH_2Cl_2 as eluant and two recrystallizations from ether/methanol 47 mg (10 %) of *(2a)* was isolated as colorless crystals.

Received: May 30, 1975 [Z 272a IE]
German version: Angew. Chem. 87, 674 (1975)

CAS Registry numbers:
(1a), 56008-67-4; *(1b)*, 56008-68-5; *(2a)*, 56008-69-6; 5-diazodibenzo[*a,d*]cycloheptene, 6141-56-6; cyclooctyne, 1781-78-8; dimethyl acetylenedicarboxylate, 762-42-5.

[*] Prof. Dr. H. Dürr and Dipl.-Chem. B. Weiss
Fachbereich 14, Organische Chemie der Universität
66 Saarbrücken (Germany)

[**] [2π,6π]-Spirenes are unsaturated monospiro compounds containing one double bond in one ring and three in the other.

[1] *H. Dürr* and *L. Schrader*, Z. Naturforsch. *24b*, 536 (1969); Chem. Ber. *103*, 1334 (1970); *H. Dürr* and *R. Sergio*, Tetrahedron Lett. *1972*, 3479; *G. Ege, ibid. 1963*, 1667.
[2] *E. E. Waali* and *W. M. Jones*, J. Org. Chem. *38*, 2572 (1973).
[3] *B. Weiss*, Diplomarbeit, Universität Saarbrücken 1974; *K. H. Pauly*, Diplomarbeit, Universität Saarbrücken 1975.

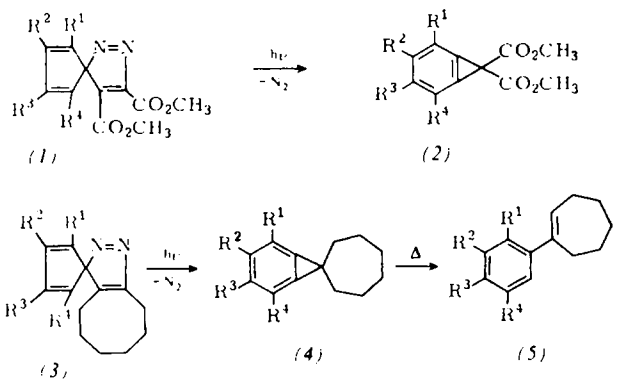
Synthesis of the First Spirocyclopropabenzene

By *Heinz Dürr* and *Heribert Schmitz*[*]

Dedicated to Professor Eugen Müller on the occasion of his 70th birthday

Photofragmentation of diaza[4π,4π]-spirenes of type *(1)* affords cyclopropa-benzenes or -naphthalenes of type *(2)* in good yields[1].

By 1,3-dipolar cycloaddition of diazocyclopentadienes to cyclooctyne[2] and subsequent photofragmentation we have succeeded analogously in synthesizing spirocyclopropabenzenes of type *(4)*, in which the cyclopropene ring should be still more strained--and the system thus more unstable--than in cyclopropabenzenes of type *(2)*. Photolysis of the diaza-[4π,4π]-spirenes *(3a)*--*(3c)*[2] was carried out in ether at −20 °C (with a high-pressure Hg lamp and a Pyrex filter); at the end of the quantitative evolution of nitrogen the spirocyclopropabenzenes *(4a)*—*(4c)* were obtained.



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

	R^1	R^2	R^3	R^4	*(4)* Yield [%]	M.p. [°C]
a	C_6H_5	C_6H_5	C_6H_5	C_6H_5	30	125–127
b	C_6H_5	H	H	C_6H_5	12 [a]	100–102 [b]
c	C_6H_5	*p*-Br-C_6H_4	*p*-Br-C_6H_4	C_6H_5	31	162–164

[a] *(4b)* rearranged to *(5b)* even during photolysis and working up.
[b] This is probably the melting point of *(5b)*.

The spirocyclopropabenzenes *(4)* were identified mainly by ^{1}H- and ^{13}C-NMR spectroscopy. In the ^{1}H-NMR spectrum the aromatic protons occur at δ = 7.2–8.1 ppm and the methylene-protons at δ = 1.0–2.4 ppm.—The rearranged product *(5)* shows also a triplet at δ = 5.95 ppm. The proton ratio accords with the structures proposed.

The compounds *(4a)* and *(4c)* are thermally stable and can be rearranged only at elevated temperatures, where other products are formed in addition to *(5)*. *(4b)*, however, rearranges quantitatively to *(5b)* in a short time even at room temperature. An orienting kinetic investigation of the thermolysis *(4b)*→*(5b)* gave $\Delta G^{\neq} = 24 \pm 1$ kcal.

Experimental:

2.00 g (5.7 mmol) of the diaza-[4π,4π]-spirene *(3b)* was dissolved in 250 ml of anhydrous ether and washed with pure nitrogen for 15 min. Irradiation was effected at −20 °C (cryostat) by a Philips HPK 125 W lamp and a Pyrex filter until the *(3b)* was completely decomposed (TLC monitoring and measurement of the amount of N_2 evolved). After the photolysis the ether was removed at the lowest temperature possible. There remained a yellow oil, from which 190 mg (11 %) of *(4b)* and 580 mg (31 %) of *(5b)* were obtained by fractional crystallization from ether at −24 °C.

Received: May 30, 1975 [Z 272b IE]
German version: Angew. Chem. 87, 674 (1975)

CAS Registry numbers:
(3a), 53359-35-6; *(3b)*, 54508-30-4; *(3c)*, 56008-70-9; *(4a)*, 56008-71-0; *(4b)*, 56008-72-1; *(4c)*, 56008-73-2; *(5b)*, 54508-37-1.

[1] *H. Dürr* and *L. Schrader*, Chem. Ber. *103*, 1374 (1970); Angew. Chem. *81*, 426 (1969); Angew. Chem. internat. Edit. *8*, 446 (1969).
[2] Cf. *H. Dürr, A. C. Ranade*, and *I. Halberstadt*, Tetrahedron Lett. *1974*, 3041.

[*] Prof. Dr. H. Dürr and Dipl.-Chem. H. Schmitz
Fachbereich 14, Organische Chemie der Universität
66 Saarbrücken (Germany)

Hazards in Using Perchloric Acid

By *Kaspar Eigenmann* and *Saleem Farooq*[*]

The distillation of a crude mixture from the attempted preparation of 4-(cyclohexylthio)phenol resulted in a violent explosion causing serious injuries to a co-worker and substantial damage to the laboratory. The preparation, which required the condensation of cyclohexylmethyl sulfoxide with phenol in 70 % aqueous perchloric acid and subsequent demethylation with potassium chloride, followed an analogous procedure to that reported in Chemical Abstracts[1]. An investigation of the possible cause of the explosion has yielded the following results which we wish to communicate to future investigators:

1. The reaction conditions given in Chemical Abstracts[1] are applicable merely to the condensation of *aryl* sulfoxides with phenols in 70 % aqueous perchloric acid and *not* to *aliphatic* sulfoxides. This becomes apparent only when reading the original literature[2]. Thus, condensation of aliphatic sulfoxides with phenols in 70 % aqueous perchloric acid takes place only in the presence of phosphorus oxychloride ($POCl_3$).
2. Sulfoxides alone can explode violently at raised temperatures (Table 1).

Table 1. Decomposition of sulfoxides (Perkin-Elmer Differential Scanning Calorimeter (DSC-1B) with gold-plated high-pressure sample pans constructed from stainless steel, heating rate of 4 °C/min).

Sulfoxide	Temperature range of decomposition [°C]	Energy of decomposition [kcal/mol]
Dimethyl sulfoxide	270–355	−10.2
Cyclohexylmethyl sulfoxide	181–255	−13.9
Methylphenyl sulfoxide	233–286	−17.8

Table 2. Decomposition of perchloric acid-phenol mixtures; apparatus and conditions as in Table 1.

Phenol [mg]	$HClO_4$ 70 % [mg]	Temperature range of decomposition [°C]	Energy of decomposition [a]
7.4	7.0	143–325	−445
12.7	8.5	102–322	−450
21.6	9.2	81–306	−415
24.4	0.4	148–215	− 25
22.3	0.4 [b]	179–235	− 20

[a] Quoted in cal per gram of mixture.
[b] +0.4 mg H_2O.

[*] Dr. K. Eigenmann and Dr. S. Farooq
Ciba-Geigy AG
CH-4002 Basel (Switzerland)

The decomposition temperature is lowered by 20 °C or more in the presence of acids depending on the acid concentration.

3. Mixtures of phenol and aqueous perchloric acid are thermally unstable and may decompose violently. The decomposition temperature depends on the content of perchloric acid (Table 2).

The formation of an ester of perchloric acid is conceivable, but has not been investigated[3].

Received: June 6, 1975 [Z 273 IE]
German version: Angew. Chem. 87, 635 (1975)

CAS Registry numbers:
Dimethyl sulfoxide, 67-68-5; cyclohexyl methyl sulfoxide, 56051-02-6; methyl phenyl sulfoxide, 1193-82-4; perchloric acid, 7601-90-3; phenol, 108-95-2.

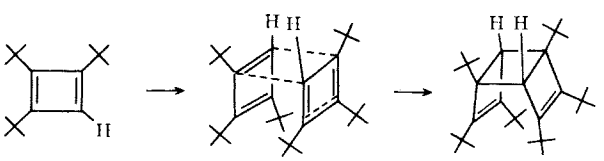
[1] Chemical Abstracts *64*, 19466d (1966).
[2] *K. Hirose* and *S. Ukai*, Yakugaku Zasshi, *86*, 187 (1966).
[3] *H. W. Wharton*, J. Am. Oil Chem. Soc. *51*, 35 (1974).

Unusual Chemical Behavior of Tri-*tert*-butylcyclobutadiene[1][**]

By *Günther Maier* and *Wolfgang Sauer*[*]

Tri-*tert*-butylcyclobutadiene *(1)*[2, 3] is the ideal model for the study of the chemical properties of the cyclobutadiene ring system: firstly, this molecule is capable of existence in the monomeric form at room temperature; secondly, it contains an unperturbed π-electron system; and thirdly, its dimerization proceeds so slowly that in competition therewith the chemical "extravagances" of this antiaromatic compound can be studied in a planned manner.

This communication describes two examples which underscore the special place of cyclobutadiene in the annulene series. One of these refers to the unusual activation parameters for the dimerization of *(1)*, the other to the fact that *(1)* undergoes ionic as well as synchronous[2] and radical[2] additions, in the ionic case behaving in a markedly carbanionoid fashion.

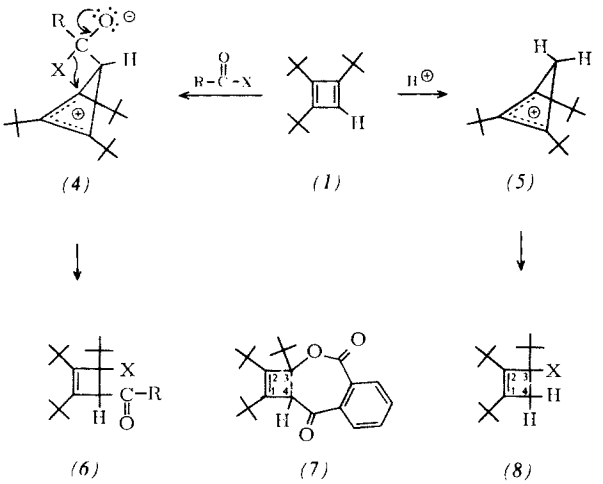


(1) *(2)* *(3)*

Dimerization of *(1)* to the tricycle *(3)* is a synchronous cycloaddition. The prognosis[4] that the activation parameters of this reaction must be unusual is confirmed by experiment. For the determination of the kinetic data we have prepared tri-*tert*-butylcyclobutadiene in a matrix of tetramethylsilane, D_{12}-cyclohexane, and D_8-tetrahydrofuran (3 : 1 : 1)[2] and, after thawing, measured the disappearance of the NMR signal of the two diagonally situated *tert*-butyl groups relative to a standard signal (hexamethylethane) between 0 and 35 °C. The regression lines obtained by a least squares program afforded $E_A = 7.8 \pm 0.9$ kcal mol^{-1}, $\log A = 2.9 \pm 0.6$, $\Delta H^{\neq} = 7.2 \pm 0.9$ kcal mol^{-1}, $\Delta S^{\neq} = -47.0 \pm 3.0$ cal K^{-1} mol^{-1}. These results are in accord with the mechanistic picture of a sterically extremely hindered activated complex *(2)*. The free energy of activation at 20 °C amounts to $\Delta G^{\neq} = \Delta H^{\neq} - T\cdot\Delta S^{\neq} = 7.2 + 13.8 = 21$ kcal mol^{-1}. The inhibition of reaction is thus given to about one-third by the activation enthalpy and two-thirds by the entropy term. This high negative activation entropy has, to the best of our knowledge, no analogy in comparable reactions[5]; it is an indication that, in spite of steric hindrance, electronic factors still predominate and force the molecule into the form *(2)*.

In the autoxidation of *(1)* oxygen is added to the more highly substituted double bond, which is unusual[2]. Remarkable also is the fact that—assuming a singlet ground state for *(1)*—this radical addition which must involve spin inversion is nevertheless faster than all the other reactions leading to stabilization of *(1)*.

Due to the pronounced donor properties of cyclobutadienes, as demonstrated by the easy formation of charge-transfer complexes in the case of tetramethylcyclobutadiene[6] and the low ionization energy of tri-*tert*-butylcyclobutadiene, we expected that cyclobutadienes would react readily with electrophilic reagents. Indeed, *(1)* reacts with carboxylic anhydrides or carbonyl chlorides to give adducts *(6)*, and on reaction with H-acidic compounds products of type *(8)* are formed.



(4) *(1)* *(5)*

(6) *(7)* *(8)*

X =	*(8a)*	*(8b)*	*(8c)*	*(8d)*	*(8e)*
	$C_6H_4(CO_2)_2$	$C_6H_5CO_2$	C_6H_5O	HO	H_3CO

The cyclobutadiene system is thus also amenable to ionic additions.

For instance, treatment of *(1)* with phthalic anhydride affords the insertion product *(7)* [m.p. 180—181 °C; IR (CCl_4): 1712, 1687 cm^{-1}; NMR (CCl_4): $\tau = 2.22$ (4H, m), 5.84 (1H, s), 8.77 (9H, s), 8.94 (9H, s), 9.02 (9H, s)]. The decision that the lactone bridge is attached to C-3 and not to C-4 is derived from the ^{13}C-NMR spectra[7]. 3,6-Dihydrophthalic anhydride also reacts with insertion into the anhydride ring although in this case a Diels-Alder reaction would also have been possible. 3,5-Dinitrobenzoyl chloride reacts smoothly, giving an adduct of type *(6)* (X = Cl; R = dinitrobenzoyl). However, *(1)* is inert towards methyl acetate. In its nucleophilicity tri-*tert*-butylcyclobutadiene is thus comparable with an organocadmium compound. In analogy to the mechanistic interpretation of protonation we assume that the nucleophilic additions of *(1)* to carboxylic acid derivatives occur by way of intermediates of structure *(4)*.

If *(1)* is produced in a closed apparatus by low-temperature photolysis[2], allowed to warm to room temperature, and then brought into contact with phthalic acid, benzoic acid, phenol, water, or methanol, then the adducts *(8a)* to *(8e)* are formed

[*] Prof. Dr. G. Maier and W. Sauer
Fachbereich Chemie der Universität
355 Marburg, Lahnberge (Germany)

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

in good yields[8]. In the first step of the reaction a proton is probably added with formation of the homocyclopropenyl cation *(5)*[9]. Addition of the anions then leads to the adducts *(8)*. The acidity of aniline is not high enough to protonate *(1)*. The uncatalyzed addition of methanol shows, however, that tri-*tert*-butylcyclobutadiene *(1)* is to be regarded as a strongly basic hydrocarbon, its basicity being comparable to that of an alkoxide ion.

Received: July 7, 1975 [Z 285 IE]
German version: Angew. Chem. 87, 675 (1975)

CAS Registry numbers:
(1), 51067-53-9; *(3)*, 51567-04-5; *(6)* (X = Cl, R = dinitrobenzoyl), 56391-10-7; *(7)*, 56391-11-8; *(8a)*, 56391-12-9; *(8b)*, 56391-13-0; *(8c)*, 56391-14-1; *(8d)*, 56391-15-2; *(8e)*, 51067-58-4.

[1] Small Rings, Part 17.—Part 16: [6].
[2] *G. Maier* and *A. Alzérreca*, Angew. Chem. *85*, 1056 (1973); Angew. Chem. internat. Edit. *12*, 1015 (1973).
[3] *S. Masamune, N. Nakamura, M. Suda*, and *H. Ona*, J. Am. Chem. Soc. *95*, 8481 (1973).
[4] *G. Maier*, Angew. Chem. *86*, 491 (1974); Angew. Chem. internat. Edit. *13*, 425 (1974).
[5] *J. Sauer*, Angew. Chem. *79*, 76 (1967); Angew. Chem. internat. Edit. *6*, 16 (1967).
[6] *G. Maier, W. Mayer, C. Haacke*, and *R. Askani*, Angew. Chem. *85*, 1057 (1973); Angew. Chem. internat. Edit. *12*, 1016 (1973).
[7] Similar shifts of C-3 in *(7)* (87.45 ppm) and *(8d)* (82.80 ppm). We thank Dr. *S. Berger* for help with the NMR measurements.
[8] The structure of compounds *(8a)*–*(8e)* are proved by NMR, IR, UV, and mass spectra. *(8a)*—*(8c)* are readily hydrolyzed to *(8d)* m.p. 44.5 °C).
[9] *G. A. Olah, J. S. Staral*, and *G. Liang*, J. Am. Chem. Soc. *96*, 6233 (1974); *C. Krüger, P. J. Roberts, Y.-H. Tsay*, and *J. B. Koster*, J. Organometal. Chem. *78*, 69 (1974).

ABSTRACTS

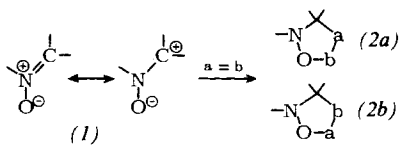
Reviews

Abstracts of selected progress reports and review articles

Alterations of skeletal muscle enzymes during aging have been investigated by *G. Kaldor* and *B. K. Min*. Old rats possess a higher Ca^{2+}-stimulated but lower Mg^{2+}-stimulated myosin A ATPase activity than young animals Significant differences were also shown in the inhibition of Mg^{2+}-stimulated myosin B ATPase by complexing agents, the number of free thiol groups in myosin, and the peroxidation of lipids in the muscle tissue. [Enzymatic Studies on the Skeletal Myosin A and Actomyosin of Aging Rats. Fed. Proc. *34*, 191—194 (1975); 13 references]

[Rd 787 IE—R]

1,3-Dipolar cycloadditions of nitrones (azomethine oxides) *(1)* are reviewed in an article by *D. St. C. Black, R. F. Crozier*, and *V. C. Davis*. Nitrones *(1)*, which are simple derivatives of carbonyl compounds, behave as 1,3-dipoles in thermal cycloadditions; they react with the multiple bonds of the dipolarophiles a=b (CC-, CS-, CP-, CN-, NS-, NP-bonds) to give five-membered heterocycles *(2a)* and/or *(2b)*. The cycloadducts obtained on heating the two components in inert solvent are not always stable and partly undergo further interesting transformations. The sequence nitrone (usually aldonitrone) → cycloadduct and cleavage often affords a new carbonyl compound. The additions of *(1)*, to alkynes, dehydrobenzene, alkenes, allenes, ketenes, nitriles, isocyanates, isothiocyanates,



carbodiimides, azetidinium and aziridinium salts, to CP-bonds (phosphoranes), to *N*-sulfinyl compounds and to iminophosphoranes are described. Several preparative examples are given. [1,3-Dipolar Cycloaddition Reactions of Nitrones. Synthesis *1975*, 205–221; 135 references]

[Rd 793 IE—M]

Chemical methods of oligonucleotide synthesis are outlined in an article by *R. I. Zhdanov* and *S. M. Zhenodarova*. A discussion of the methods for protecting functional groups (amino groups of heterocyclic bases, hydroxy groups of nucleosides and nucleotides, phosphomonoester groups of nucleotides) is followed by a section devoted to methods for the synthesis of natural internucleotide bonds: phosphorylation with halophosphates, use of activating agents (*e.g.* carbodiimides and arenesulfonic acid derivatives), and oxidation of nucleotide phosphoroamidates and nucleoside phosphites. The article closes with a discussion of methods for the synthesis of oligonucleotides: oligodeoxyribonucleotides by the blockwise or triester method; oligoribonucleotides by means of nucleoside 3′- or 5′-phosphates, by use of unprotected nucleosides and nucleotides, and ribonuclease-catalyzed syntheses. Finally, syntheses on polymer carriers are dealt with. [Chemical Methods of Oligonucleotide Synthesis. Synthesis *1975*, 222–245; 277 references]

[Rd 794 IE—M]

Homogeneous catalytic activation of C—H bonds in arenes and alkenes is reviewed in an article by *G. W. Parshall*. In the classical substitution method the reagent is actived to such an extent that the C—H bonds are attacked. Transition metal complexes with or without hydride ligands, on the other hand, attack the C—H bonds of the substrate. Thus $TaH_5[(CH_3)_2PCH_2CH_2P(CH_3)_2]_2$, like other hydride complexes, catalyzes H/D exchange in benzene; when a solution of $NbC_2H_5(C_5H_5)_2(C_2H_4)$ in D_6-benzene is heated, large amounts of deuterium appear in the ethyl and ethylene ligands. The reaction

$$C_6H_6 + Al(C_2H_5)_3 \rightarrow C_6H_5Al(C_2H_5)_2 + C_2H_6$$

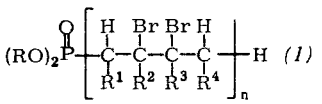
catalyzed by $NbH_3(C_5H_5)_2$, for example, has synthetic value. Even methane and ethane undergo exchange with D^+ in the presence of $PtCl_4^{2-}$. [Homogeneous Catalytic Activation of C—H Bonds. Accounts Chem. Res. *8*, 113—117 (1975); 37 references]

[Rd 796 IE—L]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Flame-resistance is conferred on thermoplastic plastics by means of bromine-containing telomeric phosphonic esters *(1)*



(1)

R = alkyl (C_1—C_8); R^1, R^2, R^3, R^4 = H, halogen, alkyl (C_1—C_4); n = an integer between 2 and 30

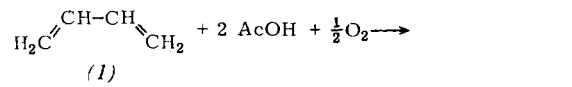
which are obtained by bromination of unsaturated telomeric phosphonic esters prepared by radical telomerization of 1,3-dienes and dialkyl phosphites. [DOS 2329924; Farbwerke Hoechst AG, Frankfurt/M]

[PR 280 IE—D]

Impact-resistant modified polyamides of the type of nylon-6 or -6,6 are obtained by dispersing in them a reaction product of an elastomer containing carboxyl groups and a diepoxide at 230 to 290 °C. The elastomer phase couples by chemical reaction to the polyamide-resin phase. The elastomers should contain 1.5 to 4 carboxyl groups per molecule; copolymerizates of acrylic acid with butadiene, chloroprene, acrylates, acrylonitrile, or methacrylonitrile are used. Suitable diepoxides are diglycidyl ethers of butanediol, resorcinol, or bisphenol A. The modified polyamides are used for the production of automobile parts such as fenders and hoods. [DOS 2356899; Ford-Werke AG, Köln]

[PR 282 IE—W]

2-Butenylene diacetate (1,4-diacetoxy-2-butene) *(2)* can be obtained by acetoxylation of butadiene *(1)* in the liquid phase at 80 °C and 30 bar with a reaction gas containing 10% of O_2. The solvent is the reactant acetic acid; the catalyst used is palladium/active charcoal/carrier to which additions of Sb, Bi, Te, and/or Se may be made. Up to 10% of the 1,2-isomer is obtained along with 90% of *(2)*. Other dienes



(1)

$$+ 2\ AcOH + \tfrac{1}{2}O_2 \longrightarrow AcOCH_2{-}CH{=}CH{-}CH_2OAc + H_2O$$

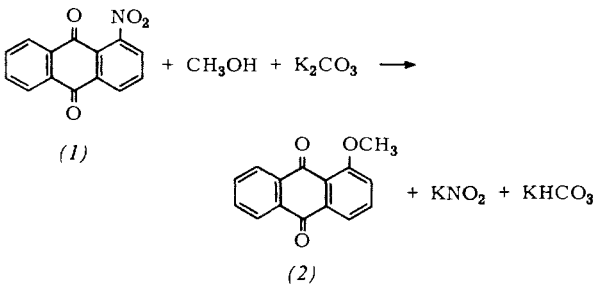
(2)

Ac = CH_3CO

such as isoprene, 2,3-dimethylbutadiene, and piperylene are converted into the corresponding esters. The products are starting materials for the preparation of diols; for example, 1,4-butanediol is obtained from *(2)*. [DOS 2424539; Mitsubishi Chemical Industries, Ltd., Tokyo (Japan)]

[PR 286 IE—G]

Anthraquinone α-methyl ethers are obtained by treatment of α-nitroanthraquinones with an excess of methanol in the presence of at least the stoichiometric amount of anhydrous potassium carbonate, in high yields per unit time and in high purity. For example, 1-methoxyanthraquinone *(2)* is



(1) *(2)*

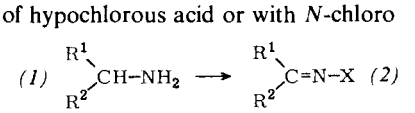
formed from 1-nitroanthraquinone *(1)* (120 °C, 6 bar, 5 h). 1,5- and 1,8-dinitroanthraquinone are similarly converted into dimethoxyanthraquinones. The yields are almost quantitative. α-Methoxyanthraquinone and its derivatives are valuable dyestuff intermediates. [DOS 2314696; Badische Anilin- & Soda-Fabrik AG, Ludwigshafen]

[PR 285 IE—G]

Process for the preparation of ethylene-propylene-diene terpolymers (ethylene-propylene rubber), consists in carrying out continuous polymerization in at least two reactors placed in series, in such a way that the reacting mixture is cooled by evaporation of ethylene and that part of the vaporized ethylene is led from at least one downstream reactor to the next upstream reactor. An advantage of the method is that the expensive vanadium catalyst is better utilized, fewer monomers are obtained, and the molecular weights are greater than after polymerization in one reactor or in several reactors arranged in series without the ethylene being circulated. [DOS 2401295; E. I. du Pont de Nemours and Co., Wilmington (USA)]

[PR 281 IE—W]

***N*-Halo ketimines** *(2)* are obtained by halogenation of primary amines *(1)* with salts of hypochlorous acid or with *N*-chloro



(1) *(2)*

R^1 = alkyl, cycloalkyl, aralkyl; $R^2 = R^1$ including other substituents; X = bromine, chlorine

amides (imides) and subsequent elimination of hydrogen halide. [DOS 2338762; Bayer AG, Leverkusen]

[PR 284 IE—K]

Radical and ionic polymerization of ethylene is effected simultaneously at 220 to 270 °C and pressures of more than 1000 bar if the catalyst used is a combination of titanium trichloride, a titanium alkoxide, and an alkylaluminum compound such as diethylaluminum chloride, sometimes with the addition of a complexing agent such as silicone oil. [DOS 2350782; Ethylene-Plastique S. A., Courbevoie (France)]

[PR 289 IE—W]

Hydrogen Bonding. By *M. D. Joesten* and *L. J. Schaad.* Marcel Dekker, Inc., New York 1974. 1st Edit., vi, 622 pp., $ 45.—.

In his foreword, *M. D. Joesten* writes that this monograph should contain a high percentage of papers on hydrogen bonds that have appeared since *Pimentel* and *McClellan's* book (The Hydrogen Bond. Freeman, San Francisco 1960). In fact the book contains almost 3000 references, and half of it is taken up by indexes and tables. Most of the English-language literature from 1960 to 1973 inclusive is handled, but that in foreign languages (German, French, Japanese, Russian, *etc.*) is almost ignored. Nevertheless, this is an invaluable bibliography. Particularly praiseworthy is the clear presentation of the thermodynamic results (40 pages), while the collection "correlations" (of, *e.g.* spectral shifts in the IR and NMR spectra) occupies only 60 pages.

Almost half of the actual text is taken up by a chapter on the theory of hydrogen bond formation, written by *L. J. Schaad*; this includes a very useful introduction to the quantum-chemical methods used, but unfortunately there is no list of contents for this section of more than 100 pages.

The price, 45 dollars, seems rather high for a book that is not printed by classical methods but produced photomechanically.

Ernst Lippert [NB 264 IE]

Mathematik für Chemiker (Mathematics for Chemists). By *H. G. Zachmann.* Verlag Chemie GmbH, Weinheim, Germany, 1974. 2nd Edit., XVIII, 664 pp., bound DM 64.—.

The second, expanded and improved edition of this notable book is now available. The fact that a new edition is required after only two years from first going to print shows that the book has found a large circle of interested readers.

In the review of the first edition[1] it was noted that in many places the text went beyond what would be required for their normal study by chemists interested mainly in preparative or analytical work and that some very elementary mathematical laws were mentioned only in passing. This choice of material is, however, by no means regrettable, since there are sufficient mathematical texts for chemists dealing with very much simpler problems.

While there is little point in repeating the table of contents, it should be noted that new chapters on n-dimensional vector space and on reciprocal space have been introduced in the section on vector calculations. In addition, the sections on the solution of differential equations and on group theory have been considerably expanded, so that in its present form the book differs considerably from the first edition. The libraries of Institutes and Seminars are recommended to obtain this, again excellently produced, volume.

Although the author has taken great trouble to remove misprints there remains, as usual, an unavoidable residue of errors that should be corrected in the next edition which will certainly soon be required.

In this connection the following may be noted: on the left-hand side of eq. (2) on p. 132 the square of the vector magnitude would be better written in the form $|a|^2$.

In Table 1 on p. 220 the range of the definition is sometimes (cf. *e.g.* the first derivations of $\tan x$, $\cot x$, $\sin^{-1} x$, and $\cos^{-1} x$) not provided with the necessary additional limitations, *i.e.* the polar positions are not excluded.

On p. 290, line 1 should read "$n-2$ and $m=3$".

The last term of the Wronski determinant [eq. (109)] on p. 475 is wrong. Correspondingly, in the text (penultimate line of the first sentence), "$y^{(n)}$" should be replaced by "$y^{(n-1)}$".

It is to be hoped that *Zachmann's* book will find a place in research and teaching that corresponds to its real value.

Perhaps at a suitable time this book can be made accessible to a large circle of students by means of a cheaper paperback edition.

Theodor Ackermann [NB 266 IE]

[1] Cf. Angew. Chem. *85*, 835 (1973); Angew. Chem. internat. Edit. *12*, 866 (1973).

Programmierte Prüfung. Chemie, Physik, Physikalische Chemie (Programmed Learning. Chemistry, Physics, and Physical Chemistry). By *W. Klein* and *H. Mayer*, Verlag Chemie, GmbH, Weinheim 1974. 1st Edit., 376 pages, paperback, DM 16.80.

Problems with several possible answers do not comprise all that can be acquired from teaching, yet they are popular because the results can be simply evaluated. In their book *Klein* and *Mayer* set out test exercises in the fields of general inorganic, organic, and physical chemistry, physics, and laboratory techniques that can be used in the training of chemistry laboratory technicians. By working through this book one can evaluate his own knowledge, since the number of points that he has accumulated fits into a scheme set up for the results of the test.

On looking carefully through the test exercises one is struck by how hard it is to find useful problems and several answers. Careless formulation leads so easily to errors. It should not be stated that atoms are the smallest particles of an element that show all the properties of the element (p. 15, problem 2), since where do single atoms have the properties of the element? Similar doubt attaches to the statement (p. 128, problem 59): Compounds with one asymmetric C atom rotate the plane of polarized light. Mesotartaric acid actually contains two asymmetric C atoms but is nevertheless optically inactive. The concept of a mole is nowadays defined differently (p. 16, problem 4), and the concept of a gram-atom is no longer used (p. 17, problem 8). Since oxidation number is defined, oxidation and reduction reactions should be described with its use. Not all reactions with hydrogen are reductions according to the expanded definition (p. 26, problem 36), *e.g.* lithium is oxidized on reaction with hydrogen.

The authors should think again about the formulations of many of the test exercises and their answers, perhaps even set them up again in relation to a modern curriculum.

In spite of some limitations, multiple-choice exercises such as the ones in this "Programmed Learning" are a great help in teaching, and it would thus be very welcome if the authors would further develop their test program.

H.-J. Schmidt [NB 267 IE]

Römpps Chemie-Lexikon (Römpp's Chemistry Lexicon). By *O.-A. Neumüller.* Franck'sche Verlagshandlung, W. Keller & Co., Stuttgart 1974. 7th Edit., Vol. 4, M—Pk, 689 pp. + 14 pp. of appendices, 207 figs., bound, DM 160.—.

Volume 4 appeared at the end of 1974, beginning with μ and ending with pK value; it contains about 100 pages more than the comparable part of the sixth edition. This expansion is due to the inclusion of new key-words, *e.g.* from the field of medicine (parkinsonism, paradontosis, gastric

juices, *etc.*), of concepts such as Nuclear Science Abstracts and partial structures, and new research fields such as lunar rocks from lunar chemistry. Furthermore, the text under some of the older existing key-words has been considerably expanded (pK value by 400%, nucleic acids by 100%) or supplemented by illustrations (offset printing). The preparations published in the "old Römpp" have been critically examined; many have been omitted because production has ceased, but new ones have been inserted (*e.g.* Parko KS 12, Parleam, Monflor). Sensibly, prices for products are omitted since they are in any case of only transitory value. In a lexicon one expects to find not only the newest key-words but also those concepts that are no longer in use but can be found in the older literature; account has been taken of this in the 7th edition: one finds, for example, parmone, the older designation of α-ionone, and masurium (now called technetium). Generally speaking, it can be reported that each key-word has been worked over completely and with great care and has been brought up to latest knowledge, while sensible abridgments are made throughout. It is not rare to find citations from 1973 and even 1974. In all this praiseworthy work on Volume 4 *O.-A. Neumüller* has been helped by *B. Bolle*, *E. Brzitwa*, *K. Esser*, and *Kurt Siekmann*.

Owing to the increased costs of production Volume 4 costs DM 35.— more than Volume 3[1]. This, however, in no way decreases the favorable impression left by turning the pages of this book. It should be available as a reference volume in their work to as many of our colleagues as possible.

Christian Weiske [NB 268 IE]

[1] Cf. Angew. Chem. *86*, 488 (1974); Angew. Chem. internat. Edit. *13*, 487 (1974).

Reactive Intermediates in Organic Chemistry. By *N. S. Isaacs*. John Wiley, London 1974. 1st Edit., XIII, 550 pp., numerous figs. and tables, bound, £ 12.00.

Unlike other books that have recently appeared on the subject of mechanistic organic chemistry, this book attempts to present its extensive field from the viewpoint of intermediates.

The volume is divided into ten chapters, of which the first (91 pp.) with the title "Physical Principles of Organic Chemistry", deals especially with the general fundamentals, *e.g.* matters of energetics and kinetics, solvent and isotope effects, methods for the detection of intermediates, stereospecificity, and a short introduction to orbital symmetry considerations. Subsequent chapters provide information on the actual intermediates: carbenium ions (108 pp.), neighboring group participation and nonclassical ions (34 pp.), carbanions (60 pp.), radicals (80 pp.), carbenes (33 pp.), dehydrobenzenes (14 pp.), tetrahedral intermediate states in reactions of carbonyl groups (23 pp.), and intermediate stages in oxidations (34 pp.). In the last chapter are collected the intermediates that are less easily assigned, for example those that are important in acid-, enzyme- or metal-catalyzed reactions. To eight chapters sufficient bibliography is assigned to provide rapid access to the literature that takes the matter further or deeper. It is good to see that at suitable places in the text there are introductions to modern spectroscopic methods (*e.g.* ESR, ^{13}C-NMR, CIDNP, and ion cyclotron resonance), but in view of the size of the book these are kept very short. The book ends with a subject index of 6 pp., which could well have been longer for a volume of more than 500 pages.

The author has consistently treated the material according to the nature of the intermediate involved, and this has the advantage that themes such as aromatic electrophilic substitution, olefin addition, and chemistry in superacid media are found presented together. Information about aromatic substitution must, however, then be sought in different chapters according to the intermediates involved. Reactions without discrete intermediates (*e.g.* S_N2 reactions, electrocyclic reactions, sigmatropic shifts that do not occur by way of ions) are only mentioned, in line with the author's intentions.

Energy parameters are given only in joules, right from the beginning of the book. An indication of the conversion factor into a unit more familiar to chemists, namely the calorie, would have made this change in practice easier to follow.

This fluently written and easily readable book is worth studying for its wide scope, particularly by younger students of organic chemistry and by those wanting to be rapidly informed about mechanistic questions in organic chemistry. However, the reader should adopt a critical attitude because misprints and inaccuracies in the structural formulas and tables are not uncommon; this should not influence too severely a wide distribution of this otherwise useful work.

Dieter Hasselmann [NH 271 IE]

Selenium. Edited by *R. A. Zingaro* and *W. Ch. Cooper*. Van Nostrand Reinhold Comp., New York 1974. 1st Edit., XVII, 835 pp., numerous figs. and tables, bound, £ 25.00.

835 pages about a single element in the periodic table: one cannot fail to be impressed by the wealth of knowledge that has been accumulated since the discovery of selenium by *Berzelius* in 1817. The discouragement that immediately sets in because of the size of the book disperses rapidly on reading. The editors have divided the material very skillfully into 16 reviews by 24 authors. What, however, would have been very useful is a readable summary of each chapter; in most of them there are passages of historical review entitled "Introduction".

The "schizophrenic chemical personality" of selenium is extensively illustrated; the organization of the book is easy to follow. After two introductory chapters on the history and occurrence of selenium and on its preparation and purification weight is first laid on description of the structure of the element in its various modifications, on its interaction with light, and on its optical and electrical properties. The second main part concerns the chemistry of selenium, and there structural problems and the organic compounds of selenium are presented in special detail. Inclusion of solid ternary metal selenides would have been desirable at this stage, since the investigation of ternary oxides and sulfides is nowadays a very wide field, so that interesting structural comparisons could have been set up. Much of the inorganic chemistry of selenium in aqueous solutions is contained in the chapter on the analysis of selenium.

The last part of the book could be described as a "Special Chapter". The topics discussed there are the element's toxicology, selenium in agriculture and in metallurgy, in xerography, in elastic and plastics materials, and in the glass industry. Again and again the many-sided properties of this element pinpoint its strange character, making it of interest to a whole series of scientific and related disciplines and to many scientists for whom this book, with its sometimes several hundered references per chapter, is a mine of information. All in all, it can be said that the book provides a pattern for future compilers of "element monographs".

Gunther Dittrich [NB 273 IE]

Houben-Weyl: Methoden der organischen Chemie. Edited by *E. Müller*. Georg Thieme Verlag, Stuttgart 1974. 4th, completely revised edit. Vol. 15: Synthese von Peptiden (Synthesis of Peptides). Edited by *E. Wünsch*, written by *M. Deffner, K.-H. Deimer, E. Jaeger, P. Stelzel, P. Thamm, G. Wendlberger*, and *E. Wünsch*. Part 1: XLIII, 1006 pp., 3 figures, 86 tables, bound, DM 540.—. Part 2: XXXVI, 806 pp., 85 figures, 67 tables, bound, DM 440.—.

The chemistry, physical chemistry, and biology of peptides and proteins have made immense strides since du Vigneaud published the first total synthesis of a peptide hormone, oxytocin, in 1953. As the universal building blocks of life, amino acids stimulated chemists to the synthesis of biologically active peptides or their partial sequences. In spite of many review articles it has become increasingly more difficult for the peptide chemist engaged in preparation work to have at his fingertips the complete arsenal of the techniques of peptide chemistry. This gap has now been filled astonishingly well by the present reference work.

Part 1 is divided into three main sections. In the first ("Classification and Nomenclature of Peptides and their Derivatives"; 28 pages) the nomenclature of amino-acid derivatives and the various types of peptides is explained clearly and in great detail. The second section ("Fundamentals of Peptide Synthesis"; 18 pages) gives the principles of peptide-bond formation (mechanistic explanation of activation systems) and the strategies for polypeptide synthesis (stepwise synthesis, condensation of fragments, universal protecting-group technique, least possible masking of unrequired functional groups, and peptide syntheses on solid and liquid polymeric carriers).

The most extensive main section (860 pages), on details of methods, treats the "Blocking and Protection of the α-Amino group" (260 pages), "Blocking and Protection of the α-Carboxyl Group" (150 pages), and "Polyfunctional Amino Acids and their Utilization in Peptide Syntheses" (360 pages). All the protecting groups of α-amino and α-carboxyl groups are presented, with consideration of the literature up to 1973 (and in part to 1974)—since the introduction of benzyloxycarbonyl protection in 1932 there have been 60 variations of protection as urethanes alone. The reactions are described with the aid of clear formula schemes and, so far as they are known, with statement of the reaction mechanisms. Critical evaluation of the protecting groups, in particular those of proved value for syntheses of natural products, as well as indications of possible side reactions and, when known, how to prevent them, together with detailed data on the stability and ease of removal provide the peptide chemist with a wealth of information; this is supplemented by many tables containing analytical data for the amino-acid derivatives known so far, as well as tables of reagents for cleavage reactions (with solvent, time, and temperature data) and also the side reactions and their avoidance. These tables are particularly valuable for the polyfunctional amino acids (Lys, Arg, Glu, Asp, Ser, Thr, Tyr, Cys, *etc.*); an excellent review is thus provided of the many combination types of α,ω-protecting groups; here too the extensive data on the stability and selective or total removal of the individual α- and ω-protecting groups illustrate the great experience of the authors and their extremely careful search of the original literature. Of greatest value are the selected experimental directions for the introduction and removal of the most important protecting groups—often several methods with a discussion of their advantages and disadvantages, depending on the amino acid used. These directions are often expanded to include the next steps in the peptide synthesis: synthesis of an activated ester, peptide coupling, selective removal of the α-amino group, selective removal or alteration of the α-carboxy protecting group, and renewed peptide coupling.

Further, short chapters deal with subsequent introduction of the α(ω)-amino group, subsequent introduction of the α-carboxyl group and the α-carboxamido group, as well as diaminodicarboxylic acids and their utilization in peptide synthesis. Moreover, there is for the first time a clear collection of information about pseudo-amino acids and their behavior in peptide synthesis, including α- and β-hydroxy acids, α- and β-thiol acids, α-(1-aza)- and β-(2-aza)-amino acids, α- and β-amino sulfonic acids, and α- and β-amino phosphonic acids.

Part 2 is devoted mainly to "Formation of the Peptide Bond" (364 pages). There is a detailed description of the many possible methods of forming the peptide bond that result from the presence of several functional groups in the amino acid molecule, and of the special requirements to ensure the necessary retention of configuration. Activation of the carboxyl group by active esters, acid anhydrides, lactims, acetals, hydroxylamino esters, anhydrides with acids of sulfur, phosphorus, silicon, or boron, by azides, diimides, azoles, acylamines, thioesters, selenoesters, or acyl halides is described and critically evaluated. Preparative examples of the preparation of activated carboxy derivatives and their use for peptide coupling, indications of their successful application to the synthesis of natural products, and finally detailed tables of the corresponding amino acid derivatives offer invaluable practical aid. Other chapters deal with the "Preparation of Heterogeneous O(S) Peptide Bonds" (30 pages), "Synthesis of Polypeptides" (30 pages) by polycondensation or copolycondensation, and "Tests for Racemization during Coupling Methods (24 pages).

In addition to chemical reactions, in peptide synthesis the "Testing and Representation of the purity of Synthetic Peptides" (274 pages) makes particular demands on the peptide chemist. A wide selection of methods of analysis and preparative separation techniques has been developed for checking the individual steps of the synthesis and for demonstrating the constitutional and configurational homogeneity of the intermediates and end products; these too are described, as are the testing for optical purity and spectroscopic and enzymatic methods. Preparative methods of purification, such as column chromatography and electrophoresis, are illustrated by examples from the synthesis of natural products and are supplemented by extensive tables that detail column packings, column dimensions, eluents, and experimental conditions.

The production, graphical presentation, tables, and the printing of both volumes are of excellent quality. Each volume contains detailed author and subject indices and a special subject index for experimental details, purification, and tests of identity. It is very welcome to find the references placed at the foot of the relevant text page, and special mention must be made of the range and the accuracy of the citations—there can hardly be any publication on peptide synthesis that has not been included. Thus, these two volumes constitute the most comprehensive and up to date review of preparative peptide chemistry, not only providing a general source of information but also, in particular, standing by to advise on special questions concerning preparations. The authors and the editor are to be congratulated without any reservations. The volumes should be by the side of every peptide chemist, not just on a shelf in the library.

Eberhard Schröder [NB 274 IE]

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 10
October 1975
Pages 655–720

Properties of Sulfur-Sulfur Bonds[**]

By Ralf Steudel[*]

Dedicated to Professor Richard C. Lord on the occasion of his 65th birthday

SS bonds are extraordinarily flexible and have properties that are observed only on isolated occasions for other homonuclear bonds: the bond lengths vary between 1.8 and 3.0 Å, the bond angles between 90 and 180°, and the dihedral angles between 0 and 180°; the bond energies amount to up to 430 kJ/mol. The SS stretching frequencies can appear over the range 177–820 cm^{-1} and force constants of 1.4 to 6.3 mdyne/Å have been calculated. This variability is illustrated with examples containing isolated and cumulated SS bonds.

1. Introduction

Sulfur-sulfur bonds are found in numerous inorganic, organic, and biologically interesting compounds. One of the causes of this may be seen in the high bond energy of SS single bonds, which at 265 kJ/mol takes third place among all homonuclear single bonds and is exceeded only by H_2 (435 kJ/mol) and the CC single bond (330 kJ/mol).

Bonds are characterized better by their lengths (d) and valence force constants (f_r) than by bond energies; these two parameters d and f_r are generally determinable more accurately and more easily, and they will therefore be used preferentially in the present review.

The simplest compounds with SS single bonds are disulfane H_2S_2 and dimethyldisulfane $(CH_3)_2S_2$, and these two molecules display many of the factors important for the structure of polysulfur compounds.

[*] Prof. Dr. R. Steudel
Institut für Anorganische und Analytische Chemie der Technischen Universität,
1 Berlin 12, Strasse des 17. Juni 135 (Germany)

[**] Based on lectures in Hoechst AG, Frankfurt/Main (Nov. 7, 74), at the Technical University Berlin (Dec. 2, 74) and at the Universities of Marburg (Jan. 6, 75), Heidelberg (Feb. 3, 75), Würzburg (Feb. 17, 75), Erlangen-Nürnberg (Feb. 18, 75), and Düsseldorf (April 9, 75, Chemiedozententagung).

2. Compounds with Isolated SS Single Bonds

2.1. Disulfane

It has been proved by electron diffraction[1] and microwave spectroscopy[2] that H_2S_2 has a molecular structure (Fig. 1) analogous to that of H_2O_2. The three bonds are formed

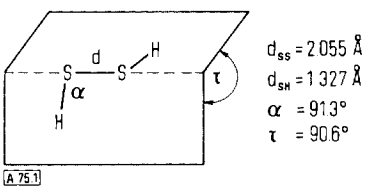


Fig. 1. Gas-phase structure of H_2S_2 (symmetry C_2).

by overlapping of the orbitals 3s, $3p_x$, and $3p_y$ of the S atoms with the H1s orbitals (orbital energies: H1s = −13.6, S3s = −20.7, and S3p = −11.7 eV)[3]. Thus, there is a free electron pair in the 3p orbital on both S atoms, this orbital being perpendicular to the two bonds (Fig. 2). In this way the possibilities shown in Fig. 3 arise for the mutual orientation of these two 3p orbitals.

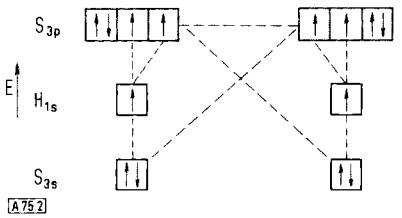


Fig. 2. Combination of the atomic orbitals of sulfur and hydrogen for the formation of the bonds in H_2S_2.

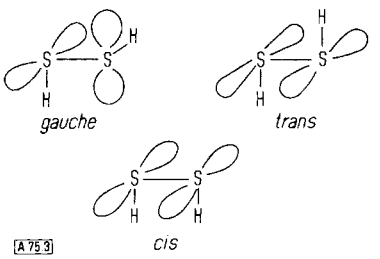


Fig. 3. Relative orientations of the p_π-electron pairs in H_2S_2 at various dihedral angles.

The appreciable size of the $3p_\pi$ orbitals leads to an interaction whose strength depends largely on the dihedral angle τ. From the overlap of these two orbitals there result two molecular orbitals that are both fully occupied (Fig. 4). Owing to the asymmetry of the splitting the destabilization of the system by the antibonding electrons in the π^*-MO is not fully compensated by stabilization of the electrons in the bonding π-MO, *i. e.* a repulsion results, and thus a weakening of the SS bond. The repulsion is greatest at $\tau=0$ and 180°, while it disappears at 90° and at 270° because of the orthogonality of the two orbitals. Each of the last-mentioned two rotamers, which are energetically equivalent, thus corresponds to an energy minimum, so that the reason for the dihedral angle $\tau=90.6°$ in H_2S_2 becomes easy to see.

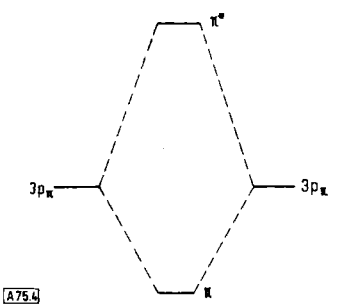


Fig. 4. Splitting of the $3p_\pi$-orbitals of the two neighboring S atoms into two molecular orbitals. The amount of the splitting depends on the dihedral angle and vanishes at $\tau=90°$.

Quantum-chemical calculations carried out by various procedures give a dependence of the total energy on the dihedral angle as illustrated schematically in Fig. 5[4–9]. The energy minimum is at about 90°. For the height of the rotation barrier at $\tau=0$ and 180° the calculations yielded very different values, but in all cases a higher energy was obtained for the *cis*-configuration (symmetry C_{2v}) than for the *trans*-configuration (symmetry C_{2h})—as could be expected from the additional repulsion of the H atoms at $\tau=0°$. The mean rotation barrier in H_2S_2 has been determined experimentally as 8—29 kJ/mol by various procedures that in some cases involved use of older, not very accurate, structural parameters[10–12].

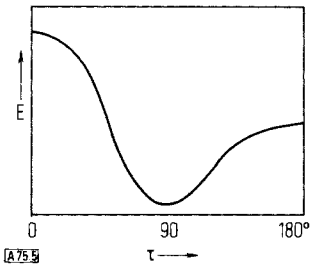


Fig. 5. Dependence of the total energy of H_2S_2 on the dihedral angle.

The above makes it clear that the H_2S_2 molecule has the optimal geometry with respect to the dihedral angle. The same is true for the bond angle, which at 91.3° is of similar small size to that in H_2S (92.2°[13]. Quantum-chemical calculations have shown that the partial charges on the H atoms in H_2S are negligibly small ($<0.05e$[14]). This finding, together with the small bulk of the H atoms, explains the small size of the bond angle, since the H···H and H···S repulsions are thereby reduced to a minimum[15]. However, considerably wider angles are to be expected when H is replaced by organyl groups or electronegative atoms (halogens).

That steric hindrance and electron-pair repulsion play a minimal role in H_2S_2 is thus derived from the values of the angles α and τ; the SS bond can thus be considered as a normal single bond, and the bond length $d=2.055$ Å can be used as a reference value for the discussion of other bond lengths. The covalent radius of the S atom follows therefrom as 1.03 Å.

2.2. Dimethyldisulfane

The structure of CH_3SSCH_3 resembles that of H_2S_2. The molecular parameters found by electron diffraction[16] and microwave spectroscopy[17] are as follows: $d_{SS}=2.03$ Å, $d_{CS}=1.81$ Å, $d_{CH}=1.10$ Å, $\alpha(CSS)=103°$, $\tau=84°$. The SS bond length corresponds to that of a single bond, especially as values of 2.05 ± 0.03 have been observed for many other disulfanes too.

The fact that the bond angle α is considerably greater than for H_2S_2 can be ascribed to repulsion between the methyl groups and the next-but-one S atoms. The C···S bond lengths at 3.0 Å are smaller than the van der Waals separation (3.4 Å), which results in mutual penetration of the atoms concerned. With $\alpha=90°$ the C···S separation would indeed be only 2.7 Å.

The dependence of the total energy on τ is similar for CH_3SSCH_3 to that for H_2S_2 (Fig. 5). The calculated[18, 19] and experimentally determined[20] rotation barriers are also of the same order of magnitude.

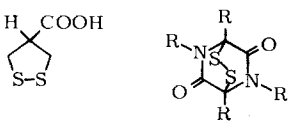
2.3. Other Disulfanes

Organyl-substituted disulfanes (RSSR) have, in general, a geometry corresponding to that of CH_3SSCH_3, and d_{SS} is usually near 2.05 Å[21]. d_{SS}, α, and τ are, however, dependent on R, which is due to various effects.

In the PE spectra of diorganyldisulfanes[18, 22, 23] a splitting of the first band is observed, corresponding to ionization

from one of the $3p_\pi$ orbitals (Fig. 4). These two orbitals—or, more accurately, the molecular orbitals formed from them—are always the highest occupied orbitals in the molecule. Since the first band in the spectrum of monosulfanes (RSR) is always unsplit, the cause of the splitting must be sought in p_π-p_π interaction. For CH_3SSCH_3 the splitting amounts to 0.24 eV, but it becomes larger if the dihedral angle is increased by steric repulsion as in $(CH_3)_3CSSC(CH_3)_3$ ($\tau = 97°$, $\Delta E = 0.65$ eV), or by inclusion of the disulfane group into a small ring, which also may cause the dihedral angle to deviate appreciably from 90° [*e.g.* for $(CH_2)_4S_2$: $\tau \approx 60°$[24], $\Delta E = 0.95$ eV].

If the dihedral angle is very greatly decreased by inclusion of the disulfane group in ring molecules, then the electron-pair repulsion becomes so much greater that an increase in the SS bond length is clearly observed, for example in the saturated rings of 1.2-dithiolane-4-carboxylic acid[25] and of sporidesmines[26, 27]:



$\tau = 27°$ $\quad$ $\tau = 8.5°$

$d_{SS} = 2.096$ Å $\quad$ $d_{SS} = 2.096$ Å

For four- and five-membered rings the normal value of the SS bond length can be set at 2.10 Å.

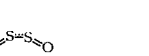
Dependence of the SS stretching vibration on the dihedral angle, as expected from the preceding results, was postulated in 1973[28] and was also made probable by calculations for the case of CH_3SSCH_3[29], but it has been disputed[30] since clearly other effects can also play a part, *e.g.* the conformation of the substituents[31].

The SS bond is found to be considerably more sensitive to substitution than, for example, the CC bond. The examples in the table below show the strong influence of halogen atoms.

	d_{SS} [Å]	d_{SX} [Å]	α [°]	τ [°]	Ref.
Br–S=S–Br	1.98	2.24	105	83.5	[32]
Cl–S=S–Cl	1.931	2.057	108.2	84.8	[33]
F–S=S–F	1.888	1.635	108.3	87.9	[34]

These compounds have the same C_2 symmetry as H_2S_2. In FSSF d_{SS} approaches the value in SSF_2 (1.86 Å), which contains the shortest SS bond of any isolable compound. This behavior of the SS bond cannot be ascribed merely to the increasing electronegativity from Br to F, since the SS bond lengths in $(CF_3)_2S_2$, $(CF_3)_2S_3$, and $(CCl_3)_2S_3$ at 2.03—2.07 Å[35, 36] are normal although the electronegativities of CF_3 and CCl_3 derived from the inductive effect in other sulfur compounds[37] amount to about 3.7 and 3.1, respectively, and thus lie between those for F and Cl.

The recently discovered S_2O_2, which surprisingly is planar in the gas phase, is also related to the substituted disulfanes[38]:



$d_{SS} = 2.024$ Å, $d_{SO} = 1.458$ Å, $\alpha = 112.7°$, $\tau = 0°$

2.4. Variation of the SS Bond Lengths in Substituted Disulfanes

Various considerations of H_2S_2 from MO theory agree in providing the sequence and τ-dependence of the molecular orbitals shown in Fig. 6 which were constructed mainly from the atomic orbitals H1s, S3s, $S3p_x$, $S3p_y$, and $S3p_z$[6, 8, 18]. The 3d orbitals of the S atom also take part to a limited extent, particularly in the lowest unoccupied MOs. The two highest occupied orbitals (3b and 4a) are antibonding with respect to the SS bond. This characteristic and the τ-dependence shown in Fig. 6 do not change if H is replaced by CH_3[8]. If electrons are withdrawn by electronegative substituents, the occupation of these two antibonding orbitals is first diminished and the SS bond thus becomes stronger.

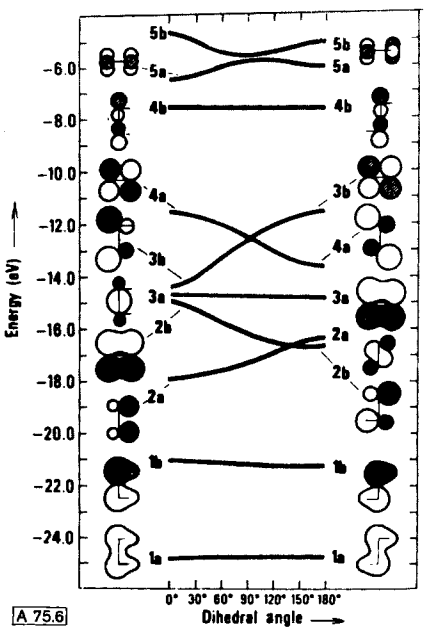


Fig. 6. Calculated orbitals for the H_2S_2 molecule and dependence of the MO eigenvalues on the dihedral angle. The shaded and the unshaded regions of the MOs have different signs. In the ground state all the MOs except 4b, 5a, and 5b are doubly occupied [8].

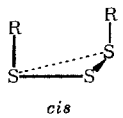
On the other hand, the lowest unoccupied MO of H_2S_2 *(4b)* is also antibonding with respect to the SS bond. Substituents that delocalize electrons in the S_2 unit should thus weaken the SS bond. In this way the deviations of the bond lengths in disulfanes from the normal value of 2.055 Å can be interpreted qualitatively.

3. Compounds Containing Cumulated SS Bonds

3.1. Structures

Among the many compounds with sulfur chains, the structures of the polysulfanes H_2S_n and dihalopolysulfanes S_nCl_2 and S_nBr_2 (all with $n > 2$) have not yet been elucidated; fluoropolysulfanes[39] and iodopolysulfanes[40] are unstable and cannot be obtained in the pure form. However, there are numerous diorganylpolysulfanes R_2S_n on which structural investigations have been carried out. Homocyclic[41] and heterocyclic[42] compounds containing cumulated SS bonds are also known.

The following geometric forms are possible for trisulfanes of the type R—S—S—S—R:



cis

trans (d und l)

The two *trans*-forms are mirror images of one another (d- and l-forms). Both *cis*- and *trans*-trisulfanes are known. With longer sulfur chains the arrangements can be all-*trans* or all-*cis* or in some form (designated "motif") alternatively *cis* or *trans*, and furthermore d-*trans* should be distinguished from l-*trans*. An all-*cis*-form exists in S_8[43] and is required for geometric reasons also for other, small, nonplanar rings; however, so far it has been demonstrated only for S_6[44], since the structures of S_7, S_9, S_{10}, and S_{11} have not yet been clarified[45]. S_{12} is the smallest ring so far with a regular alternating *cis-trans*-arrangement[46, 47] (Fig. 7). α-S_{18}, β-S_{18}, and S_{20} contain complicated motifs[47].

Fig. 7. Structures of S_6, S_8, and S_{12}. The atoms lie alternately in two or three parallel planes.

Table 1. Nuclear separations d_{SS} and q, valence angles α, dihedral angles τ, valence force constants f_r, and interaction constants f_{rr} for S_8, S_{12}, and S_6.

	S_8	S_{12}	S_6
d_{SS} [Å]	2.060 [a]	2.053	2.057
q [Å]	3.33	3.29	3.20
α [°]	108.0 [a]	106.6	102.2
τ [°]	98.8 [b]	87.5 [b]	74.5 [b]
f_r [mdyne/Å]	2.37	2.37	2.24
f_{rr} [mdyne/Å]	0.61	0.58	0.53

[a] Corrected for librations (uncorrected values: d_{SS} = 2.047 Å, q = 3.32 Å, α = 108.1°, τ = 98.6°).
[b] Calculated by the author from α.

In symmetrical ring molecules such as S_6, S_8, and S_{12}, structural data for which are given in Table 1, the bond and dihedral angles are no longer independent of one another, since for a given α ring closure is only possible at a value of τ that is completely predetermined, being dependent on the ring size and the motif[48]. Thus, in certain circumstances the dihedral angle cannot assume its optimal value, namely that corresponding to the minimum of the torsion potential. In sulfur chains and rings this optimal value is no longer 90°, since in these structures the p_π orbitals of the next-but-one atoms also overlap, to the greatest extent at τ = 90° or 270° (cf. Fig. 8). One can thus expect that the optimal dihedral angle will be somewhat larger or smaller than 90°. Unfortunately, the structure of any gaseous compound containing sulfur chains is not known. However, it follows from the structures derived by electron diffraction for S_2Cl_2 and S_2Br_2, in which the same interaction exists, that the energy minimum is reached at τ ≈ 85°.

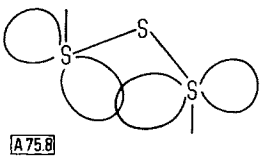


Fig. 8. Interaction of the $3p_\pi$-orbitals of next-but-one atoms in sulfur chains.

Because of the electron-pair repulsion between next-but-one atoms, the bond angle α departs from 90° in sulfur chains and rings. In most cases it is in the neighborhood of 106°. The colorless diamagnetic cation S_4^{2+} shows, however, that sulfur rings can also be stable when embodying quite different values of α and τ. On the basis of its Raman spectrum[49] and analogy with the square planar ions Se_4^{2+} and Te_4^{2+}, the ion S_4^{2+} probably has D_{4h} symmetry. Thus α = 90° and τ = 0°. d_{SS} can be estimated from the frequencies of the stretching vibrations (a_{1g}: 584, b_{1g}: 530, e_u: 460 cm^{-1}) by equation (4) to be 2.00 Å[50]. This value corresponds to the four-center π-bond assumed for this compound (cf. Fig. 9).

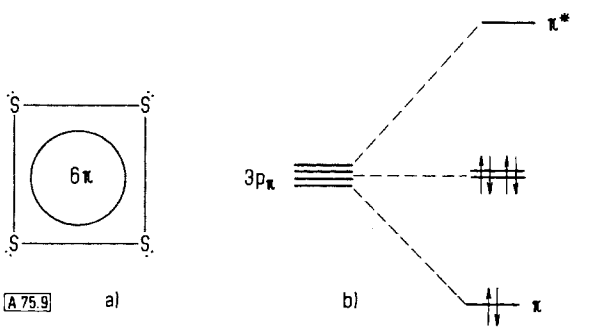


Fig. 9. Structure of the ion S_4^{2+} (a) and splitting of the four $3p_\pi$-atomic orbitals (b).

Although the electron-pair repulsions are different between nearest atoms as well as next-but-one neighboring atoms, the SS bond lengths in S_8, S_{12}, and S_6 are almost the same, although a slight trend toward weakening of the bond can be recognized if the uncorrected values are compared. The distance q between next-but-one nearest neighbors is greatest in S_8 and smallest in S_6, which corresponds to the stability sequence (Table 1).

3.2. Force Constants

S_6, S_8, and S_{12} are of particular interest at this point, because it was for these compounds that accurate force constants for cumulated SS bonds could first be determined. In all three cases the calculations are based on a modified Urey-Bradley force field. The Urey-Bradley force constants first determined were used for the calculation of the valence force constants that are a measure of forces retaining the atomic separations and angles in a molecule[51–53]:

f_r Bond stretching
f_{rr} Interaction between neighboring bonds.

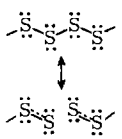
From the values in Table 1 it can be recognized that the forces retaining the separations in the SS bond are considerably smaller than those for the CC single bond (f_r(C—C) ≈ 4.4

mdyne/Å[54]). The SS bond is thus "softer" than the CC bond, since the action of a given force leads to a larger extension or compression of the former. It is therefore not surprising that inductive and other effects influence the SS bond much more strongly than would be expected from experience with carbon compounds.

With the aid of simplifying assumptions required because of the disparity between the number of observed molecular vibrations and the number of force constants, the f_r(SS) were calculated for H_2S_2 and $(CH_3)_2S_2$ to be 2.5 and 3.1 mdyne/Å, respectively[55, 56].

For S_8, S_{12}, and S_6, whose thermal and probably also thermodynamic stability decreases in that order, the values of f_r reflect the stability relationships correctly, *i.e.* the bond strength is greatest in S_8.

The values of the interaction constants f_{rr} are surprisingly high (Table 1). These constants denote the influence of bond stretching or compression on neighboring bonds. A positive value denotes that extension of an SS bond leads to a shortening of the neighboring bonds, which can be interpreted by assuming that the valence electrons rearrange during the vibration:



At 0.5—0.6 mdyne/Å the f_{rr}(SS) is very much larger than, *e.g.* f_{rr}(C—C)=0.10 mdyne/Å obtained for cyclohexane[54], and smaller values are also found even for comparable compounds such as $SiCl_4$ (0.23), PCl_3 (0.29), and SCl_2 (0.16)[57]. The strong bond-bond interaction must therefore be regarded as a characteristic property of cumulated sulfur bonds. The following consequences follow from the high value of f_{rr}:

1. If an SS bond in a sulfur chain is stretched under the influence of substituents, then the neighboring bonds are shortened, *i.e.* the bond lengths alternate.

2. SS bonds in sulfur chains are even "softer" than corresponds to the value of f_r, since approximately only the force $f_r - f_{rr}$ is required for the stretching of a bond with simultaneous contraction of the neighboring bond(s).

3. The dissociation energy for breaking a bond in a sulfur chain is considerably smaller than the bond energy (the arithmetical mean of all dissociation energies), since energy is gained by strengthening of the neighboring bond(s).

Proof of these statements will be given in the following sections.

Between the valence force constants f_r and the SS bond length we have the relationship:

$$f_r \cdot d^{7.26} = 460 \qquad (1)$$

which in log-log coordinates gives a straight line (Fig. 10). The corresponding equation

$$\log f_r = 2.66 - 7.26 \log d \qquad (2)$$

(d in Å, f_r in mdyne/Å) is valid for isolated as well as cumulated SS bonds[50]. By using this equation we can test the approximate values of f_r obtained under simplifying assumptions: thus, the f_r for SSF_2 (d_{SS}=1.86) was determined as 5.0[58] and for S_2O (d_{SS}=1.88) as 4.7 mdyne/Å[59], in good agreement with values calculated from equation (2) (calcd.: 5.1 and 4.7 mdyne/Å, respectively).

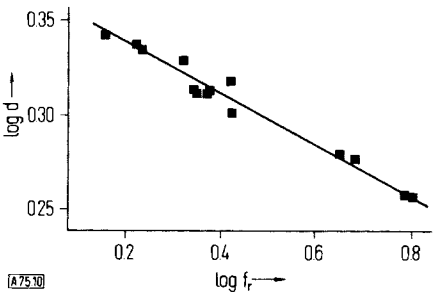


Fig. 10. Dependence of the force constants f_r [mdyne/Å] of SS bonds on the nuclear separations d [Å].

3.3. Stretching Frequencies ν_{SS}

From equation (1) it may be surmised that a relationship also exists between ν_{SS} and d_{SS}. For diatomic molecules or ions (S_2, S_2^-, S_2^{2-} *etc.*) ν_{SS} depends only on f_r, and by plotting ν_{SS} for BaS_2 and seven different states of S_2 against d_{SS} we obtain a straight line corresponding to the equation:

$$d_{SS} = 2.57 - 9.47 \times 10^{-4} \cdot \nu_{SS}; \quad 400 < \nu_{SS} < 820 \qquad (3)$$

where ν_{SS} is in cm^{-1} and d is in Å (cf. Fig. 11)[50].

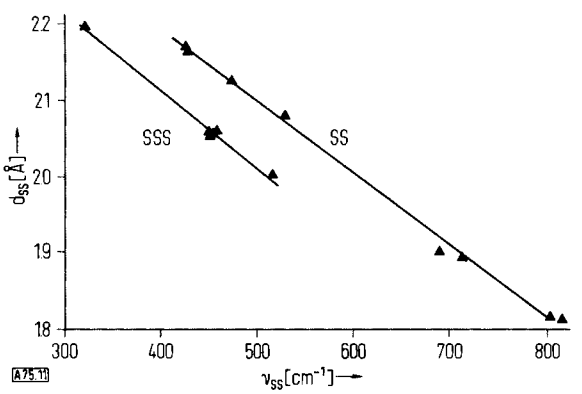


Fig. 11. Dependence of the stretching vibration ν_{SS} of sulfur-sulfur bonds on the nuclear separations d. The upper curve (SS) applies to diatomic and the lower (SSS) to triatomic and polyatomic molecules S_n.

The stretching vibrations of cumulated SS bonds are determined not only by f_r but also by f_{rr}, so that a second relationship is obtained for such systems provided that f_{rr} is approximately constant (Fig. 11). This is the case for sulfur rings, and for S_6, S_8, S_{12}, and S_8O we have[50]:

$$d_{SS} = 2.53 - 1.041 \times 10^{-3} \cdot \nu_{SS}; \quad 300 < \nu_{SS} < 530 \qquad (4)$$

This equation can be used to derive SS bond lengths from the vibrational spectra of compounds that contain cumulated SS bonds but whose structures have not yet been studied. In this way, for example, the bond lengths in S_7 were found to be between 2.00 and 2.15 Å[60].

If an SS bond is flanked by heterobonds as in H_2S_2, $(CH_3)_2S_2$, S_2O, and SSF_2, neither of equations (3) and (4)

is valid, and the stretching frequencies ν_{SS} then lie between the two straight lines in Fig. 11.

3.4. Dissociation Energies and Bond Energies

H_2S_2 and aliphatic disulfanes contain the most stable SS single bonds known so far, the dissociation energies D(SS) being as follows: H_2S_2 272, $(CH_3)_2S_2$ 281, $(C_2H_5)_2S_2$ 289, and $(n\text{-}C_3H_7)_2S_2$ 285 kJ/mol[61]; these values are accurate to within about 25 kJ/mol.

The dissociation energies of tri-, tetra- and other polysulfanes are appreciably smaller. For example, the D(SS) for the central bond in $(CH_3)_2S_4$ amounts to only 151 kJ/mol[62], and for S_8 the first dissociation energy, *i.e.* the energy of the ring cleavage reaction, was determined as 138 ± 4 kJ/mol[63-66]. These findings are explained by the stabilization, discussed above, of radicals formed by homolysis, in which the unpaired electron participates in a π-bond as long as at least one SS bond is present[67, 68]. In the radicals —S—S· the two highest occupied molecular orbitals corresponding to Fig. 4 are occupied by only three electrons in all, so that a partial π-bond is formed. The energy gained by this bonding is saved in the dissociation. For the radical anion S_3^- this multiple bond can be recognized directly from the values of ν_{SS} or d_{SS} (see Section 4.1).

A consequence of the easy homolysis of cumulated SS bonds is that already from 172 °C upward free radicals can be detected in liquid sulfur by ESR spectroscopy[65, 69]. Furthermore, it can now be understood why so many polysulfur compounds decompose even on gentle heating (S_6, S_7, S_9, S_{10}, S_{11}, S_{12}, H_2S_n, S_nCl_2, R_2S_n with $n>4$). For the conversion of polymeric sulfur ("crystex") into S_8 an activation energy of ≥ 130 kJ/mol has been determined, a value corresponding to the dissociation energy of S_8, *i.e.* homolysis of an SS bond is in fact the rate-determining step[70]. The half-life of the change is 50 h at 76 °C and 1 h at 92 °C. However, in many S_n systems a heterolytic ring cleavage[71], catalyzed by H_2S, SO_2, amines, and other compounds, must be taken into account as a competing reaction.

Investigations into the polymerization of liquid sulfur have shown that the heat of the reaction:

$$\cdot S_n + S_m \rightarrow \cdot S_{n+m}$$

(*i. e.* the reaction of radicals with rings) is extraordinarily small (13 kJ/mol[64]). This provides an additional explanation of the instability of many S_n compounds, since a kind of chain reaction is possible after homolysis of an SS bond has been initiated by light or heat.

The mean bond energy of S_8 can be calculated as 265 kJ/mol[72-75] from the heat of the reaction:

$$\tfrac{1}{8}S_8(g) \rightarrow S(g)$$

The same value is found for sulfanes H_2S_n[73, 76] and for aliphatic disulfanes and polysulfanes R_2S_n[20].

The heat of formation of the very labile S_6 (compared with S_8) corresponding to:

$$\tfrac{6}{8}S_8(g) \rightarrow S_6(g)$$

amounts to about 26 kJ/mol[72], *i. e.* in S_6 each bond is only *ca.* 4 kJ/mol weaker than in S_8. The enthalpy difference, still not measured, between S_8 and S_{12} must be very small because of their identical f_r values, and this accords with the fact that S_{12} is completely stable at 25 °C[77].

4. SS Bonds with Coordination Numbers <2 and >2 for the S atoms

4.1. Coordination Number 1

Sulfur atoms with a coordination number of 1 are found in a series of ions S_n^{2-}, in thiosulfate $S_2O_3^{2-}$, and in the following compounds containing multiple SS bonds:

	d_{SS} [Å]	f_r(SS) [mdyne/Å]	Ref.
	1.892	4.9	[78]
	1.882	4.7	[59, 79]
	1.860	5.0	[34, 58]

In these molecules, which correspond to O_2, SO_2, and SOF_2, the singly coordinated S atom takes part in one σ- and one π-bond and possesses an electron octet. S_2 has an electron configuration analogous to that of O_2 that corresponds to a double bond; the properties of the molecule accord with this description ($D_{298}=429$ kJ/mol). One of the excited states of S_2 ($^3\Sigma_u^-$) has the shortest and strongest SS bond yet discovered: d(SS) = 1.810 Å and $f_r = 6.3$ mdyne/Å[78].

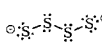
The radical anions S_2^- and S_3^-, which have been unambiguously identified by spectroscopy, assume a position intermediate between those of (a) the molecules S_2 and S_3 detectable in sulfur vapor and (b) the ions S_2^{2-} and S_3^{2-} discussed below[80-84]. S_3^- is responsible for the blue color of ultramarine. The bond lengths in these two particles can be calculated by equations (3) and (4), respectively, from the stretching vibrations observed in the Raman spectra[50]:

	ν_{SS} [cm^{-1}]	d_{SS} [Å]
S_2^-	600	2.00
S_3^-	580 } 533 }	1.95

These show that multiple bonds are present in both these ions, as indeed is to be expected from comparison of the two series $S_2/S_2^-/S_2^{2-}$ and $S_2O/S_3^-/S_3^{2-}$.

π-Bonds of the type just mentioned are formed only in special circumstances. Unless there is an electron deficiency, the singly coordinated S atom takes part only in a σ-bond (see following Table).

The structures of the polysulfide ions show that, even when there is an excess of electrons, the S atoms have little tendency to delocalize their free electrons into the orbitals of the neighboring atoms through coordinative π-bonds. This slight tendency also appears in the structures of $(SiH_3)_2S$[88] and $(GeH_3)_2S$[89] which, unlike $(SiH_3)_2O$ and $(GeH_3)_2O$, give no sign of π-bonding. The ions $S_2O_3^{2-}$ and $CH_3SO_2S^-$, how-

	Compound	d_{SS} [Å]	α [°]	τ [°]	Ref.
	SrS_2	2.08			[85]
	BaS_2	2.126			[85]
	SrS_3	2.050	108.3		[85]
	BaS_3	2.076	114.9		[85]
	Na_2S_4 (a)	2.074	109.8 (a)	97.8 (a)	[86]
	$BaS_4 \cdot H_2O$ (b)	2.061 2.074	104.1 (b)	76.4 (b)	[87]

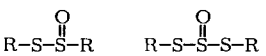
ever, containing both a strongly negatively charged S atom attached to a strongly positively charged S atom, are exceptions from this situation:

	Compound	d_{SS} [Å]	Ref.
	$K_2S_2O_3 \cdot \frac{1}{2}H_2O$	2.00	[90]
	$Na_2S_2O_3 \cdot 5H_2O$	1.95	[91]
	$NaSSO_2CH_3 \cdot H_2O$	1.98	[92]

In these two cases partial SS π-bonds are clearly present, since the short bond lengths cannot be ascribed to the high coordination number of one of the S atoms (cs. Section 4.3).

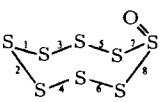
4.2. Coordination Number 3

The simplest compounds of this kind are of the type



Such molecules are known with R = an organic group, but their structures have not yet been determined.

The most interesting compound containing cumulated SS bonds with threefold-coordinated sulfur is S_8O, whose structure and bond relationships have been studied in detail. The molecular structure resembles the S_8 ring in rhombic sulfur, but the SS bond lengths are markedly differentiated—the structure is symmetrical about the mirror plane of the molecule:



Bond	d_{SS} [Å]	ν_{SS} [cm^{-1}]	f_r [mdyne/Å]
1, 2	2.05	423, 438,	2.27
3, 4	2.07	474, 474	
5, 6	2.00	512, 516	2.66
7, 8	2.20	300, 340	1.45

The bond lengths[93] and force constants[94] show that introduction of the O atom causes drastic changes in the neighboring SS bonds. Because of bond interaction, the bond lengths have alternating values, but as their distance from the O atom increases the differences decrease.

Two well-known sulfur derivatives with a coordination number of 3 are the dithionite and the disulfite ion:

	Compound	d_{SS} [Å]	ν_{SS} [cm^{-1}]	Ref.
	$Na_2S_2O_4$	2.39	229	[95, 96]
	$K_2S_2O_5$	2.209	310	[97, 98]

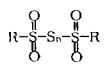
Both contain extremely weak SS bonds which determine the properties of their salts. Thus, $S_2O_4^{2-}$ dissociates in water into radical anions even at 25 °C[99]:

$$S_2O_4^{2-} \rightleftharpoons 2SO_2^- ; \quad K_D = 0.63 \times 10^{-9} \text{ mol/l}$$

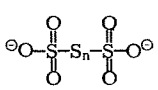
SO_2^- is isoelectronic with S_3^- (cf. Section 4.1). The central bond in $S_2O_4^{2-}$ is the longest "bearing" SS bond yet discovered, this designation denoting a bond which on dissociation leads to two molecular fragments.

4.3. Coordination Numbers > 3

Bonds connecting twofold- and fourfold-coordinated S atoms exist in the following sulfane dioxides:

	R	d_{SS} [Å]	Ref.
	p-C_6H_4Br	2.09	[100]
	$C_{14}H_{12}$	2.048	[101]
	C_6H_5 ($n=1$)	2.07	[102]
	CH_3 ($n=2$)	2.06 (S—S) 2.10 (S—SO_2)	[103]

Inorganic analogs are the polythionate ions:



Five corresponding salts with $n=2$, 3, or 4 have bond lengths d(S—SO_3) of 2.11—2.12 Å, being thus distinctly longer than the d(S—S) bond lengths of 2.02—2.05 Å[104–108].

SS bonds are also longer than normal if both S atoms have a high coordination number and no longer themselves dispose of lone electron pairs. This follows from the structures of some dithionates and of S_2F_{10}:

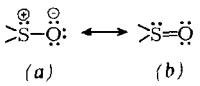
Compound	d_{SS} [Å]	ν_{SS} [cm^{-1}]	Ref.
$Li_2S_2O_6 \cdot 2H_2O$	2.14		
$Na_2S_2O_6 \cdot 2H_2O$,		281	[109–112]
$K_2S_2O_6$,			
$SrS_2O_6 \cdot 4H_2O$	2.15		
S_2F_{10}	2.21	247	[113, 114]

4.4. Causes of Weakening of the SS Bond with Increasing Coordination Number

The following considerations merit discussion as causes of the long SS bond lengths in the compounds described in Sections 4.2 and 4.3:

1. According to experience to date, the coordination number of the atoms in SS bonds is increased only where O, F, or Cl is involved. Thus, all the compounds in question are overloaded with lone electron pairs, whose mutual repulsion must play an important role. Since, however, the SF bond lengths in SF_2 and SOF_2 and the SN bond lengths in $S[N(CH_3)_2]_2$ and $SO[N(CH_3)_2]_2$ are identical within each pair, although here too nonbonding electron pairs are neighbors, a weak bond (small f_r) such as S forms with S or Cl but not with F, O, N, or C, is clearly a prerequisite for bond extension. In fact, d(SCl) is somewhat greater in $SOCl_2$ (2.08 Å) than in SCl_2 (2.01 Å)[114].

2. In most of the compounds with coordination number > 2, two positively charged S atoms occur side by side, whereby again a repulsion results. The positive charge in the SO derivatives can be ascribed not only to the electronegativity difference but also to resonance structures of type (*a*).



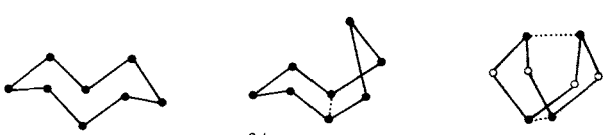
(*a*) (*b*)

3. The most interesting explanation of the very long SS bonds in the dithionite ion and analogous compounds is the assumption of partial delocalization of the nonbonding O-electron pairs into an antibonding molecular orbital of the SS bond[115, 116]. A strengthening of the SO and a weakening of the SS bond are produced, in accord with the observations.

5. Extremely Long SS Bonds

5.1. Ring-bridging Bonds

In S_8 the distance between the two atoms separated by the maximal number of bonds amounts to 4.7 Å. By oxidation of S_8 one obtains the ion S_8^{2+}—also cyclic—in which the S···S separation across the ring amounts to only 2.86 Å, which unambiguously denotes a partial bond possessing π-symmetry with respect to the neighboring SS bonds[117]. Owing to this partial bond the valence angles at the two corners of the ring furthest removed from the S···S bond are reduced from 106° in S_8 to 93°:



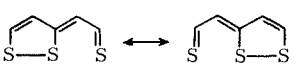
S_8 S_8^{2+} in $S_8(AsF_6)_2$ S_4N_4

The structures of S_8 and S_8^{2+} are closely related to that of S_4N_4[118], which shows a cage with *two* S···S partial bonds. These two bonds are not only indicated by their lengths of 2.58 Å but are also confirmed by MO calculations[119, 120], according to which the cage structure of S_4N_4 is mainly due to the attraction between the S atoms. Because of the molecular geometry according to which the SS bonds are oriented perpendicular to the neighboring SN bonds, we must assume that the former are p-p-bonds while 3s, 3p, and 3d orbitals of the S atoms participate in the SN bonds.

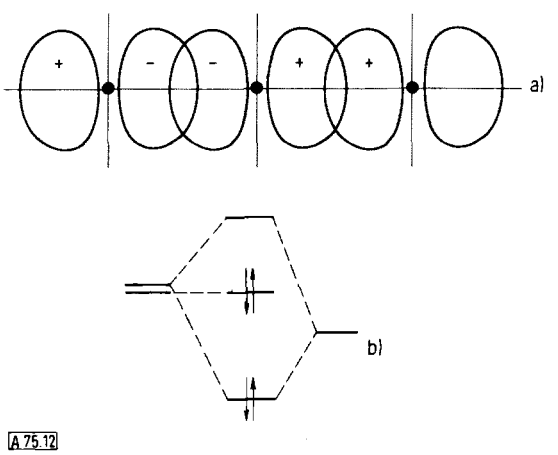
According to simplified MO calculations the differing structures of S_8, S_8^{2+}, and S_4N_4 are due mainly to the differing numbers of valence electrons (48, 46, and 44, respectively). Addition of each pair of electrons to S_4N_4 breaks in each case one of the SS bonds with the formation of two additional free electron pairs: owing to the mutual repulsion of these electrons the S_4N_4 cage opens first halfway (S_8^{2+}) and then completely (S_8).

5.2. Linear Multisulfur Systems

According to an X-ray structure determination[121], thiothiophthene contains the bicyclic ring system:



The SS separations in the almost linear S_3 unit are equal and unusually large (2.351 Å). Bonding-nonbonding resonance has therefore been assumed between these atoms, as is also postulated for other linear systems (*e.g.* I_3^-, HF_2^-). Three 3p orbitals overlap simultaneously in the SS direction and form a three-center, four-electron π-bond (Fig. 12). Such a bond corresponds to an SS separation considerably greater than the normal value of 2.10 Å.



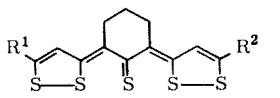
A 75.12

Fig. 12. Three-center bonding between three linearly arranged S atoms. a) Combination of atomic orbitals to give a bonding molecular orbital; b) energy level scheme.

Similarly long SS bonds have also been shown to exist in symmetrically and in unsymmetrically substituted derivatives of thiothiophthene. The two SS separations are not always identical, but may differ by up to 10%[122]. According to a theoretical investigation[123] 3d-orbital participation in the π-system of thiothiophthene causes not only a considerable stabilization but also a slight asymmetry of the nuclear separations in the S_3 unit. Linear multisulfur systems with four and five S atoms have also been synthesized, and the structures of the resulting compounds[124, 125] show that multicenter bonds exist also in these groups. Here the SS separations vary between the limits of 2.1 and 3.0 Å. In the case of larger separations we can hardly speak of a bond any longer. It was observed

that an O atom as a chain member does not participate in multicenter bonding.

A typical example of a compound with a linear S_n chain is illustrated below.



$R^1 = C(CH_3)_3$
$R^2 = C_6H_5$

d_{SS}[Å]: 2.16 2.55 2.62 2.14

5.3. The Range of SS Interactions

The examples in the two preceding sections indicate that SS bonds can bridge distances of up to 3.0 Å. This is confirmed by the results obtained by PE spectroscopy[126] and calculations of force constants[60] between next-but-one nearest neighbors in S_n chains, since there separations up to 3.3 Å occur and since these forces, like bonds, arise owing to orbital overlap. Sulfur atoms separated from one another by more than 3.3 Å, *e.g.* by two S atoms or two methylene groups, are in general no longer able to partake in "through-space" interactions, although they sometimes do partake in "through-bond" interactions.

For S_6[44], S_8[44], S_8O[93], S_{12}[127], S_{18}[47], and S_{20}[47] the smallest intermolecular SS separations amount to 3.2—3.5 Å, which corresponds approximately to the van der Waals separation of 3.5—3.6 Å derived for H_2S and CS_2[128]. The transition from SS bonds to dispersion forces can thus be an almost continuous process. The bond energy of the van der Waals interaction can be estimated from the heat of sublimation of S_8[129] to be 13 kJ per mol of S atoms.

6. Future Outlook

The variability of the bonding between two S atoms, illustrated by numerous examples above, can lead us to expect future syntheses to provide new compounds some of which will contain "unusual" SS bonds. However, in addition to further development of preparative sulfur chemistry there appears to be a need for a more accurate characterization of compounds that are already known. The structures of such elementary substances as S_4^{2+}, S_7, S_9, S_{10}, S_{11}, S_{16}^{2+}, H_2S_3, H_2S_4, S_3Cl_2, *etc.* are so far unknown. No force constants have been calculated for these compounds or for S_8^{2+}, S_4N_4[130], linear multisulfur systems, or for most of the inorganic oxo ions mentioned above. The dearth of thermodynamic data is also evident. In these three areas, important for the characterization of SS bonds, there is a large experimental backlog to be worked off. We may also hope that more accurate model calculations on simple systems will uncover the factors responsible for the great variations in SS bonding in some of the compounds discussed in this review, but it remains to be seen how far the widespread demand for "lucid explanations" will be satisfied.

Received: December 18, 1975 [A 75 IE]
German version: Angew. Chem. *87*, 683 (1975)
Translated by Express Translation Service, London

[1] *M. Winnewisser* and *J. Haase*, Z. Naturforsch. *23a*, 56 (1968).
[2] *G. Winnewisser*, *M. Winnewisser*, and *W. Gordy*, J. Chem. Phys. *49*, 3465 (1968).
[3] *H. B. Gray*: Elektronen und chemische Bindung. W. de Gruyter, Berlin 1973.
[4] *M. E. Schwartz*, J. Chem. Phys. *51*, 4182 (1969).
[5] *A. Veillard* and *J. Demuynck*, Chem. Phys. Lett. *4*, 476 (1970).
[6] *D. B. Boyd*, J. Phys. Chem. *78*, 1554 (1974).
[7] *I. H. Hiller*, *V. R. Saunders*, and *J. F. Wyatt*, Trans. Faraday Soc. *66*, 2665 (1970).
[8] *D. B. Boyd*, J. Am. Chem. Soc. *94*, 8799 (1972).
[9] *D. W. Davies*, Chem. Phys. Lett. *28*, 520 (1974).
[10] *R. L. Redington*, J. Mol. Spectrosc. *9*, 469 (1962).
[11] *F. Fehér* and *K. Seyfried*, Z. Anorg. Allg. Chem. *322*, 162 (1963).
[12] *H. Mackle* and *P. A. G. O'Hare*, Trans. Faraday Soc. *59*, 309 (1963).
[13] *H. C. Allen* and *E. K. Plyler*, J. Chem. Phys. *25*, 1132 (1956).
[14] *D. G. Carroll*, *A. T. Armstrong*, and *S. P. McGlynn*, J. Chem. Phys. *44*, 1865 (1966).
[15] In spite of the small bond angle, the H···H distance in H_2S, 1.91 Å is appreciably larger than that in H_2O (1.52 Å; $\alpha = 104.5°$).
[16] *B. Beagley* u. *K. T. McAloon*, Trans. Faraday Soc. *67*, 3216 (1971).
[17] *D. Sutter*, *H. Dreizler*, and *H. D. Rudolph*, Z. Naturforsch. *20a*, 1676 (1965).
[18] *G. Wagner* and *H. Bock*, Chem. Ber. *107*, 68 (1974).
[19] *H. Yamabe*, *H. Kato*, and *T. Yonezawa*, Bull. Chem. Soc. Jpn. *44*, 604 (1971).
[20] *W. N. Hubbard*, *D. R. Douslin*, *J. P. McCullough*, *D. W. Scott*, *S. S. Todd*, *J. F. Messerly*, *I. A. Hossenlopp*, *A. George*, and *G. Waddington*, J. Am. Chem. Soc. *80*, 3547 (1958).
[21] *P. Laur* in *A. Senning*: Sulfur in Organic and Inorganic Chemistry, Vol. 3. M. Dekker, New York 1972, p. 91.
[22] *R. J. Colton* and *J. W. Rabalais*, J. Electron Spectrosc. Relat. Phenom. *3*, 345 (1974).
[23] *A. D. Baker*, *M. Brisk*, and *M. Gellender*, J. Electron Spectrosc. Relat. Phenom. *3*, 227 (1974).
[24] *O. Foss*, *K. Johnsen*, and *T. Reistad*, Acta Chem. Scand. *18*, 2345 (1964).
[25] *O. Foss*, *A. Hordvik*, and *J. Sletten*, Acta Chem. Scand. *20*, 1169 (1966).
[26] *A. Hordvik*, Acta Chem. Scand. *20*, 1885 (1966).
[27] *J. Friedrichsons* and *A. McL. Mathieson*, Acta Crystallogr. *18*, 1043 (1965).
[28] *H. E. VanWart*, *A. Lewis*, *H. A. Scheraga*, and *F. D. Saeva*, Proc. Nat. Acad. Sci. USA *70*, 2619 (1973).
[29] *H. E. VanWart*, *L. L. Shipman*, and *H. A. Scheraga*, J. Phys. Chem. *78*, 1848 (1974).
[30] *R. B. Martin*, J. Phys. Chem. *78*, 855 (1974).
[31] *H. Sugeta*, *A. Go*, and *T. Miyazawa*, Chem. Lett. *1972*, 83; Bull. Chem. Soc. Jpn. *46*, 3407 (1973).
[32] *E. Hirota*, Bull. Chem. Soc. Jpn. *31*, 130 (1958).
[33] *B. Beagley*, *G. H. Eckersley*, *D. P. Brown*, and *D. Tomlinson*, Trans. Faraday Soc. *65*, 2300 (1969).
[34] *R. L. Kuczkowski*, J. Am. Chem. Soc *86*, 3617 (1964).
[35] *H. J. M. Bowen*, Trans. Faraday Soc. *50*, 452 (1954).
[36] *H. J. Berthold*, Z. Kristallogr. *116*, 290 (1961).
[37] *R. Steudel*, Z. Naturforsch. *26b*, 750 (1971).
[38] *F. J. Lovas*, *E. Tiemann*, and *D. R. Johnson*, J. Chem. Phys. *60*, 5005 (1974).
[39] *F. Seel*, Adv. Inorg. Chem. Radiochem. *16*, 297 (1974).
[40] *J. P. Danehy* in *A. Senning*: Sulfur in Organic and Inorganic Chemistry, Vol. 1. M. Dekker, New York 1971, p. 327.
[41] *E.g.* S_4^{2+}, S_6, S_7, S_8, S_8^{2+}, S_9, S_{10}, S_{11}, S_{12}, S_{16}^{2+}, S_{18}, S_{20}.
[42] *E.g.* S_7Se, S_7NH, $S_6(NH)_2$, $S_5(NH)_3$, S_7TeCl_2, S_7TeBr_2, $(C_5H_5)_2TiS_5$, $(C_5H_5)_2WS_4$, $(NH_4)_2Pt(S_5)_3 \cdot 2H_2O$, $S_{11}N_2$.
[43] *A. Caron* and *J. Donohue*, Acta Crystallogr. *18*, 562 (1965).
[44] *J. Donohue*, *A. Caron*, and *E. Goldish*, J. Am. Chem. Soc. *83*, 3748 (1961).
[45] *M. Schmidt*, Angew. Chem. *85*, 474 (1973); Angew. Chem. internat. Edit. *12*, 445 (1973).
[46] *A. Kutoglu* and *E. Hellner*, Angew. Chem. *78*, 1021 (1966); Angew. Chem. internat. Edit. *5*, 965 (1966).
[47] *M. Schmidt*, *E. Wilhelm*, *T. Debaerdemaeker*, *E. Hellner*, and *A. Kutoglu*, Z. Anorg. Allg. Chem. *405*, 153 (1974); *T. Debaerdemaeker* and *A. Kutoglu*, Cryst. Struct. Commun. *3*, 611 (1974).
[48] *F. Tuinstra*: Structural Aspects of the Allotropy of Sulfur and the Other Divalent Elements. Waltman, Delft 1967.
[49] *R. J. Gillespie*, *J. Passmore*, *P. K. Ummat*, and *O. C. Vaidya*, Inorg. Chem. *10*, 1327 (1971).
[50] *R. Steudel*, Z. Naturforsch. *30b*, 281 (1975).
[51] *D. W. Scott*, *J. P. McCullough*, and *F. H. Kruse*, J. Mol. Spectrosc. *13*, 313 (1964).
[52] *L. A. Nimon* and *V. D. Neff*, J. Mol. Spectrosc. *26*, 175 (1968).
[53] *R. Steudel* and *D. F. Eggers*, Spectrochim. Acta *A 31*, 879 (1975).
[54] *K. B. Wiberg* and *A. Shrake*, Spectrochim. Acta *A 29*, 583 (1973).
[55] *B. P. Winnewisser* and *M. Winnewisser*, Z. Naturforsch. *23a*, 832 (1968).
[56] *D. W. Scott* and *M. Z. El-Sabban*, J. Mol. Spectrosc. *31*, 362 (1969).
[57] *H. Siebert*: Anwendungen der Schwingungsspektroskopie in der anorganischen Chemie. Springer, Berlin 1966.
[58] *R. D. Brown* and *G. P. Pez*, Spectrochim. Acta *A 26*, 1375 (1970).

[59] *R. D. Brown, G. P. Pez,* and *M. F. O'Dwyer,* Aust. J. Chem. *18,* 627 (1965).
[60] *R. Steudel,* Spectrochim. Acta *A 31,* 1065 (1975).
[61] *H. Mackle,* Tetrahedron *19,* 1159 (1963).
[62] *I. Kende, T. L. Pickering,* and *A. V. Tobolsky,* J. Am. Chem. Soc. *87,* 5582 (1965).
[63] *T. K. Wiewiorowski, A. Parthasarathy,* and *B. L. Slaten,* J. Phys. Chem. *72,* 1890 (1968).
[64] *A. V. Tobolsky* and *A. Eisenberg,* J. Am. Chem. Soc. *81,* 780 (1959).
[65] *D. M. Gardner* and *G. K. Fraenkel,* J. Am. Chem. Soc. *78,* 3279 (1956).
[66] *J. A. Poulis, C. H. Massen,* and *D. Van der Leeden,* Trans. Faraday Soc. *58,* 474 (1962).
[67] *F. Fairbrother, G. Gee,* and *G. T. Merall,* J. Polymer Sci. *16,* 459 (1955).
[68] *G. Bergson,* Ark. Kemi *18,* 409 (1961).
[69] *D. C. Konigsberger* and *T. De Neef,* Chem. Phys. Lett. *4,* 615 (1969).
[70] *A. V. Tobolsky* and *W. J. MacKnight:* Polymeric Sulfur and Related Polymers. Wiley-Interscience, New York 1965, p. 96.
[71] *R. E. Davis* in *G. Nickless:* Inorganic Sulphur Chemistry. Elsevier, Amsterdam 1968, p. 85.
[72] *D. A. Johnson* in *A. Senning:* Sulfur in Organic and Inorganic Chemistry, Vol. 2. M. Dekker, New York 1972, p. 37.
[73] *H. Mackle* and *P. A. G. O'Hare,* Tetrahedron *19,* 961 (1963).
[74] *T. L. Allen,* J. Chem. Phys. *31,* 1039 (1959).
[75] *J. Berkowitz* in *B. Meyer:* Elemental Sulfur. Wiley-Interscience, New York 1965, p. 125.
[76] *F. Fehér* and *G. Winkhaus,* Z. Anorg. Allg. Chem. *292,* 210 (1957).
[77] *M. Schmidt* and *E. Wilhelm,* Angew. Chem. *78,* 1020 (1966); Angew. Chem. internat. Edit. *5,* 964 (1966).
[78] *B. Meyer, D. Jensen,* and *T. Oommen* in *A. Senning:* Sulfur in Organic and Inorganic Chemistry, Vol. 2. M. Dekker, New York 1972, p. 13.
[79] *E. Tiemann, J. Hoeft, F. J. Lovas,* and *D. R. Johnson,* J. Chem. Phys. *60,* 5000 (1974).
[80] *J. Rolfe,* J. Chem. Phys. *49,* 4193 (1968).
[81] *W. C. Holton* and *M. de Witt,* Solid State Commun. *7,* 1099 (1969).
[82] *W. Holzer, W. F. Murphy,* and *H. J. Bernstein,* J. Mol. Spectrosc. *32,* 13 (1969).
[83] *T. Chivers* and *I. Drummond,* Inorg. Chem. *11,* 2525 (1972); Chem. Soc. Rev. *3,* 233 (1973).
[84] *F. P. Daly* and *C. W. Brown,* J. Phys. Chem. *77,* 1859 (1973).
[85] *H. G. v. Schnering* and *N.-K. Goh,* Naturwissenschaften *61,* 272 (1974); *N. K. Goh,* Dissertation, Universität Münster 1974; *S. Yamaoka, J. T. Lemley, J. M. Jenks,* and *H. Steinfink,* Inorg. Chem. *14,* 129 (1975).
[86] *R. Tegman,* Acta Crystallogr. *B 29,* 1463 (1973).
[87] *S. C. Abrahams* and *J. L. Bernstein,* Acta Crystallogr. *B 25,* 2365 (1969).
[88] *K. Almenningen, K. Hedberg,* and *R. Seip,* Acta Chem. Scand. *17,* 2264 (1963).
[89] *C. Glidewell, D. W. H. Rankin, A. G. Robiette, G. M. Sheldrick, B. Beagley,* and *S. Cradock,* J. Chem. Soc. *A 1970,* 315.
[90] *L. Csordás,* Acta Chim. Acad. Sci. Hung. *62,* 371 (1969); cited after [21].
[91] *V. M. Padmanabhan, V. S. Yadava, Q. D. Navarro, A. Garcia, L. Karsono, Il-Hwan Suh,* and *L. S. Chien,* Acta Crystallogr. *B 27,* 253 (1971).
[92] *O. Foss* and *A. Hordvik,* Acta Chem. Scand. *18,* 619 (1964).
[93] *R. Steudel, P. Luger, H. Bradaczek,* and *M. Rebsch,* Angew. Chem. *85,* 452 (1973); Angew. Chem. internat. Edit. *12,* 423 (1973); Chem. Ber., in press.
[94] *R. Steudel* and *D. F. Eggers,* Spectrochim. Acta *A 31,* 871 (1975).
[95] *J. D. Dunitz,* Acta Crystallogr. *9,* 579 (1956).
[96] *A. Simon* and *H. Küchler,* Z. Anorg. Allg. Chem. *260,* 161 (1949); ν_{SS} assigned by the present author.
[97] *I. Lindqvist* and *M. Mörtsell,* Acta Crystallogr. *10,* 406 (1957).
[98] *A. W. Herlinger* and *T. V. Long,* Inorg. Chem. *8,* 2661 (1969); ν_{SS} assigned by the present author.
[99] *S. Lynn, R. G. Rinker,* and *W. H. Corcoran,* J. Phys. Chem. *68,* 2363 (1964).
[100] *J. H. Noordik* and *A. Vos,* Recl. Trav. Chim. Pays-Bas *86,* 156 (1967).
[101] *G. H. Wahl, J. Bordner, D. N. Harpp,* and *J. G. Gleason,* Acta Crystallogr. *B 29,* 2272 (1973).
[102] *A. McL. Mathieson* and *J. M. Robertson,* J. Chem. Soc. *1949,* 724.
[103] *H. Sörum,* Acta Chem. Scand. *7,* 1 (1953).
[104] *O. Foss* and *A. Hordvik,* Acta Chem. Scand. *12,* 1700 (1958).
[105] *O. Foss* and *H. Zachariasen,* Acta Chem. Scand. *8,* 473 (1954).
[106] *O. Foss* and *K. Maroy,* Acta Chem. Scand. *19,* 2219 (1965).
[107] *K. Maroy,* Acta Chem. Scand. *25,* 2580 (1971).
[108] *K. Maroy,* Acta Chem. Scand. *27,* 1684 (1973).
[109] *W. G. Palmer,* J. Chem. Soc. *1961,* 1552.
[110] *I. Berthold* and *A. Weiss,* Z. Naturforsch. *22a,* 1440 (1967).
[111] *E. Stanley,* Acta Crystallogr. *9,* 897 (1956).
[112] *R. N. Hargreaves* and *E. Stanley,* Z. Kristallogr. *135,* 399 (1972).
[113] *R. B. Harvey* and *S. H. Bauer,* J. Am. Chem. Soc. *75,* 2840 (1953).
[114] *R. E. Dodd, L. A. Woodward,* and *H. L. Roberts,* Trans. Faraday Soc. *53,* 1545 (1957).
[115] *R. D. Brown* and *R. D. Harcourt,* Aust. J. Chem. *16,* 737 (1963).
[116] *R. D. Harcourt,* Theor. Chim. Acta *3,* 194 (1965).
[117] *C. Davies, R. J. Gillespie, J. J. Park,* and *J. Passmore,* Inorg. Chem. *10,* 2781 (1971).
[118] *B. D. Sharma* and *J. Donohue,* Acta Crystallogr. *16,* 891 (1963).
[119] *P. Cassoux, J.-F. Labarre, O. Glemser,* and *W. Koch,* J. Mol. Struct. *13,* 405 (1972).
[120] *R. Gleiter,* J. Chem. Soc. *A 1970,* 3174.
[121] *L. K. Hansen* and *A. Hordvik,* Acta Chem. Scand. *24,* 2246 (1970).
[122] *A. Hordvik* and *L. J. Saethre,* Acta Chem. Scand. *24,* 2261 (1970); and literature cited therein.
[123] *R. Gleiter* and *R. Hoffmann,* Tetrahedron *24,* 5899 (1968).
[124] *J. Sletten,* Acta Chem. Scand. *A 28,* 499 (1974); and literature cited therein.
[125] *J. Sletten* and *M. Velsvik,* Acta Chem. Scand. *27,* 3881 (1973); and literature cited therein.
[126] *J. H. D. Eland:* Photoelectron Spectroscopy. Butterworths, London 1974, p. 203.
[127] *A. Kutoglu,* private communication (1975).
[128] *A. Bondi,* J. Phys. Chem. *68,* 441 (1964).
[129] *J. Berkowitz* and *W. A. Chupka,* J. Chem. Phys. *40,* 287 (1964).
[130] The normal coordinate analysis carried out for S_4N_4 [131] seems to be erroneous, since some of the force constants have unlikely values, *e.g.* $f_t(SS) = 1.61$ mdyne/Å whereas 0.46 mdyne/Å would be expected from eq. (1). The SS stretching vibrations are at 177 and 213 cm^{-1}.
[131] *J. Bragin* and *M. V. Evans,* J. Chem. Phys. *51,* 268 (1969).

Heterocycles as Structural Units in New Optical Brighteners

By Alfons Dorlars, Carl-Wolfgang Schellhammer, and Joseph Schroeder[*]

Dedicated to Professor Siegfried Petersen on the occasion of his 65th birthday

Optical brighteners are used in detergents, textiles, paper, plastics, and paints. Most optical brighteners contain heterocycles such as coumarins, 2-pyrazolines, naphthalimides, pyrazoles, triazoles, oxadiazoles, and triazines. In this article the syntheses, properties, and applications of new optical brighteners are described with references to patent literature.

1. Introduction

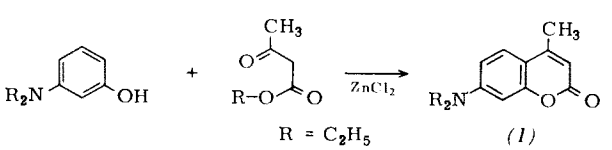
Optical brighteners are colorless fluorescent dyestuffs that absorb in the near ultraviolet (3500—3900 Å) and fluoresce in the violet to blue region of the spectrum (4250—4450 Å). Thus, by their use the reflection deficit of yellowish substrates can be compensated and even overcompensated. The first review of organic fluorescent dyes and their industrial use in this Journal appeared 26 years ago[1], and since then new substrates that require brightening have come into use; the increased demands on fastness to light and to other agents in use have, however, been satisfied by research in the laboratories of the dyestuffs industry, and the results are recorded in patent applications. Reference should also be made to some reviews of the whole field[2].

Except for some linearly extended, conjugated carbocyclic systems such as derivatives of distyrylbenzene and 4,4'-distyrylbiphenyl, the optical brighteners that are used industrially contain heterocycles. The heterocycle may play either of two roles: the basic skeleton of the brightener may be a heterocycle, for example in coumarin derivatives or 2-pyrazoline derivatives, or alternatively, the fluorescence of a conjugated system may be increased and shifted bathochromically. We can thus distinguish between heterocycles themselves capable of fluorescence and heterocycles attached to conjugated systems that can fluoresce. Admittedly there is an overlap in many cases, but nevertheless we shall use this classification in the present attempt to review, from the patent literature, the heterocycles used as structural units in the new optical brighteners.

2. Synthesis of Heterocyclic Systems Themselves Capable of Fluorescence

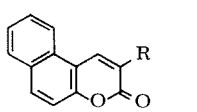
2.1. Synthesis of Coumarins and 2-Quinolones

One of the oldest optical brighteners based on coumarin is 7-(diethylamino)-4-methylcoumarin *(1)*, which is prepared by the Pechmann coumarin synthesis from *m*-(diethylamino)-phenol and ethyl acetoacetate.

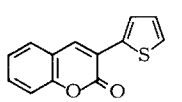


R = C_2H_5 *(1)*

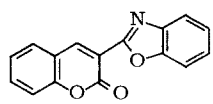
Numerous variants of compounds *(1)* that carry hydrogen or a methanesulfonyl or butanesulfonyl group in place of the *N*-ethyl group are also useful brighteners[3]. Work on compounds of type *(1)* has utilized the observation that coumarin derivatives fluoresce strongly when an electron-donor substituent is present in position 7[4]. Coumarins also fluoresce strongly if C-5 and C-6 are annelated to benzo rings as in *(2a)*—*(2c)*[5], or if a 2-thienyl *(3)*[6] or 2-benzoxazolyl group *(4)*[7] is present in position 3. The fluorescence of 3,4-, 6,7-, and 7,8-benzo-annelated coumarins is much weaker than that of compounds of type *(2)*.



(2a), R = C_6H_5[9]
(2b), R = $COOC_2H_5$[10]
(2c), R = $COOC_4H_9(n)$[11]



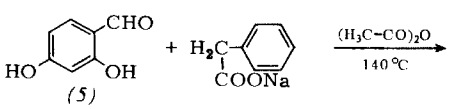
(3)



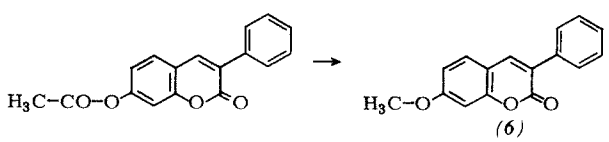
(4)

More powerful brightening effects or better light fastness is obtained with derivatives of 3-phenyl- or 3-heterocyclyl-coumarins. These compounds also must have electron-donor substituents if they are to fluoresce optimally; this condition is satisfied by alkoxy, alkylthio[12], or acylamino groups or heteroaryl containing an excess of π-electrons; these may be in the *p*-position of the 3-phenyl ring or in the 7-position of the coumarin.

7-Alkoxy-3-phenylcoumarins *(6)* are prepared by the Perkin-Oglialoro synthesis[13] from resorcylaldehyde *(5)* and sodium phenylacetate with subsequent hydrolysis of the intermediate product by alkylation of the hydroxyl group[14].



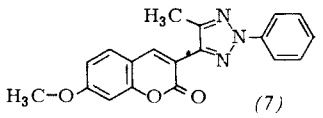
(5)



(6)

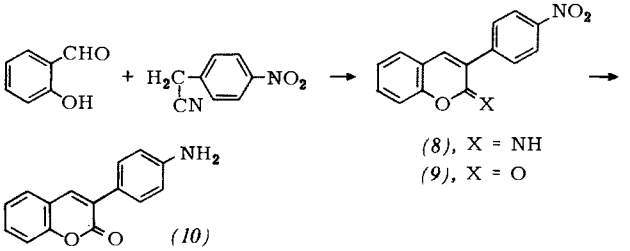
Substituted phenylacetic acids[15] or 4,4'-biphenyldiacetic acid[16] may replace the phenylacetic acid. 7-Alkoxy-3-heterocyclylcoumarins such as *(7)* are obtained from 4-alkoxysalicylaldehydes and the corresponding substituted acetic acids[17].

[*] Dr. A. Dorlars, Dr. C.-W. Schellhammer, and Dr. J. Schroeder
Bayer AG, Wissenschaftliche Laboratorien
509 Leverkusen (Germany)



(7)

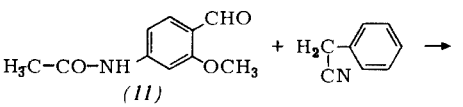
3-(*p*-Aminophenyl)coumarin *(10)* is prepared by Knoevenagel condensation[18] of salicylaldehyde with *p*-nitrobenzyl cyanide, giving the iminocoumarin *(8)*, followed by hydrolysis to *(9)* and catalytic reduction[19].



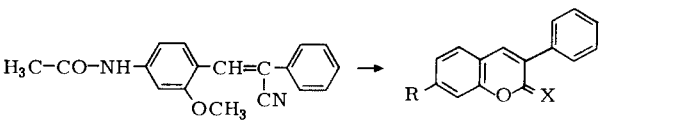
(8), X = NH
(9), X = O

(10)

7-Amino-3-phenylcoumarin *(14)* can be obtained by successive Knoevenagel condensation of the substituted benzaldehyde *(11)* with benzyl cyanide, giving the acrylonitrile derivative *(12)*, cyclizing ether fission by aluminum chloride in benzene to give *(13)*, and acid hydrolysis[20].



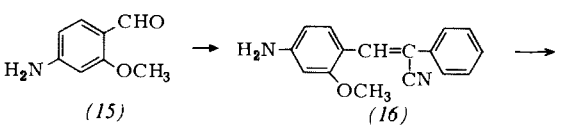
(11)



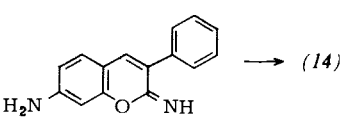
(12)

(13), X = NH, R = NH-CO-CH_3
(14), X = O, R = NH_2

The synthesis of *(14)* can be simplified by adding benzyl cyanide to an alkaline solution of 4-amino-2-methoxybenzaldehyde *(15)* as obtained on treatment of 2-methoxy-4-nitrotoluene with sodium disulfide in aqueous-alcoholic alkali[21]; the acrylonitrile derivative *(16)* is isolated and is cyclized by aluminum chloride in benzene to *(17)*[22], whence *(14)* is finally obtained by acid hydrolysis.

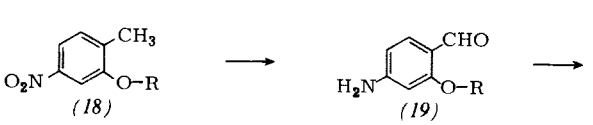


(15) *(16)*

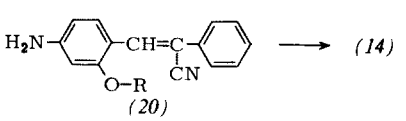


(17)

If the synthesis of *(14)* is started from the sulfamidic ester *(18)*, the aldehyde *(19)* is obtained on treatment with sodium disulfide, and with benzyl cyanide this gives *(20)*; heating of *(20)* with 50% sulfuric acid then affords *(14)*[23].

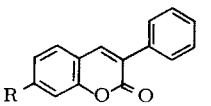


(18) *(19)*



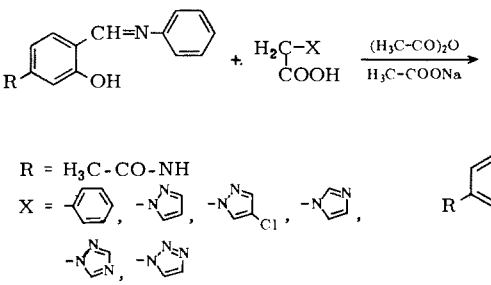
R = SO_2-N(CH_3)$_2$ *(20)*

Precursors of *(14)*, namely 7-nitro- *(21)*[24] and 7-(acetylamino)-3-phenylcoumarin *(22)* can be prepared by Perkin-Oglialoro synthesis.



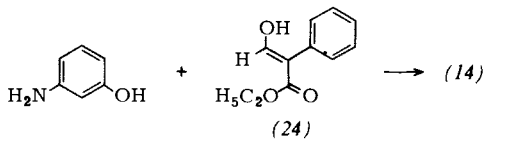
(21), R = NO_2
(22), R = NH-CO-CH_3

Since 4-nitro- and 4-(acetylamino)salicylaldehyde are not readily available industrially, 4-(acetylamino)salicylideneaniline[25] can be used as the aldehyde component. This variant of the synthesis affords 7-(acetylamino)coumarin derivatives *(23)*[26] and is particularly suitable for the preparation of coumarins carrying heterocyclic groups attached in the nitrogen in position 3.

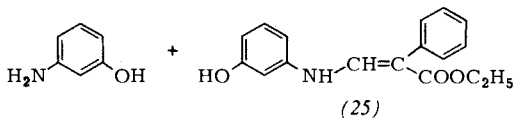


(23)

(14) is also accessible by processes that resemble the Pechmann coumarin synthesis[27]. Thus, it is obtained when ethyl 3-hydroxy-2-phenylacrylate *(24)* is added slowly to *m*-aminophenol in boiling 1,2-dichlorobenzene[28] or in nitrobenzene containing aluminum chloride[29].



(24)

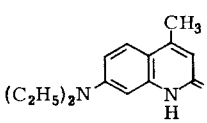


(25)

When the acrylic ester derivative *(25)* is heated with *m*-aminophenol to 165 °C, *(14)* is obtained without the addition of a catalyst[30].

The coumarin derivatives *(10)* and *(14)* are merely intermediates; they become optical brighteners only on acylation of the amino group or on incorporation into heteroaromatic compounds having an excess of π-electrons (see Section 3.9).

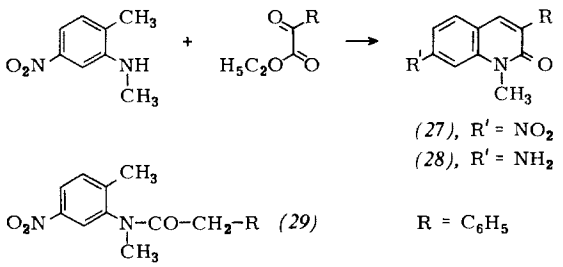
7-(Diethylamino)-4-methyl-2-quinolone *(26)* which is structurally similar to *(1)* also fluoresces strongly[4, 31].



(26)

The industrially useful properties of 2-quinolone derivatives are also improved by the presence of a phenyl group in position 3. 7-Amino-1-methyl-3-phenyl-2-quinolone *(28)* can be pre-

pared by condensing 2-(methylamino)-4-nitrotoluene with ethyl phenylglyoxalate and reducing the intermediate product *(27)* or by treating the phenylacetamide *(29)* with sodium disulfide in an alkaline-alcoholic medium[33].



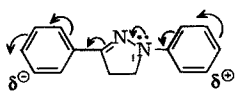
(27), R' = NO_2
(28), R' = NH_2

(29) R = C_6H_5

The fluorescence maxima of 7-amino-3-phenyl-2-quinolone derivatives are shifted hypsochromically from those of the corresponding coumarin derivatives; for this reason 7-(dimethylamino)-1-ethyl-3-phenyl-2-quinolone, which is prepared by methylating the 7-amino compound with formaldehyde/hydrogen, is an optical brightener[34], whereas 7-(dimethylamino)-3-phenylcoumarin is too highly colored.

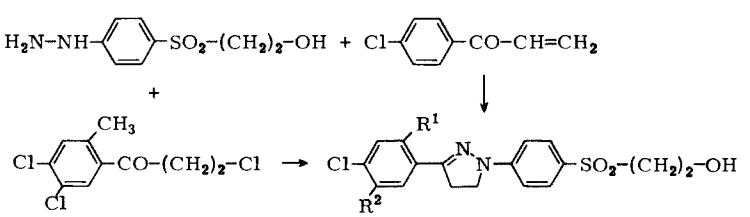
2.2. Syntheses of 2-Pyrazolines

The industrially useful brighteners in this class of compounds are derived from 1,3-diphenyl-2-pyrazoline, which is a fluorescing system in its own right. Some authors describe this grouping as a chromophore:



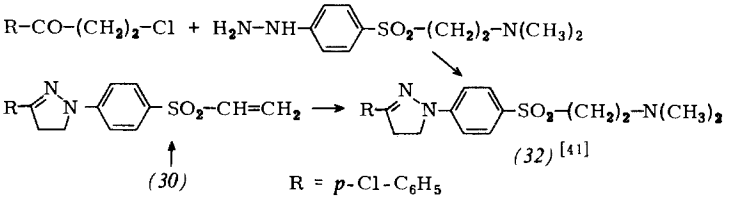
The $2p_z$ electrons of the N-1 atom are then considered to interact with the π-electrons of the C=N bond[35]. Other workers believe that the strong interaction of 1,3-diphenyl-2-pyrazoline[37] with light is better described by assuming intramolecular charge transfer (ICT)[36] in the directions indicated by the arrows in the formula. There have been studies of the influence of structure, solvent, and temperature on this fluorescence[38].

Industrial syntheses of 1,3-diphenyl-2-pyrazolines, *e.g. (30)* and *(31)* employ phenyl vinyl or β-chloroethyl phenyl ketone, or alternatively Mannich bases from acetophenone and formaldehyde with secondary amines and substituted phenylhydrazines, as the starting materials.



(30), $R^1 = R^2 = H$[39]
(31), $R^1 = CH_3$, $R^2 = Cl$[40]

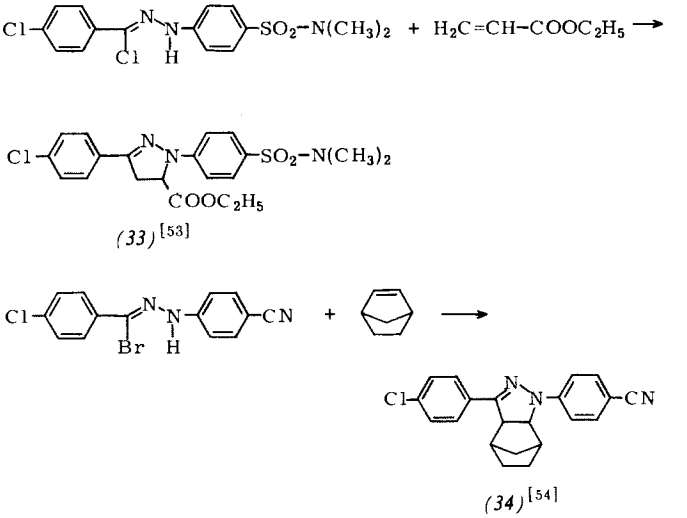
1,3-Diphenyl-2-pyrazolines containing functional groups are synthesized from substituted phenylhydrazines or by changes effected on the preformed pyrazoline. Thus, *(32)* can be obtained *via* the two routes shown.



(30) R = *p*-Cl-C_6H_5 *(32)*[41]

The upper portion of Table 1 shows the variations in substituents introduced into the 1-phenyl ring; the lower portion lists the industrially important 2-pyrazoline derivatives.

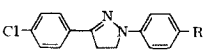
1,3-Diphenyl-2-pyrazoline-5-carboxylic acid derivatives *(33)* and pyrazoline derivatives *(34)* disubstituted in positions 4 and 5 are occasionally synthesized by 1,3-dipolar addition.



(33)[53]

(34)[54]

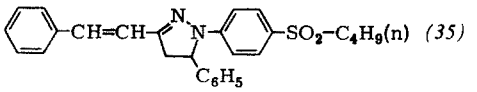
Table 1. 3-(*p*-Chlorophenyl)-1-phenyl-2-pyrazolines substituted in the 1-phenyl ring ($A^\ominus$ = anion). Top: Illustrations of the variants. Below: Industrially important brighteners.



R	Ref.
$COO-CH_2-CH=CH_2$	[42]
$COO-CH_2-COO-C_2H_5$	[43]
$SO_2-NH-(CH_2)_3-\overset{\oplus}{N}(CH_3)_2-(CH_2)_2-OH$ $A^\ominus$	[44]
$SO_2-NH-(CH_2)_2-SO_3H$	[45]
$SO_2-NH-(CH_2)_2-\overset{\oplus}{S}(CH_3)_2$ $A^\ominus$	[46]
$SO_2-(CH_2)_2-N$ heterocycle	[47]
$SO_2-(CH_2)_n-SO_3H$	[48, 39]
SO_2-OCH_3	[49]
SO_2-N N-R	[50]
$SO_2-(CH_2)_2-COO-(CH_2)_2-\overset{\oplus}{N}(CH_3)_3$ $A^\ominus$	[51]
$SO_2-(CH_2)_2-COO-(CH_2)_2-\overset{\oplus}{S}(CH_3)_2$ $A^\ominus$	[52]
COOH	[55]
$COOCH_3$	[55]
SO_2-NH_2	[56]
$SO_2-NH-(CH_2)_3-\overset{\oplus}{N}(CH_3)_3$ $CH_3SO_4^\ominus$	[57]
$SO_2-(CH_2)_2-SO_3H$	[39]
$SO_2-(CH_2)_2-NH-CO-CH_3$	[58]
$SO_2-(CH_2)_2-SO_3H$ [a]	[40]
$SO_2-(CH_2)_2-O-CH(CH_3)-CH_2-\overset{\oplus}{N}H(CH_3)_2$ $Cl^\ominus$	[59]
SO_2-CH_3	[41]
$SO_2-C_4H_9(n)$	[60]

[a] Further substituents: 2-methyl and 5-chlorine in the 3-phenyl ring.

Mixing[61] 1,3-diphenyl-2-pyrazolines whose fluorescence has a red tint with the 1,5-diphenyl-3-styryl-2-pyrazolines *(35)* that can be obtained from dibenzylideneacetone and relevant phenylhydrazines permits any desired hue of white to be introduced.

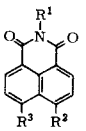


(35)

2.3. Syntheses of Naphthalimides

Naphthalimides with electron-donor substituents on C-4 and C-5 fluoresce strongly. Whereas the 4-acetylamino derivatives *(36)* to *(38)* whiten to a green tint, the alkoxy derivatives such as *(39)* and *(40)* produce neutral white shades on synthetic materials (Table 2).

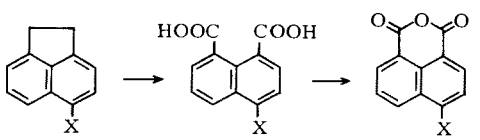
Table 2. Naphthalimide-type brighteners.



	R^1	R^2	R^3	Ref.
(36)	Alkyl	NH—CO—CH_3	H	[62]
(37)	Alkyl	NH—CO—NH—C_6H_5	H	[62]
(38)	H, Alkyl	N(CH_3)—CO—CH_3	H	[63]
(39)	Alkyl	OCH_3	H	[64]
(40)	Alkyl	OC_2H_5	OC_2H_5	[65]

Numerous variants of the naphthalimide whitening agents of types *(39)* and *(40)* are known and make it possible to meet the requirements of industrial application more adequately[64, 66–73]. In order that 4-methoxynaphthalimide derivatives can also be used for acid-modified polyacrylonitrile fibers numerous variants have been prepared, containing basic and, in particular, quaternary ammonium groups[74–81].

The starting material for industrial syntheses of naphthalimide derivatives is acenaphthene that has been sulfonated, nitrated, or chlorinated in position 7 [thus giving *(41)*] and then oxidized to the naphthalic acids *(42)* by dichromate[82]. On drying, these acids are converted into their anhydrides *(43)*.

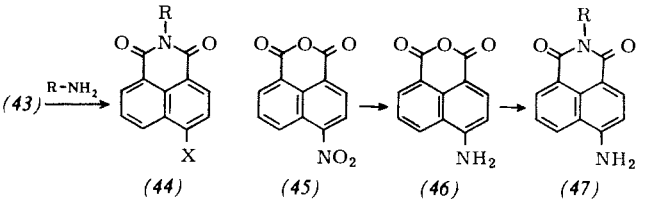


(41) *(42)* *(43)*

X = SO_3H, NO_2, Cl

4-Chloronaphthalic anhydride *(43)*, X=Cl, is also formed on chlorination of naphthalic acid at pH 7.3[82], and mild treatment with ammonia or aliphatic amines gives the imides *(44)*[83].

The sulfonic acid group or halogen atom of *(44)* can be replaced by an amino, hydrazino, or hydroxyl group[84]; all three substituents X in *(44)* can be caused to react with sodium methoxide to afford *(39)*[85]. The amine *(47)* that

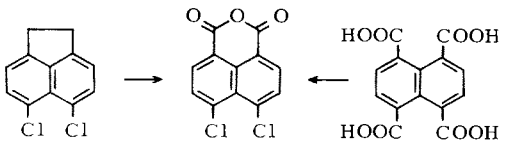


(43) *(44)* *(45)* *(46)* *(47)*

X = SO_3H, NO_2, Cl

serves for the production of the brighteners *(36)*—*(38)* can also be synthesized from *(45)* by way of the amine *(46)*[86].

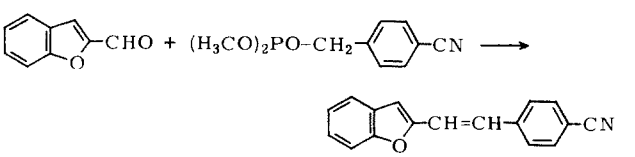
4,5-Dichloronaphthalic anhydride *(49)*, the intermediate for brighteners of type *(40)*[87], is obtained by oxidizing 5,6-dichloroacenaphthene *(48)*[88] or by treating 1,4,5,8-naphthalenetetracarboxylic acid *(50)* with sodium hypochlorite[89].



(48) *(49)* *(50)*

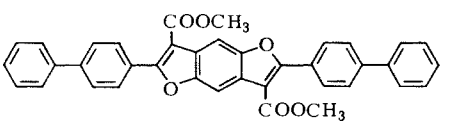
2.4. Synthesis of Other Fluorescing Heterocyclic Systems

Among the heterocycles with one heteroatom the derivatives of benzofuran acting as optical brighteners occupy much space in the patent literature. 2-Phenylbenzofuran is formally a *trans*-fixed stilbene[90]; the 2-phenyl group may be replaced by styryl, stilbenyl, or benzazolyl groups. *p*-(2-Benzofurylvinyl)-benzonitrile *(51)* is formed on condensation of 2-benzofurancarbaldehyde with dimethyl 4-cyanobenzylphosphonate in the presence of an alkali metal alkoxide[91].



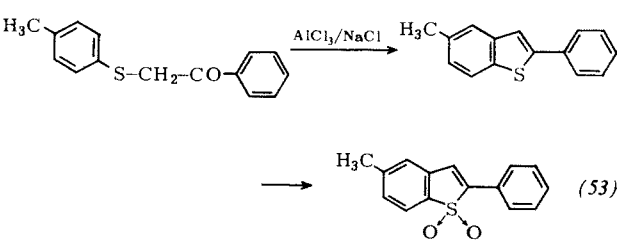
(51)

Benzodifurans can also be useful brighteners, an example being *(52)*[92] which is formed in a redox reaction of methyl *p*-phenylbenzoylacetate with *p*-benzoquinone.



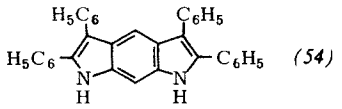
(52)

Utilizable fluorescence is also shown by derivatives of benzothiophene *e.g.* 5-methyl-2-phenylbenzothiophene *S,S*-dioxide *(53)*[93]. Chlorite-resistant brighteners can be derived, in particular, from dibenzothiophene *S,S*-dioxide[94].



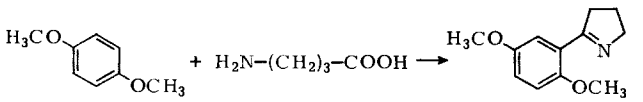
(53)

Among the fluorescing nitrogenous heterocycles the benzodipyrrole *(54)* is especially readily accessible—from *m*-phenylenediamine and benzoin[95].



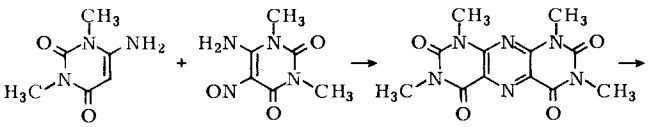
(54)

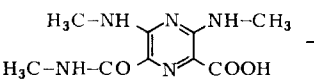
Fluorescence is also, surprisingly, shown by 2-(2,5-dimethoxyphenyl)-1-pyrroline *(55)*, which can be synthesized by condensing 4-aminobutyric acid with hydroquinone dimethyl ether in polyphosphoric acid[96].

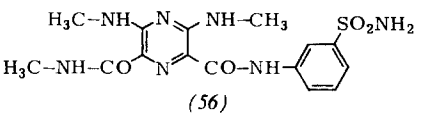


(55)

Optical brigtheners are also found among the derivatives of pyrazine, an example being the diaminopyrazinedicarboxylic acid derivative *(56)*[97].

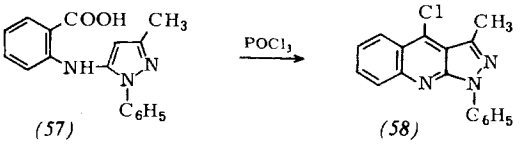






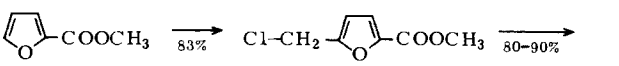
(56)

Pyrazoloquinolines such as *(58)*, which can be used as whitening agents, are formed when pyrazoles such as *(57)* are heated with phosphorus oxychloride[98].

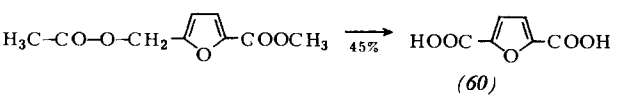


(57) *(58)*

Some brighteners are also found among the derivatives of 2,5-furandicarboxylic acid *(60)* and of 2,5-thiophenedicarboxylic acid *(63)*. Compound *(60)* can be prepared in 50% yield from tetrahydroxyadipic acid (*e.g.* mucic acid or a sugar acid) by treatment with concentrated acids[99] or from methyl 2-furancarboxylate *(59)*[100] *via* several steps.

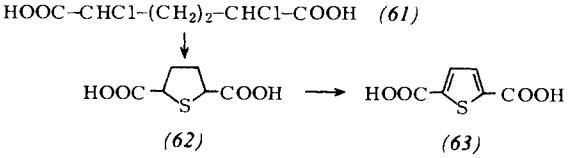


(59)



(60)

(60) and *(63)* are also formed on carboxylation of the potassium salts of the corresponding monocarboxylic acids (in the presence of CdF_2 at 320 °C/50 atm)[101]. More importance attaches to the synthesis of *(63)* which starts from 2,5-dichloroadipic acid *(61)* and proceeds by way of the tetrahydro-2,5-thiophenedicarboxylic acid *(62)*[102].

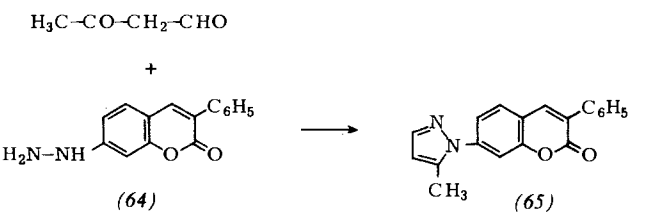


(62) *(63)*

3. Syntheses of Heterocycles Attached to Fluorescing Conjugated Systems

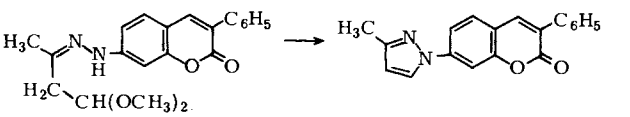
3.1. Conjugated Systems Containing 1-Pyrazolyl or 2-Indazolyl Groups

Whereas nowadays pyrroles do not play any part as substituents of fluorescing conjugated systems, the 1-pyrazolyl group is a constituent of some important optical brighteners. 1-Pyrazolyl derivatives are obtained by treating β-dicarbonyl compounds with the relevant substituted hydrazines. For example, the 5-methyl-1-pyrazolyl derivative *(65)* is obtained by reaction of acetoacetaldehyde with 7-hydrazino-3-phenylcoumarin *(64)*, which is itself obtained by diazotization of *(14)* and subsequent reduction by sulfite[103].



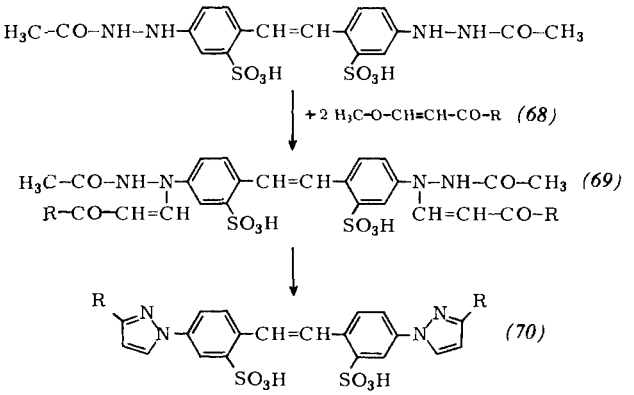
(64) *(65)*

Since, however, compounds containing a 5-substituted 1-pyrazolyl group have less advantageous properties than the 3-substituted analogs, special techniques must be applied to provide the compounds containing 3-substituted 1-pyrazolyl groups. If the aldehyde is replaced by its dimethyl acetal and the mineral acid used for cleavage of the acetal grouping is added only after the formation of the ketone hydrazone *(66)*, then the 3-methyl-1-pyrazolyl derivative *(67)* is obtained[103].



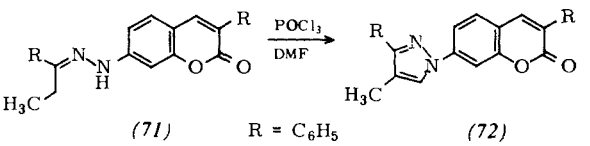
(66) *(67)*

Analogous reactions are undergone by 7-hydrazinocoumarins containing heterocycles such as 1,2,4-triazole or 4-chloropyrazole in position 3[104], or *N*-alkyl-4-hydrazinonaphthalimides[105]. In place of oxoaldehyde acetals, alkyl or aryl 3-chlorovinyl ketones may also be used. To synthesize the 3-substituted 1-pyrazolyl derivative from 2-methoxyvinyl phenyl ketone *(68)*, the hydrazine used is first acylated in the β-position and thus the desired compound *(70)* is obtained by way of the intermediate *(69)*[106].



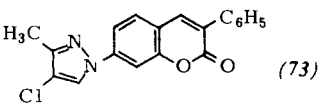
R = C_6H_5

Pyrazoles disubstituted in positions 3 and 4, *e.g.* *(72)*, can be prepared by Vilsmeier formylation of ketone hydrazones such as *(71)*[107]. *(67)* can be chlorinated by sulfuryl

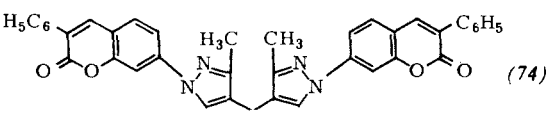


(71) R = C_6H_5 *(72)*

chloride in tetrachloroethane, yielding *(73)*[108], or it can be converted into *(74)* by means of formaldehyde/toluenesulfonic acid[109].

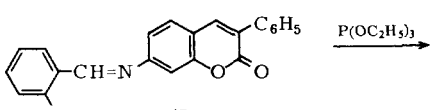


(73)

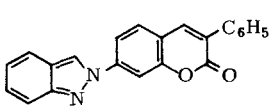


(74)

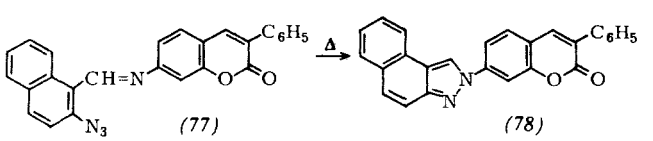
7-(2-Indazolyl)coumarins suitable as optical brighteners are accessible by conversion of *(14)* into *(75)* by reaction with *o*-nitrobenzaldehyde and subsequent cyclization to yield *(76)* by heating with triethyl phosphite; or *(14)* may be condensed with, *e.g.* 2-azido-1-naphthaldehyde, yielding *(77)*, from which nitrogen can be removed thermally with the production of *(78)*[110].



(75)



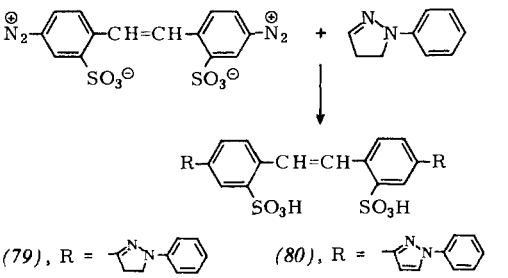
(76)



(77) *(78)*

3.2. Conjugated Systems Containing 3-Pyrazolyl Groups

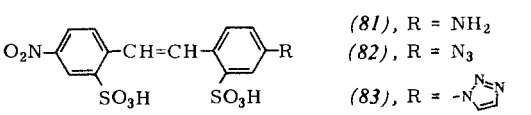
By coupling diazotized 4,4'-diamino-2,2'-stilbenedisulfonic acid ("flavic acid") with 1-phenyl-2-pyrazoline one obtains compound *(79)*, whence *(80)* results on dehydrogenation[111].



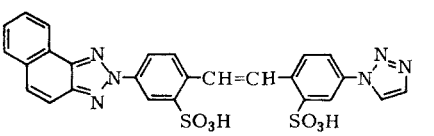
(79), R = *(80)*, R =

3.3. Conjugated Systems Containing 1,2,3-Triazol-1-yl Groups[111a]

The known synthesis of 1,2,3-triazol-1-yl compounds by the addition of azides to alkines has been mastered also by industry, so that we meet such compounds among stilbene as well as among coumarin derivatives. The intermediate *(83)* needed for the manufacture of the bis(triazolyl) brightener *(84)* is obtained from the 4-amino-4'-nitro-2,2'-stilbenedisulfonic acid *(81)* that is readily available industrially by diazotization and coupling with toluenesulfonamide; the azide *(82)* then obtained with loss of toluenesulfinic acid[112a] can be converted into *(83)* by acetylene under slight pressure[112].

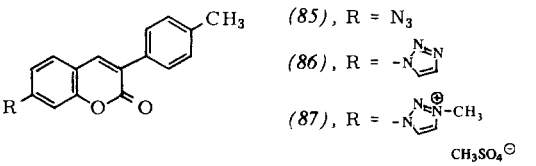


(81), R = NH_2
(82), R = N_3
(83), R =



(84)

The compound *(86)* is obtained similarly from 7-azido-3-(*p*-tolyl)coumarin *(85)* by the addition of acetylene, and with dimethyl sulfate it gives the quaternary derivative *(87)*[113].

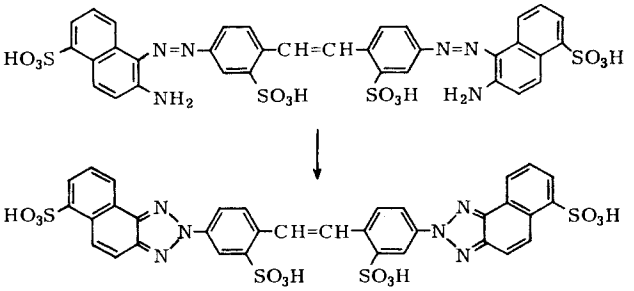


(85), R = N_3
(86), R =
(87), R =

3.4. Conjugated Systems Containing 1,2,3-Triazol-2-yl Groups

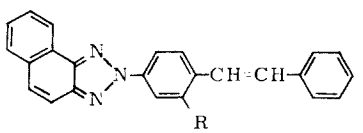
The great stability of the 1,2,3-triazol-2-yl group bonded by its central N atom has long been known from the chemistry of dyes for the cases of annelated triazolyl groups and in particular of benzo- and naphtho[1,2-*d*]triazoles. Attempts to achieve stability to hypochlorite bleaching solutions and improved light fastness by incorporating the N-atoms of flavic acid into the heteroaromatic system of the naphthotriazole have proved successful. The first representative of this class of compounds, *(88)*, is prepared by coupling diazotized flavic

acid with 2-naphthylamine-5-sulfonic acid and oxidation of the resulting *o*-aminoazo dye with hypochlorite or copper(II) salts[114].



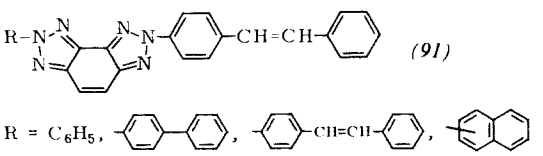
(88)

The marked greenish tint of *(88)* can be shifted in the direction of neutral white by dispensing with one of the naphthotriazole groups, although this is at the cost of efficiency. The compound *(89)* is stable to hypochlorite bleaching liquors and peroxides; it is suitable for whitening cellulose and polyamide from washing baths[115].



(89), R = SO_3H
(90), R = CN

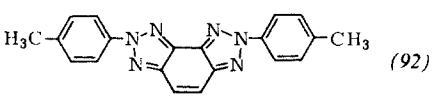
The cyano compound *(90)* is used as polyester brightener[116]. *(89)* and *(90)* are prepared analogously to *(88)*[116a]. The patent literature contains numerous variants of the compound types *(88)*—*(90)*[116b], *e. g. (84)*. Moreover, the benzobis(triazole)stilbene compounds *(91)* have been developed as polyester brighteners[117].



(91)

R = C_6H_5,

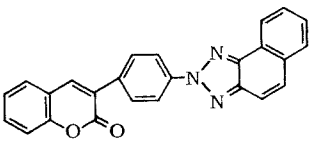
These compounds *(91)* are prepared by coupling 5-amino-2-(*p*-tolyl)-benzotriazole with diazotized *p*-toluidine or with the diazo component corresponding to the group R, and are then cyclized, *e. g.* to *(92)*. The methyl groups can be condensed with benzylideneaniline in dimethylformamide in the presence of strong bases (KOH), yielding the distilbenyl compound ("anil synthesis")[118].



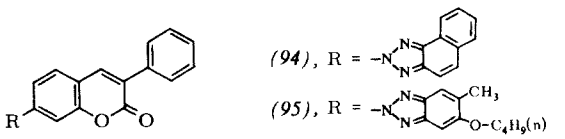
(92)

In the coumarin series too this procedure leads to effective brighteners. The naphtho[1,2-*d*]triazole compounds *(93)*[119] and *(94)*[120] obtainable from the amines *(10)* and *(14)*, respectively, are polyester brighteners, while the compound *(95)* accessible from diazotized *(14)* and 3-butoxy-*p*-toluidine brightens PVC well[121].

The monocyclic 1,2,3-triazol-2-yl group is very stable and capable of varied substitution and it brings new possibilities into the chemistry and technology of optical brighteners. This can be illustrated by some examples from the stilbene series (Table 3).

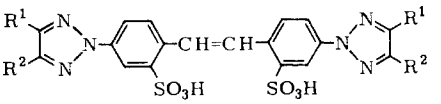


(93)



(94), R =
(95), R =

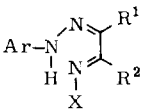
Table 3. Brighteners containing 1,2,3-triazol-2-yl groups.



	R^1	R^2	Ref.
(96)	NH—CO—C_6H_5	H	[122]
(97)	C_6H_5	H	[123]
(98)	C_6H_4—$SO_3H(p)$	H	[124]
(99)	CH=CH—C_6H_5	H	[125]
(100)	C_6H_5	C_6H_5	[123]
(101)	C_6H_5	$COOC_2H_5$	[126]

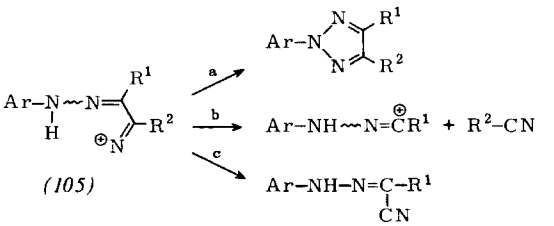
While *(96)* confers white tints on cotton and polyamides with good effect[122], derivatives without the carboxamide group, *e.g. (97)*, give clear neutral white shades that are light-fast and resistant to hypochlorite bleach liquors[123]. The tetrasulfonic acid *(98)* produced by subsequent sulfonation of *(97)* is equally stable and is so far the only water-soluble stilbene brightener that can be used in a reactant resin form without the necessity of wasteful after-washing. Compounds *(99)*, *(100)*, and *(101)* are good brighteners for polyamides. Sulfonamides derived from disulfonic acids of type *(97)* are suitable for brightening polyester materials to be spun[126a].

Synthesis of the 1,2,3-triazol-2-yl derivatives *(96)*—*(100)* is best achieved by *Pechmann* cyclization[127] of α-hydroxyimino hydrazones *(102)*, which in turn can be provided by coupling diazotized arylamines—here especially flavic acid—with reactive methylene compounds, *e.g.* nitroacetaldoxime ($R^1 = NO_2$, $R^2 = H$)[122, 128], or by condensing aromatic hydrazines, here 4,4'-dihydrazino-2,2'-stilbenedisulfonic acid, with the readily available α-hydroxyimino ketones ($R^1 = C_6H_5$, $R^2 = H$, *etc.*)[129].



(102), X = OH
(103), X = O-Acyl
(104), X = H

Four configurations can, in general, be considered for α-hydroxyimino hydrazones such as *(102)*: *syn*- and *anti*-hydrazones can take part in triazole ring closure, especially the *syn*-hydrazone *anti*-oxime. For this synthesis the hydroxyimino group is acylated, giving *(103)*, *e. g.* by acetic anhydride, urea[130],

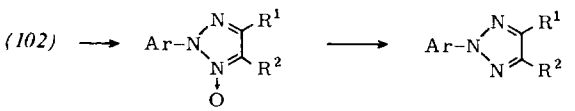


(105)

or isocyanates[131]; after nucleofugal departure of the acyloxy anion an intermediate *(105)* is obtained, which can stabilize itself in several ways, in which a part is played by the possible removal of the *N*-proton that is capable of hydrogen-bridge formation.

The products may be not only the desired triazoles by reaction (a) but also, from *anti*-hydrazones and/or aromatic R^2, the acylhydrazines by reaction (b) (Beckmann cleavage), or, further, by reaction (c) when $R^2=H$, the hydrazonoglyoxylonitriles and subsequent products therefrom. For high yields of triazole the reaction conditions must thus be carefully optimized in each individual case.

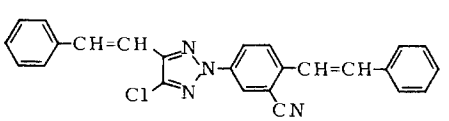
The compound *(101)* is advantageously obtained by oxidative cyclization of the coupling product of diazotized flavic acid with β-aminocinnamic ester *(104)*, $R^1=C_6H_5$, $R^2=COOC_2H_5$[126]. In some cases higher yields of triazole are obtained more easily if the hydroxyimino hydrazones *(102)* are first cyclized with dehydrogenation to triazole N^1-oxides *(106)*[132], *e.g.* by copper(II) salts, and these oxides are then reduced to the triazoles *(107)*.



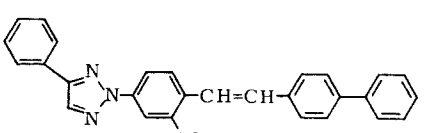
(106) *(107)*

(108), R^2 = Cl
(109), R^2 = O–CO–CH_3
(110), R^2 = CH_2–O–CO–CH_3

Treatment of the reactive triazole N^1-oxides *(106)* with hydrogen chloride or phosphorus chlorides leads, when $R^2=H$, to chlorotriazoles *(108)*[133]; reaction with acetic anhydride leads analogously to acetoxytriazoles *(109)*[134], and, when $R^2=CH_3$, to acetoxymethyl derivatives *(110)*[135]. An example of an optical brightener of type *(108)* is compound *(111)*, which is obtained by condensation of 4-hydrazino-2-stilbenecarbonitrile with α-(hydroxyimino)benzylideneacetone, dehydrogenation of the hydroxyimino hydrazone to the triazole N^1-oxide and finally treatment with hydrogen chloride[136a].



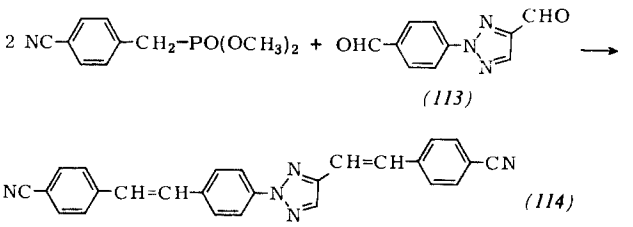
(111)



(112)

As examples of long-chain monotriazolylstilbenes may be cited the cotton brightener *(112)*[136] and the spun-polyester brightener *(114)*. Whereas *(112)* can be prepared, analogously to *(97)*, from 4-hydrazino-4′-phenyl-2-stilbenesulfonic acid, *(114)*[136b] is obtained from the dialdehyde *(113)* by carbonyl olefination[136c].

(113) and numerous substituted derivatives thereof can be prepared in good yields by Rosenmund reduction of dicarboxylic acid chlorides.

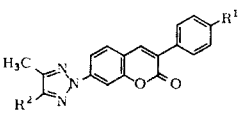


(113)

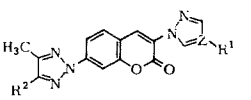
(114)

In the coumarin series combination with 1,2,3-triazol-2-yl groups leads to products that are particularly suitable as polyester brighteners. A selection of characteristic examples is given in Table 4.

Table 4. Brighteners of coumarin type containing 1,2,3-triazol-2-yl groups.



(115)-*(117)*

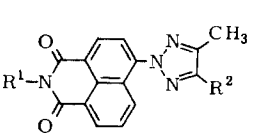


(118)-*(121)*

	R^1	R^2	Z	Ref.
(115)	H	C_6H_5	—	[137]
(116)	H	C_6H_4–C_6H_5(*p*)	—	[137a]
(117)	–$(CH_2)_n$–	C_6H_5	—	[142]
(118) [a]	H	CH=CH–C_6H_5	C	[138]
(119)	H	C_6H_5	C	[139]
(120)	Cl	C_6H_5	C	[140]
(121)	—	C_2H_5	N	[141]

[a] H in place of CH_3.

Compounds *(115)*—*(121)* are prepared from 3-phenyl- or 3-heterocyclyl-7-hydrazinocoumarins by condensation with α-hydroxyimino-propiophenone, -benzylideneacetone, -*p*-phenylpropiophenone or -diethyl ketone, with subsequent cyclodehydration of the resultant hydroxyimino hydrazones. Naphthalimide derivatives carrying a monocyclic 1,2,3-triazol-2-yl group in position 4 have also been described as polyester brighteners. Since this class of compounds already fluoresces at rather long wavelengths, bathochromic substituents should not be introduced into the triazole nucleus. The best results are obtained with *(122a)*[143] or, even better, *(122b)*[144], where R^1 is ethyl or butyl in both cases.



(122a), R^2 = Cl
(122b), R^2 = H

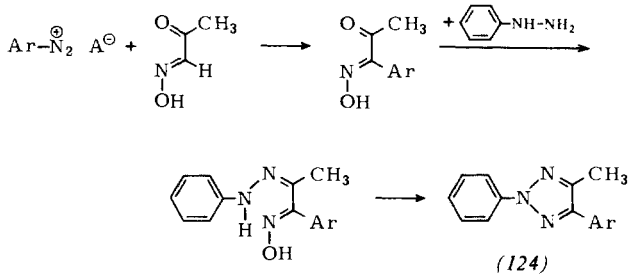
The starting material for these compounds is *N*-ethyl- or *N*-butyl-4-hydrazinonaphthalimide, which is condensed with hydroxyiminoacetone to yield the α-hydroxyimino hydrazone *(102)*. For the preparation of *(122a)* the next step is dehydrogenation to the *N*-oxide *(106)*, which then yields the halotriazole *(108)* as described above. *(122b)* can also be obtained in the usual way. However, if the readily accessible anti-acetoximino-acetone *(123)* is used as the starting material, *(122b)*

H_3–CO–O–N=CH–CO–CH_3 *(123)*

is formed in 90% yield in a one-stage reaction[144a]; but it should be mentioned that this procedure cannot be applied to hydroxyiminoaryl ketones.

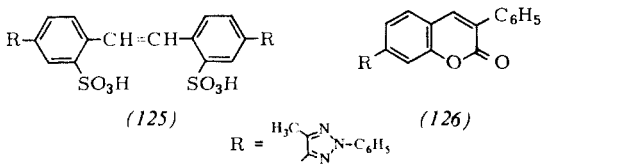
3.5. Conjugated Systems Containing 1,2,3-Triazol-4-yl Groups

Since hydroxyimino ketones—especially hydroxyiminoacetone—can be readily arylated by diazo compounds[145], fluorescing systems containing amino groups (Ar—NH_2) can be linked to a 1,2,3-triazolyl group attached through its atom C-4, yielding compounds of type *(124)*.



(124)

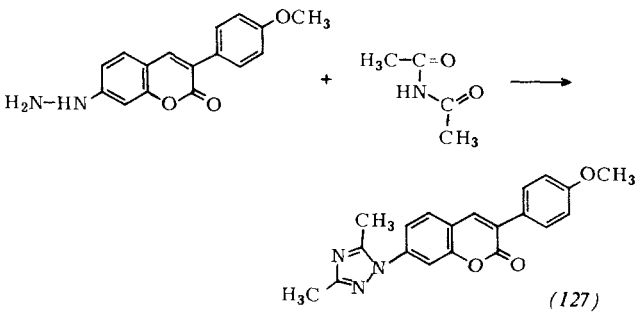
However, brighteners of this type, *e.g.* *(125)*[146] and *(126)*[147], have not become important, because in the first place their effect is somewhat smaller than that of the 1,2,3-triazol-2-yl analogs *(97)* and *(115)* and, secondly, they are considerably harder to prepare.



(125) *(126)*

3.6. Conjugated Systems Containing 1,2,4-Triazol-1-yl Groups

7-(1,2,4-Triazol-1-yl)coumarins, *e.g.* *(127)* are formed on treatment of 7-hydrazinocoumarins with formamide or diacetamide.



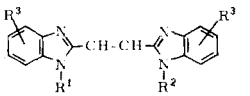
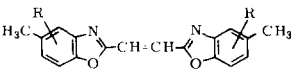
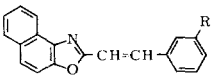
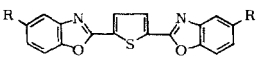
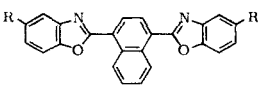
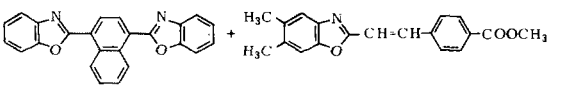
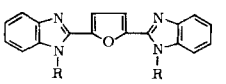
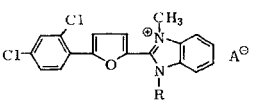
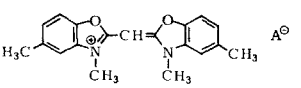
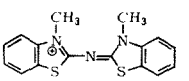
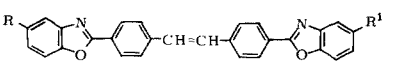
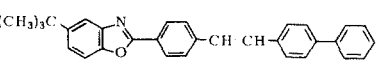
(127)

(127) can be quaternized on the triazolyl group and then used as a brightener for polyacrylonitrile[148]. Stilbene derivatives containing sulfo groups and 1,2,4-triazol-1-yl groups have also been described[149].

3.7. Conjugated Systems Containing 2-Benzimidazolyl, 2-Benzoxazolyl, or 2-Benzothiazolyl Groups

Although so far conjugated systems containing monocyclic 2-imidazolyl, 2-oxazolyl[150], or 2-thiazolyl groups have been of no industrial importance, numerous optical brighteners are derived from the benzo- or naphtho-annelated derivatives. More than 600 patents record such compounds, their main use being to provide white shades on synthetic fibers and plastics. Examples are collected in Table 5.

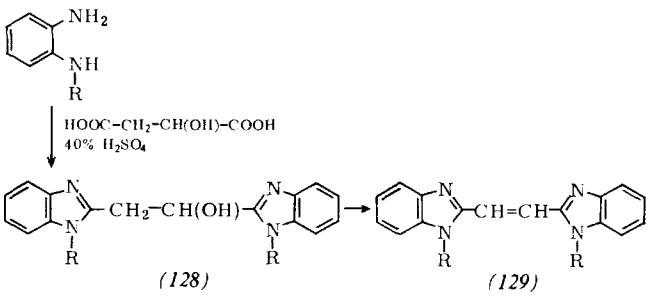
Table 5. Brighteners containing 2-benzimidazolyl, 2-benzoxazolyl or 2-benzothiazolyl groups. $A^{\ominus}$ = anion.

	Substituents	Ref.
	$R^1 = R^2 = R^3 = H$	[151]
	$R^1 = R^2 = H$, $R^3 = SO_3H$	[152]
	$R^1 = R^2 = CH_3$, $R^3 = SO_3H$	[152]
	$R^1 = R^3 = H$, $R^2 = CH_2CH_2OH$	[153]
	R = H	[154]
	R =	[155]
	R = H	[156]
	R = Cl	[157]
	R = H	[158]
	R = $C(CH_3)_3$	[159]
	R = $COOCH_3$	[160]
		[161]
	R = H	[162]
	R = CH_3	[163]
	R = C_6H_5	[164]
		[165]
		[166]
	R = H, CH_3	[167]
		[168]

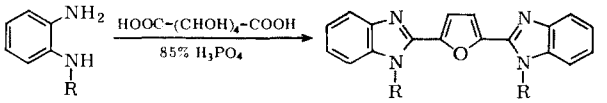
Many carbocyclic or heterocyclic systems that, like benzoxazole, themselves fluoresce weakly, are converted on combination with a 2-benzoxazolyl group into compounds showing outstanding fluorescence. There the benzoxazole produces not only an extension of the resonating system but also a lowering of the $S\pi\pi^*$ level below the usual lowest $Tn\pi^*$ level of double bond systems with a distinct decrease in the life of the excited singlet. The combination of these two effects leads to fluorescence[169].

3.7.1. Aqueous Acids as Cyclizing Agents

Aqueous acids can be used only in the synthesis of 2-benzimidazolyl derivatives. Good yields are obtained in, *e. g.*, the reaction of *o*-phenylenediamines with carboxylic acids in 40% sulfuric acid[152] or in 85% phosphoric acid[163].



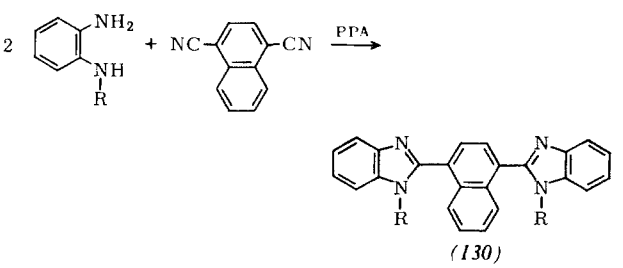
(128) *(129)*



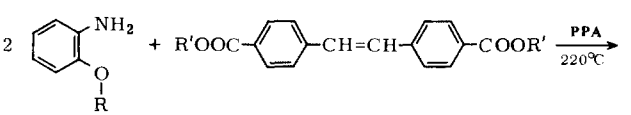
Water can be removed from the malic acid derivatives *(128)*, yielding *(129)*, by heating in tetralin[152] or by treatment with urea in glacial acetic acid[170].

3.7.2. Polyphosphoric Acid (PPA) as Cyclizing Agent

PPA containing 85% of P_2O_5 is an efficient cyclizing agent for the synthesis of benzazoles. By means of PPA, mono- or dicarboxylic acids and their amides, esters, or nitriles can be converted into benzazoles such as *(130)*[172], and *(131)*[174] on treatment with *o*-phenylenediamines, *o*-aminophenols, *o*-aminophenyl ethers or *o*-aminothiophenols at 100—200 °C with exclusion of air[151, 158, 171, 172]. The limits of this reaction are set by the sensitivity of the reactants to PPA.



(130)



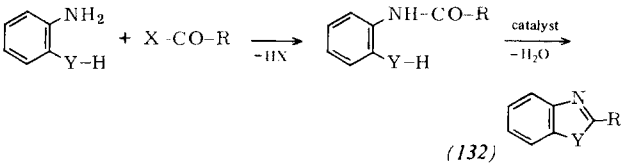
(131)

R = H, CH_3, R' = H, C_2H_5

3.7.3. Boric Acid, Toluenesulfonic Acid, or Zinc Chloride as Cyclizing Agent

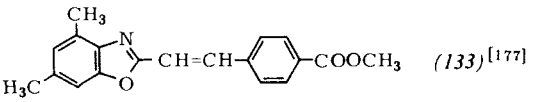
Problems of corrosion can be decreased by replacing the PPA for removal of water with boric acid, toluenesulfonic acid, or zinc chloride in an inert solvent as the catalyst. Ring closure to compounds of type *(132)* occurs as formulated.

In practice, equimolar amounts of the carboxylic acid or its ester for example, can be melted together with the amine component at 180—200 °C with exclusion of air[162, 175].

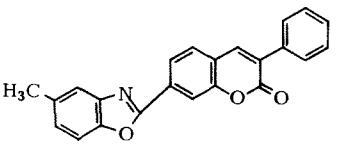


(132)

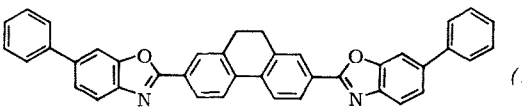
It is also possible to treat a carbonyl chloride (produced in some cases *in situ*[176]) with the amine component, and then to cyclize the resulting amide (after isolation, if necessary) by addition of the catalyst[154, 158, 160, 173]. Compounds *(133)*—*(135)* are examples of this (for solvents see references[173, 179-183]).



(133)[177]



(134)[178]

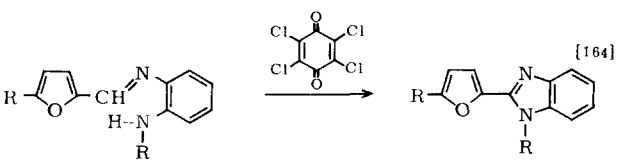


(135)[173]

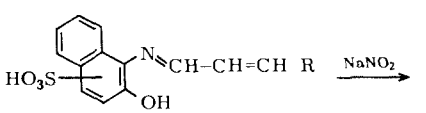
A particularly elegant variation is to treat equimolar amounts of carboxylic acid and amine components by stepwise heating in solvents while the water produced is distilled off[179, 184].

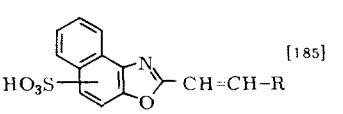
3.7.4. Oxidative Ring Closures

Schiff bases from *o*-aminophenols or *o*-phenylenediamines and aromatic aldehydes can be oxidized to benzoxazoles and benzimidazoles, respectively, in inert solvents by means of chloranil[164], sodium nitrite in glacial acetic acid[185], potassium permanganate[186], or lead(IV) salts[187].



[164]

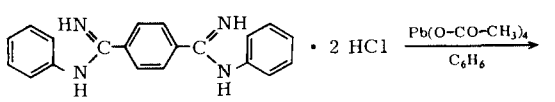




[185]

R = C_6H_5

This oxidative ring closure succeeds even with *N*-arylamidinium salts *(136)*, although with only moderate yields.

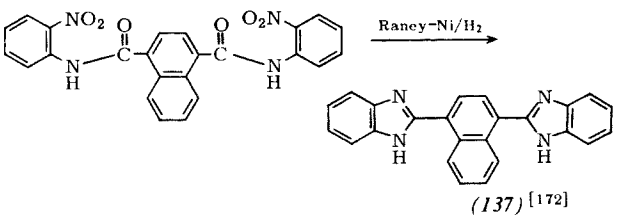


(136)

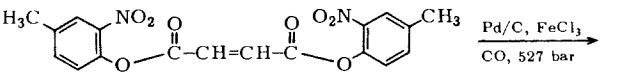
[188]

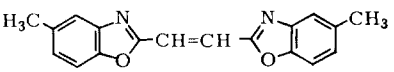
3.7.5. Reductive Ring Closures

Ring closure of derivatives of *o*-nitroanilines[172, 190] or *o*-nitrophenols[189, 191], to benzimidazoles such as *(137)* or benzoxazoles such as *(138)*, respectively, under reducing conditions can also be effected.



(137) [172]

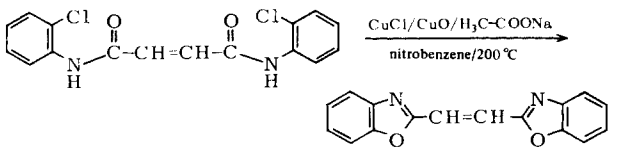




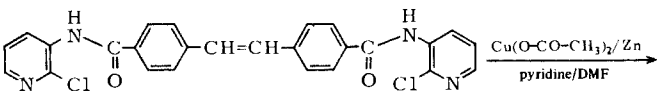
(138) [189]

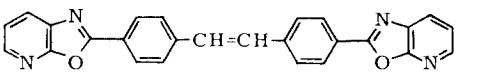
3.7.6. Benzoxazoles from *o*-Haloanilides

In recent years benzoxazole syntheses have been described that start from *o*-haloanilides. These compounds are heated with copper salts in the presence of bases, yielding the desired compounds *(139)* and *(140)*.



(139) [192]

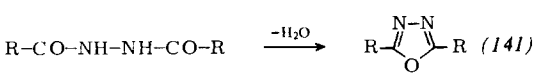




(140) [193]

3.8. Conjugated Systems Containing 1,3,4-Oxadiazole-1,2,4-Oxadiazole, or 1,3,4-Thiadiazole Derivatives

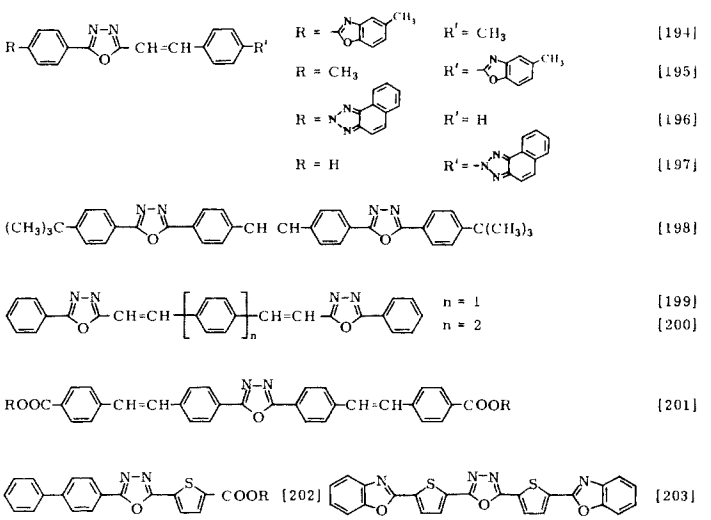
1,3,4-Oxadiazole derivatives are often mentioned in the patent literature as components in optical brighteners. 1,3,4-Oxadiazoles *(141)* are obtained on removing water from diacylhydrazines *e. g.* with thionyl chloride, oleum, or phosphorus oxychloride.



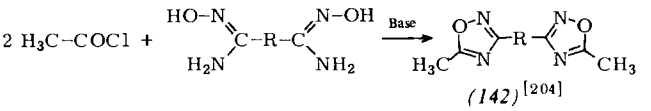
(141)

Treatment of diacylhydrazines with P_2S_3 or P_2S_5 yields 1,3,4-thiadiazole derivatives. Table 6 shows a selection of 1,3,4-oxadiazoles.

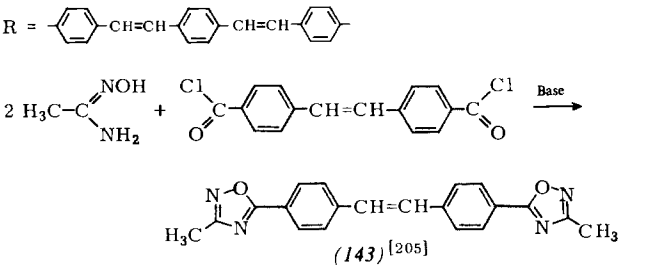
Table 6. Brighteners containing 1,3,4-oxadiazolyl groups.



1,2,4-Oxadiazoles such as *(142)* and *(143)* were only recently used as building units for optical brighteners; they have the fluorescing system attached to C-3 or C-5. The cyclization is effected in nitrobenzene.



(142) [204]



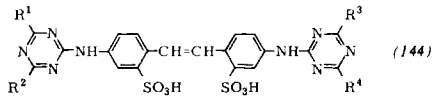
(143) [205]

3.9. Conjugated Systems Containing Triazinylamino Groups

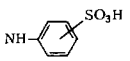
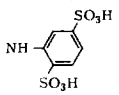
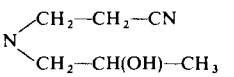
While simple acylation products of flavic acid, *e. g.* those given by substituted benzoyl chlorides[206] or phenyl isocyanate[207], have lost their importance, products acylated by the *s*-triazino group *(144)*[208] have become dominant. The almost unlimited number of combinations of the substituents R^1—R^4 permits satisfaction of almost any demand over a very broad spectrum of industrial uses. Table 7 gives a collection of characteristic compounds of this class.

Triazinylflavic acid derivatives *(144)* are prepared industrially by treating 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride) with flavic acid and any desired amine, ammonia, or alcohol—in the case of the amines in an aqueous medium and without isolation of the intermediates[218]. The bond strength between the chlorine atoms to be exchanged and the triazine ring depends on the nucleophilic character of the other substituents; this makes it possible to carry out an industrial one-step process in such a way that no disturbing yellowish to greenish by-products are formed, *e. g.* by coupling of two stilbenyl groups to one triazinyl group. The cyanuric chloride is thus usually treated with flavic acid only in the second stage[219].

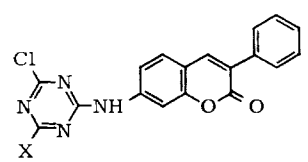
Table 7. Brighteners of type *(144)* containing *s*-triazinylamino groups.



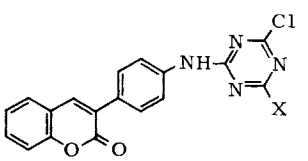
(144)

$R^1=R^3$	$R^2=R^4$	Use	Ref.
$N(CH_2-CH_2-OH)_2$	Cl	polyamide	[209]
$N(CH_2-CH_2OH)_2$ $NH-(CH_2)_2-SO_3H$	OCH_3	cellulose, wool, silk, cotton	[210]
$N(CH_3-CH_2-CH_2-SO_3H$	$O-(CH_2)_2-O-CH_3$	paper coating (casein)	[211]
$NH-C_6H_5$	NH_2	cellulose (exhaustion process)	[212]
$NH-C_6H_5$	$N(CH_2-CH_2-OH)_2$	polyamide, cellulose fabrics made from mixed fibers	[212, 213]
$NH-C_6H_5$	morpholino	detergent for cellulose	[214]
	$N(CH_2-CH_2OH)_2$	cellulose (Foulard process), paper pulp	[215]
$NH-C_6H_5$	OCH_3	polyamide, cotton	[216]
		cellulose, acid-resistant	[217]

The aminocoumarins *(14)* and *(10)* can also be acylated by cyanuric chloride, yielding *(145)* and *(146)*, respectively.



(145), X = Cl
(147), X = $N(C_2H_5)_2$

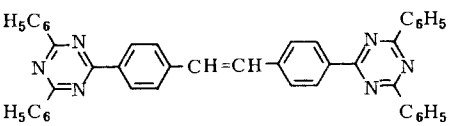


(146), X = Cl
(148), X = $N(C_2H_5)_2$

On exchange of the chlorine atom for a diethylamino group, the plastic brighteners *(147)*[220] and *(148)*[221] are obtained.

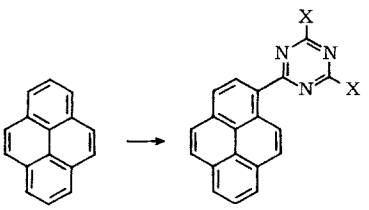
3.10. Conjugated Systems Containing *s*-Triazin-2-yl Groups

Treatment of 4,4'-stilbenedicarbonyl dichloride with benzonitrile and ammonium chloride in *o*-dichlorobenzene in the presence of aluminum chloride gives the bis(triazinyl) derivative *(149)*[222]. This high-melting compound is suitable as a brightener for polyesters that are to be spun.



(149)

The synthesis of dimethoxy(pyrenyl)-*s*-triazine *(151)* proceeds differently: for example, cautious treatment of pyrene with cyanuric chloride in the presence of aluminum chloride gives *(150)*, whose remaining chlorine atoms are finally replaced by methoxy groups[223].



(150), X = Cl
(151), X = OCH_3

4. Conclusion

Optical brighteners are used in four areas: as constituents in detergents, for whitening paper, for textile finishing, and for the brightening of plastics and paints. The demands on a brightener intended to improve the appearance of cotton and polyamide in the washing process are dictated by the local washing habits. Brighteners are required that will be withdrawn from the alkaline wash bath at the boiling point, at 50—60 °C, or at room temperature; the brighteners should be stable to peroxides and often to hypochlorite bleach solutions. Other important characteristics of brighteners used in washing machines—and the same applies equally to all areas of application—are naturally also easy availability and thus a favorable price. These demands are met partly by triazinylflavic acid derivatives of type *(144)* and partly by triazolylstilbenesulfonic acid derivatives such as *(84)*, *(89)*, or *(97)*[224].

In the paper industry too, it would no longer be conceivable to dispense with whiteners. They are either added to the paper pulp or applied by means of a starch or casein-containing surface layer. Suitable paper whiteners have proved to be, here too, triazinylflavic acid derivatives of type *(144)*, particularly those that are unaffected by fillers such as China clay and are as acid-resistant as possible.

The type of the brightener used in textile finishing varies with the material to be treated; representatives of all the classes of compounds discussed above will be encountered.

For brightening cotton, the most important textile fiber, compounds of type *(144)* are again used, for improved cotton the triazolylstilbenedisulfonic acid derivative *(98)* is particularly suitable. Polyamides are advantageously brightened by derivatives of 2-pyrazoline containing sulfonic acid, sulfonamide, or alkylsulfonyl groups, by triazinylflavic acid derivatives of type *(144)*, or by *(97)*. Derivatives of 2-pyrazoline and bis(benzoxazolyl)thiophene are available to produce whites on cellulose acetate fibers. These brighteners and also derivatives of naphthalimide, of bis(benzimidazolyl)furan and of coumarin, particularly those containing basic groups, are suitable for brightening polyacrylonitrile.

In keeping with the importance of polyester fibers a wide choice of brighteners for this material is available[225]. Among them we find stilbene derivatives such as *(90)*, naphthalimide derivatives such as *(39)* and *(40)*, as well as coumarin derivatives and numerous brighteners containing benzoxazolyl groups.

Wholly synthetic fibers can also be brightened during the spinning process, and this is probably the technically most elegant process. Again among the brighteners applied during spinning—these must be particularly fast to light and stable at elevated temperatures—we find representatives of the most varied types of compounds, namely compounds of type *(144)* (as free sulfonic acids) for brightening polyamide, 2-pyrazoline derivatives for brightening cellulose acetates, polyamide, or polyacrylonitrile, and benzoxazolylstilbene, benzoxazolylnaphthalene, and coumarin derivatives such as *(94)* for brightening polyester fibers. The situation for plastics brighteners is very similar.

Optical brighteners have been used for about 30 years without any harmful side effects having been reported. Nevertheless, it is only recently that ecological and toxicological doubts about these products, which are especially easily detected because of their fluorescence, were disposed of at a scientific Hearing in Stockholm[226].

In this review it has been possible to discuss only a selection from the chemistry of brighteners. The diversity of classes of brighteners and the matching of individual products to industrial requirements have been possible only because of the great variety of heterocyclic chemistry.

Received: July 1, 1975 [A 81 IE]
German version: Angew. Chem. *87*, 693 (1975)
Translated by Express Translation Service, London

[1] *S. Petersen*, Angew. Chem. *61*, 17 (1949).
[2] *R. Zweidler*, Textilveredlung *4*, 75 (1969); *A. K. Sarkar:* Fluorescent Whitening Agents. Merrow Publishing Co. Ltd., Watford 1971; *H. Gold* in *K. Venkataraman:* The Chemistry of Synthetic Dyes. Academic Press, New York 1971, Vol. 5, pp. 535ff.
[3] Austrian Pat. 175871 (1950), Sandoz; DBP 842074 (1946), Ciba, Inv. *F. Ackermann*; DBP 946449 (1952), Bayer, Inv. *H. Gold* and *S. Petersen.*
[4] *B. N. Mattoo*, Trans. Faraday Soc. *52*, 1184 (1956); *C. E. Wheelock*, J. Am. Chem. Soc. *81*, 1348 (1959); *H. Umemoto*, *T Kitano*, and *K. Konishi*, Kogyo Kagaku Zasshi *73*, 1146 (1970).
[5] *P. I. Petrovich* and *N. A. Borisevich*, Isv. Akad. Nauk SSSR, Ser. Fiz. *27*, 703 (1963).
[6] DBP 1262206 (1961), Bayer, Inv. *R. Raue* and *A. Brack.*
[7] DBP 1222014 (1960), Ciba, Inv. *E. A. Siegrist*, *P. Liechti*, and *M. Dünnenberger.*
[8] *H. Umemoto et al.* Kogyo Kagaku Zasshi *74*, 2123 (1971).
[9] USSR-Pat. 186501 (1965), Inv. *P. I. Petrovich* and *A. G. Emel'yanov.*
[10] DBP 1090624 (1955), Inv. *R. Raue et al.:* USSR-Pat. 165750 (1963), Inv. *P. I. Petrovich.*
[11] DBP 1275983 (1956), BASF, Inv. *F. Mühlbauer et al.*
[12] French Pat. 1565731 (1967), Hickson & Welch.
[13] *J. R. Johnson*, Org. React. *1*, 210 (1942).
[14] DBP 1102694 (1960), Bayer, Inv. *R. Raue.*
[15] US-Pat. 3351482 (1965), Bayer, Inv. *R. Raue*; Belg. Pat. 703813 (1966), Hickson & Welch, Inv. *A. K. Sarkar.*
[16] DOS 2240037 (1971), Ciba-Geigy, Inv. *P. Liechti.*
[17] DBP 1296121 (1961), Bayer, Inv. *R. Raue* and *H. Gold*; DOS 2329991, 2355116 (1972), Ciba-Geigy, Inv. *H. Schläpfer.*
[18] *J. R. Johnson*, Org. React. *1*, 226 (1942).
[19] *W. E. Solodar* and *M. Green*, J. Org. Chem. *23*, 103 (1958); *E. Profft* and *K. Stuehmer*, Arch. Pharm. *300*, 1 (1967).
[20] DBP 1020636 (1955), Geigy, Inv. *H. Häusermann.*
[21] *J. J. Blanksma*, Rec. Trav. Chim. Pays-Bas *29*, 408 (1910).
[22] US-Pat. 3514471 (1968), Showa Chem. Ind., Inv. *T. Yanagisawa* and *O. Kotoyori.*
[23] DOS 1793262 (1968), Inv. *H. Knupfer* and *C.-W. Schellhammer.*
[24] *N. V. Subba Rao* and *V. Sundaramurthy*, Proc. Indian Acad. Sci., Sect. A *54*, 321 (1961).
[25] *A. A. Goldberg* and *R. S. Theobald*, J. Chem. Soc. *1954*, 2641; *H. Ichibagase*, J. Pharm. Soc. Jap. *75*, 1477 (1955).
[26] DBP 1293160 (1964), Bayer, Inv. *C.-W. Schellhammer*, *K.-W. Müller*, and *R. Raue.*
[27] *S. Sethna* and *R. Phadke*, Org. React. *7*, 1 (1953).
[28] Czechoslovak Pat. 141903 (1968), Inv. *J. Pirkl.*
[29] US-Pat. 3322794 (1964), Geigy, Inv. *J. Haeberli.*
[30] US-Pat. 3356689 (1966), Geigy, Inv. *J. Haeberli.*
[31] US-Pat. 2616855 (1952), Procter & Gamble, Inv. *C. E. Wheelock.*
[32] DOS 1469225 (1964), Bayer, Inv. *W.-D. Wirth*, *H. Knupfer*, and *C.-W. Schellhammer.*
[33] DAS 1278385 (1965), Bayer, Inv. *H. Knupfer et al.*
[34] Belg. Pat. 679188 (1965), Bayer, Inv. *H. Knupfer*, *W.-D. Wirth*, and *C.-W. Schellhammer.*
[35] *R. N. Nurmukhametov* and *V. B. Tishenko*, Opt. Spectrosc. (USSR) *23*, 43 (1967).
[36] *S. V. Tsukerman*, *E. G. Buryakovskaya*, and *V. F. Lavrushin*, Opt. Spectrosc. (USSR) *26*, 299 (1969).
[37] *S. R. Sandler* and *K. C. Tsou*, J. Chem. Phys. *39*, 1062 (1963).
[38] *I. H. Leaver*, Mol. Photochem. *5*, 411 (1973); *I. H. Leaver* and *D. E. Rivett*, *ibid. 6*, 113 (1974); *Z. Raciszewski* and *J. F. Stephan*, J. Am. Chem. Soc. *91*, 4338 (1969); *A. Z. Karimova et al.*, J. Appl. Spectrosc. (USSR) *11*, 1334 (1969).
[39] DAS 1419329 (1962), Hoechst, Inv. *E. Schinzel* and *K.-H. Lebkücher.*
[40] DOS 2011552 (1970), 2142564 (1971), Hoechst, Inv. *H. Mengler*, *E. Schinzel*, and *G. Rösch*; DOS 2145019 (1971), Hoechst, Inv. *H. Mengler.*
[41] US-Pat. 3378389 (1962), Bayer, Inv. *C.-W. Schellhammer* and *A. Wagner*; Austrian Pat. 251532 (1964), Hoechst.
[42] Netherlands Pat. 6906448 (1959), Bayer.
[43] Brit. Pat. 1209631 (1967), ICI, Inv. *G. H. Keats.*
[44] DOS 2050725 (1970), Bayer, Inv. *G. Boehmke* and *H. Theidel.*
[45] DOS 2403308 (1973), Sandoz, Inv. *J. J. Bolton*, *F. Fleck*, and *A. V. Mercer.*
[46] DOS 2158304 (1970), Ugine Kuhlmann, Inv. *A. M. S. Domergue*, *G. R. H. Mingasson*, and *R. F. M. Sureau.*
[47] DOS 1670980 (1968), Bayer, Inv. *M. Hajek.*
[48] DOS 1670988 (1968), Bayer, Inv. *M. Hajek.*
[49] DOS 1695103 (1966), Ciba, Inv. *S. Rosenberger*, *E. Troxler*, and *H. Häusermann.*
[50] DOS 1802642 (1967), Ciba, Inv. *E. Troxler* and *H. Häusermann.*
[51] DOS 2235073 (1971), Sandoz, Inv. *F. Fleck*, *P. S. Littlewood*, and *A. V. Mercer.*
[52] DOS 2248772 (1971), Sandoz, Inv. *H. Aebli.*
[53] DOS 1900349 (1969), BASF, Inv. *K. Adelsberger*, *E. Hahn*, and *H. Scheuermann.*
[54] DOS 2217259 (1971), Ciba, Inv. *M. Stagi.*
[55] DAS 1104483 (1955), Bayer, Inv. *A. Wagner* and *S. Petersen.*
[56] DAS 1090683 (1956), Bayer, Inv. *A. Wagner* and *S. Petersen.*
[57] Brit. Pat. 906960 (1960), Bayer.
[58] DOS 1670722 (1966), Hoechst, Inv. *E. Schinzel*, *S. Bildstein*, and *K. H. Lebkücher.*
[59] DOS 1904424 (1969), Hoechst, Inv. *G. Rösch et al.*
[60] DOS 2310446 (1973), Bayer, Inv. *J. Schroeder* and *C.-W. Schellhammer.*
[61] DOS 1923702 (1969), Hoechst, Inv. *H. Mengler et al.*: DOS 1904424 (1969), Hoechst, Inv. *G. Rösch et al.*: French Pat. 2219945 (1973), Bayer, Inv. *J. Schroeder* and *C.-W. Schellhammer.*
[62] US-Pat. 2600080 (1946), GAF, Inv. *M. O. Shrader*; DBP 1019274 (1953), BASF, Inv. *E. Tolksdorf*, *F. Schubert*, and *E. Kern*; DBP 1023169 (1958), BASF, Inv. *E. Tolksdorf*, *F. Schubert*, and *E. Kern*; DBP 1068260 (1959), BASF, Inv. *E. Hold.*
[63] Jap. Pat. 6515468 (1962), Mitsubishi, Inv. *J. Okada* and *I. Yasuda.*
[64] DOS 1445961 (1961), Mitsubishi, Inv. *T. Kasai et al.*; DOS 1419350 (1962), Mitsubishi, Inv. *T. Kasai.*
[65] Jap. Pat. 7113963 (1968), Mitsubishi, Inv. *S. Kasai.*
[66] Jap. Pat. 7000774 Jap. Pat. 7034438 (1967), Mitsubishi, Inv. *H. Okada* and *M. Kaneko.*
[67] DOS 2064159 (1969), Sumitomo, Inv. *S. Hotta* and *T. Akamatsu*; DOS 2043662 (1970), BASF, Inv. *H. Scheuermann.*
[68] Jap. Pat. 7134509, Jap. Pat. 7138418 (1968), Mitsubishi, Inv. *H. Okada*, *S. Imahori*, and *S. Hirako.*
[69] Jap. Pat. 7213382 (1967), Teijin Ltd., Inv. *F. Takabayashi* and *N. Ito.*
[70] Jap. Pat. 7002672, Jap. Pat. 6918955 (1967), Nippon Kayaku, Inv. *T. Noguchi* and *K. Tsukamoto*; Jap. Pat. 7227777 (1969), Mitsubishi, Inv. *H. Okada* and *S. Imahori*; Jap. Pat. 7213383 (1967), Teijin Ltd.
[71] Jap. Pat. 7223706 (1968), Nippon Kayaku, Inv. *T. Noguchi*, *K. Tsukamoto*, and *T. Matsunaga*; Jap. Pat. 7142506 (1968), Mitsubishi, Inv. *H. Okada* and *M. Kaneko.*
[72] DOS 1470051 (1963), Mitsubishi, Inv. *H. Senshu* and *M. Yamashita.*
[73] Jap. Pat. 6820971 (1964), Seisan Kaihatsu, Inv. *R. Kimura* and *T. Yabuuchi.*
[74] Jap. Pat. 7035595 (1967), Nippon Kayaku, Inv. *T. Noguchi* and *T. Matsunaga*; DOS 1928286 (1969), Mitsubishi, Inv. *H. Okada et al.*
[75] DOS 1939620 (1969), Ugine Kuhlmann, Inv. *G. R. H. Mingasson.*
[76] Jap. Pat. 6918957, Jap. Pat. 7002674 (1967), Nippon Kayaku.

[77] Jap. Pat. 6918956 (1967), Nippon Kayaku, Inv. *T. Noguchi, K. Tsukamoto*, and *D. Matsunaga*.
[78] French Pat. 1541050 (1967), Ugine Kuhlmann, Inv. *G. R. H. Mingasson et al.*
[79] DOS 1795091 (1967), Ugine Kuhlmann, Inv. *G. R. H. Mingasson* and *A. Domergue*.
[80] French Pat. 1557945 (1968), Nippon Kayaku; Jap. Pat. 7002668 (1967), Nippon Kayaku, Inv. *T. Noguchi* and *D. Matsunaga*.
[81] DOS 1419350 (1962), Mitsubishi, Inv. *T. Kasai et al.*
[82] Review: *H. Gold* in *K. Venkataraman:* The Chemistry of Synthetic Dyes. Academic Press, New York 1971, Vol. 5, p. 620.
[83] DOS 2242513 (1972), Hoechst, Inv. *W. Deucker* and *H. Tröster*; DOS 2302372 (1973), Hoechst, Inv. *W. Deucker* and *H. Tröster*.
[84] Jap. Pat. 7308309 (1971), Mitsubishi, Inv. *H. Okada* and *M. Kaneko*.
[85] Belg. Pat. 612955 (1961), *T. Kasai*.
[86] *M. Okazaki et al.*, Yûki Gosei Kagaku Kyôkai Shi *14*, 455 (1956).
[87] *T. Kasai* and *K. Himeno*, Kogyo Kagaku Zasshi *72*, 1128 (1969).
[88] Jap. Pat. 7405333 (1969), Nippon Kagaku, Inv. *T. Noguchi* and *S. Matsunaga*.
[89] DAS 1154799 (1962), Hoechst, Inv. *H. Sieber*.
[90] *K. Oka, T. Hinohara*, and *K. Matsui*, Kogyo Kagaku Zasshi *71*, 1010 (1968).
[91] DOS 2105305 (1971), Hoechst, Inv. *W. Sahm, E. Schinzel*, and *G. Rösch*.
[92] DOS 2306515 (1973), Bayer, Inv. *P. Hartmann*.
[93] Brit. Pat. 871351 (1956), O. Dann.
[94] French Pat. 1558762 (1967), Bayer.
[95] US-Pat. 2980549 (1956), GAF, Inv. *E. Craig*.
[96] DAS 1111188 (1959), Hoechst, Inv. *W. Koller* and *P. Schlack*.
[97] DBP 1087609 (1957), Geigy, Inv. *A. F. Daglish, P. Vonderwahl*, and *G. A. Tollotson*.
[98] DBP 1222885 (1962), Bayer, Inv. *G. Wolfrum et al.*
[99] DAS 1253275 (1961), Ciba, Inv. *E. Matter*.
[100] *G. Gonis* and *E. D. Amstutz*, J. Org. Chem. *27*, 2947 (1962).
[101] US-Pat. 2900386 (1956), Henkel, Inv. *B. Raecke et al.*
[102] Belg. Pat. 611897 (1960), Ciba; Swiss. Pat. 437347 (1961), Ciba, Inv. *P. Liechti, A. E. Siegrist*, and *E. Maeder*.
[103] DBP 1276588 (1961), Geigy, Inv. *H. Häusermann*; French Pat. 1320597 (1961), Geigy.
[104] DOS 1942926 (1969), Bayer, Inv. *C.-W. Schellhammer*; US-Pat. 3663560 (1967), Bayer, Inv. *C.-W. Schellhammer, A. Dorlars*, and *W.-D. Wirth*; DOS 2040189 (1970), Bayer, Inv. *A. Dorlars* and *H. Gold*.
[105] DBP 1469220 (1964), Bayer, Inv. *C.-W. Schellhammer* and *A. Wagner*.
[106] DBP 1594850 (1967), Bayer, Inv. *A. Dorlars* and *O. Neuner*.
[107] DOS 2131788 (1971), Bayer, Inv. *J. Schroeder* and *C.-W. Schellhammer*.
[108] DOS 1932256 (1968), Geigy, Inv. *G. Kabas* and *R. Zweidler*.
[109] DOS 1931757 (1968), Geigy, Inv. *J. A. Gurney*.
[110] Brit. Pat. 1200852 (1968), Bayer, Inv. *U. Fetzer* and *C.-W. Schellhammer*.
[111] DOS 1695119 (1967), Geigy, Inv. *H. Häusermann* and *E. Troxler*.
[111a] Information about triazoles will be found in review articles: *F. R. Benson* and *W. L. Savell*, Chem. Rev. *46*, 1 (1950); *T. L. Gilchrist* and *G. E. Gymer*, Advan. Heterocycl. Chem. *16*, 33 (1974).
[112] DBP 1008248 (1955), Bayer, Inv. *H. Gold* and *O. Bayer*.
[112a] Cf. Houben-Weyl: Methoden der Organischen Chemie. Thieme, Stuttgart 1965. 1. Edit., Vol. X/3, pp. 809f.
[113] DAS 1282591 (1963), Bayer, Inv. *C.-W. Schellhammer, R. Raue*, and *H. Gold*.
[114] DBP 911368 (1948), Bayer, Inv. *H. Gold* and *S. Petersen*.
[115] DBP 942395 (1951), Geigy, Inv. *E. Keller, R. Zweidler*, and *H. Häusermann*.
[116] DBP 1052405 (1956), Geigy, Inv. *R. Zweidler* and *E. Keller*; Belg. Pat. 664606 (1964), Geigy; DBP 1220381 (1960); GAF, Inv. *A. F. Strobel* and *S. C. Catino*.
[116a] DBP 1065838 (1957), Geigy, Inv. *H. Häusermann*; DBP 846849 (1948), Geigy, Inv. *H. Häusermann* and *R. Zweidler*; DAS 1218436 (1961), GAF, Inv. *J. A. Cofrancesco*.
[116b] DBP 955686 (1952), Geigy, Inv. *R. Zweidler* and *E. Keller*.
[117] US-Pat. 3157644 (1956), GAF, Inv. *F. Marschall, H. B. Freyermuth*, and *W. W. Williams*; DOS 2148017, DOS 2148018, DOS 2148512 (1970), Ciba-Geigy, Inv. *A. E. Siegrist*.
[118] *A. E. Siegrist*, Helv. Chim. Acta *50*, 906 (1967), and further communications.
[119] DBP 1234224 (1963), Sandoz, Inv. *F. Fleck, H. Balzer*, and *H. Aebli*.
[120] DOS 1470242 (1962), Sandoz, Inv. *F. Fleck, H. Balzer*, and *H. Aebli*.
[121] DOS 1519471 (1965), Bayer, Inv. *W.-D. Wirth, H. Knupfer*, and *C.-W. Schellhammer*.
[122] DOS 1519461 (1965), Bayer, Inv. *A. Dorlars, O. Neuner*, and *R. Pütter*.
[123] DBP 1279636 (1965), Bayer, Inv. *A. Dorlars, O. Neuner*, and *R. Pütter*.
[124] French Pat. 1567496 (1967), Bayer, Inv. *A. Dorlars* and *O. Neuner*.
[125] DOS 2213754 (1971), Ciba-Geigy, Inv. *G. Kabas, H. Schläpfer*, and *I. Fletcher*.
[126] DBP 1287550 (1966), Bayer, Inv. *A. Dorlars* and *O. Neuner*.
[126a] DOS 2032172 (1970), Bayer, Inv. *A. Dorlars* and *O. Neuner*.
[127] *H. v. Pechmann*, Liebigs Ann. Chem. *262*, 270 (1891).
[128] DBP 1168437 (1962), Hoechst, Inv. *R. Mohr* and *M. Zimmermann*.
[129] US-Pat. 3697596, US-Pat. 3697597 (1968), Bayer, Inv. *A. Dorlars*.
[130] DBP 1670914 (1967), Bayer, Inv. *A. Dorlars* and *O. Neuner*; DOS 2242784 (1972), Bayer, Inv. *H. Gold* and *U. Claussen*.
[131] DOS 2210261 (1972), Bayer, Inv. *U. Claussen, H. Gold*, and *J. Schroeder*.
[132] DOS 1695122 (1967), Geigy, Inv. *R. Kirchmayr, H. Heller*, and *J. Rody*.
[133] DOS 2029096, DOS 2029142, DOS 2029157 (1969), Geigy, Inv. *R. Kirchmayr* and *H. Schläpfer*.
[134] *O. Neuner*, Bayer, unpublished.
[135] DOS 2112198 (1970), Ciba-Geigy, Inv. *R. Kirchmayr*.
[136] DOS 2213839 (1971), Ciba-Geigy, Inv. *G. Kabas, H. Schläpfer*, and *I. Fletcher*.
[136a] DOS 1795073 (1967), Ciba-Geigy, Inv. *K. Weber et al.*
[136b] DOS 2258276 (1972), Bayer, Inv. *A. Dorlars* and *O. Neuner*.
[136c] DAS 1108219 (1959), BASF, Inv. *W. Stilz* and *H. Pommer*; DAS 1112072 (1959), BASF, Inv. *W. Stilz, H. Pommer*, and *K.-H. König*.
[137] DAS 1794396 (1966), Bayer, Inv. *O. Neuner et al.*
[137a] US-Pat. 3869469 (1972), Bayer, Inv. *O. Neuner* and *A. Dorlars*.
[138] DOS 2159797 (1970), Ciba-Geigy, Inv. *R. Zweidler et al.*
[139] DOS 1670969 (1968), Bayer, Inv. *A. Dorlars* and *W.-D. Wirth*.
[140] DOS 2037854 (1970), Bayer, Inv. *A. Dorlars* and *C.-W. Schellhammer*.
[141] DOS 1670999 (1968), Bayer, Inv. *A. Dorlars, C.-W. Schellhammer*, and *W.-D. Wirth*.
[142] DOS 2335218 (1973), Bayer, Inv. *J. Schroeder*.
[143] DOS 2226524 (1972), Bayer, Inv. *A. Dorlars, A. Vogel*, and *C.-W. Schellhammer*.
[144] DOS 1670810 (1967), Bayer, Inv. *A. Dorlars* and *C.-W. Schellhammer*.
[144a] DOS 2310123 (1973), Bayer, Inv. *A. Dorlars*.
[145] Cf. *R. Pütter* in Houben-Weyl: Methoden der Organischen Chemie. Thieme, Stuttgart 1965. 1. Edit., Vol. X/3, pp. 185ff.
[146] DOS 2062383 (1969), Sandoz, Inv. *H. Balzer et al.*
[147] US-Pat. 3686202 (1968), Ciba-Geigy, Inv. *R. Kirchmayr* and *J. Rody*.
[148] French Pat. 1551662 (1967), Bayer, Inv. *C.-W. Schellhammer*.
[149] DOS 1919209 (1969), Hoechst, Inv. *A. Horn, E. Schinzel*, and *G. Rösch*.
[150] DOS 2050771 (1969), Sumitomo, Inv. *M. Matsuo, S. Sagaguchi*, and *T. Akamatsu*.
[151] DAS 1105423 (1958), Ciba, Inv. *M. Dünnenberger* and *A. E. Siegrist*.
[152] DAS 1039064 (1954), Ciba, Inv. *A. E. Siegrist* and *F. Ackermann*.
[153] DAS 1090167 (1957), Ciba, Inv. *M. Dünnenberger* and *A. E. Siegrist*.
[154] DAS 1090214 (1955), Ciba, Inv. *F. Ackermann* and *A. E. Siegrist*; DAS 1040555 (1956), Ciba, Inv. *F. Ackermann, M. Dünnenberger*, and *A. E. Siegrist*.
[155] DOS 1419312 (1960), Daito Chem. Ind., Inv. *K. Konishi et al.*
[156] French Pat. 1336949 (1961), Mitsui.
[157] US-Pat. 3597364 (1962), Mitsui Toatsu, Inv. *I. Okubo* and *M. Tsujimoto*.
[158] DAS 1166197 (1959), Ciba, Inv. *M. Dünnenberger, A. E. Siegrist*, and *E. Maeder*.
[159] Swiss Pat. 439292, Swiss. Pat. 492818 (1961), Ciba, Inv. *E. Maeder, P. Liechti, A. E. Siegrist*, and *M. Dünnenberger*.
[160] DOS 1795602 (1966/67), Hoechst, Inv. *H. Frischkorn, U. Pintschorius*, and *H. Behrenbruch*; DOS 1745622 (1966), Hoechst, Inv. *H. Frischkorn, U. Pintschovius*, and *H. Behrenbruch*.
[161] DAS 1594855 (1967), Hoechst, Inv. *G. Rösch, E. Schinzel*, and *O. Smerz*.
[162] DAS 1086237 (1958), Ciba, Inv. *M. Dünnenberger* and *A. E. Siegrist*.
[163] DAS 1147232 (1958), Ciba, Inv. *M. Dünnenberger, A. E. Siegrist*, and *E. Maeder*.
[164] DOS 1469227 (1964), Bayer, Inv. *H. Harnisch* and *R. Raue*; DOS 1545846 (1965), Bayer, Inv. *H. Harnisch* and *R. Raue*.
[165] Brit. Pat. 736452 (1952), Geigy.
[166] DAS 1089721 (1959), BASF, Inv. *H. Balli et al.*, DAS 1144280 (1961), BASF, Inv. *M. Seefelder* and *H. G. Reppe*.
[167] DAS 1445694 (1962), Kodak, Inv. *D. G. Hedberg et al.*, DAS 1445699 (1963), Kodak, Inv. *M. S. Bloom*.
[168] Austrian Pat. 270567 (1965), Ciba.
[169] *A. Reiser et al.*, J. Am. Chem. Soc. *94*, 2414 (1972).
[170] DAS 1067441 (1957), Ciba, Inv. *A. E. Siegrist*.
[171] US-Pat. 2985611 (1956), Am. Cyanamid, Inv. *D. W. Hein, R. J. Alheim*, and *J. J. Leavitt*; Jap. Pat. 7001891 (1965), Osaka Seika, Inv. *T. Tonegawa* and *S. Iono*; DDR-Pat. 94998 (1971), *J. Liebscher* and *H. Hartmann*; Jap. Pat. 7138417 (1968), Showa Chem. Ind., Inv. *K. Matsui, K. Otaguro*, and *E. Kobayashi*.
[172] Belg. Pat. 717988 (1967), Hoechst.
[173] DOS 2344841 (1972), Ciba-Geigy, Inv. *K. Weber*.
[174] DAS 1288608 (1963), Sumitomo, Inv. *T. Kinoshita*.
[175] DAS 1109177 (1958), Ciba, Inv. *M. Dünnenberger, A. E. Siegrist*, and *E. Maeder*.
[176] DOS 1519486 (1964), Nippon Kayaku, Inv. *N. Ono, S. Serizawa*, and *M. Sumitani*.
[177] French Pat. 1532087 (1966), Hoechst.
[178] DOS 1594830 (1965), Ciba, Inv. *E. Maeder* and *A. E. Siegrist*.
[179] DOS 1949334 (1968), Ciba, Inv. *E. Matter*.

[180] DAS 1253222 (1962), Ciba, Inv. *E. Maeder et al.*
[181] DOS 2237874 (1971), Ciba, Inv. *H. R. Meyer.*
[182] DOS 1470289 (1963), Sumitomo, Inv. *M. Ohkawa, Y. Yamakawa*, and *T. Kinoshita.*
[183] Jap. Pat. 6830193 (1965), Nisso Chem. Ind., Inv. *G. Hayakawa* and *G. Mochizuki.*
[184] DOS 1795157 (1967), Ciba, Inv. *E. Matter.*
[185] US-Pat. 3341529 (1964), Am. Cyanamid, Inv. *B. G. Buell.*
[186] US-Pat. 3767663 (1970), Am. Cyanamid, Inv. *H. X. Kaempfen* and *S. County.*
[187] DOS 2230077 (1971), Morton Norwich Prod., Inv. *K. J. Hayes.*
[188] US-Pat. 3206468 (1968), Merck Co., Inv. *V. J. Grenda.*
[189] DOS 2047998 (1969), Am. Cyanamid, Inv. *A. G. Mohan* and *R. K. Madison.*
[190] DOS 2159469 (1970), Ciba, Inv. *H. Schläpfer.*
[191] DAS 1232922 (1960), Ciba, Inv. *M. Dünnenberger et al.*
[192] DAS 1445861 (1961), Hodogaya, Inv. *M. Lizecka et al.*
[193] DOS 2003575 (1969), Am. Cyanamid, Inv. *H. X. Kaempfen.*
[194] Jap. Pat. 7041629 (1967), Osaka Seika, Inv. *S. Jono* and *T. Fujino.*
[195] Jap. Pat. 7422929 (1967), Osaka Seika.
[196] Jap. Pat. 7041630 (1967), Osaka Seika, Inv. *S. Jono* and *T. Fujino.*
[197] Jap. Pat. 7108785 (1966), Osaka Seika, Inv. *K. Tonegawa, S. Seino*, and *T. Fujino*; Jap. Pat. 6920268 (1966), Osaka Seika, Inv. *K. Tonegawa, J. Jono*, and *T. Fujino.*
[198] French Pat. 1445769 (1964), Ciba.
[199] DOS 2356611 (1972), Ciba, Inv. *H. R. Meyer.*
[200] DOS 2350570 (1972), Ciba, Inv. *H. R. Meyer.*
[201] DOS 1594824 (1965), Ciba, Inv. *A. E. Siegrist et al.*
[202] DAS 1238874 (1962), Ciba, Inv. *A. E. Siegrist et al.*
[203] Brit. Pat. 1115325 (1965), Ciba.
[204] DOS 1955374 (1969), BASF, Inv. *H. Scheuermann.*
[205] DOS 1958778 (1969), BASF, Inv. *H. Scheuermann.*
[206] US-Pat. 2089413 (1934), ICI, Inv. *C. Praine, J. A. Radley*, and *L. P. Rendel.*
[207] DRP 746569 (1940), IG Farbenindustrie, Inv. *S. Petersen, O. Bayer*, and *B. Wendt.*
[208] DRP 731558, 752677 (1940), IG Farbenindustrie, Inv. *B. Wendt.*
[209] DBP 814902 (1947), ICI, Inv. *D. A. W. Adams* and *R. H. Wilson.*
[210] DBP 848496 (1949), Ciba, Inv. *F. Ackermann*; DBP 1183882 (1960), Bayer, Inv. *J. Hagemann* and *W. Schölermann.*
[211] DBP 1444015 (1963), Bayer, Inv. *H. Gold, E. Lehmann*, and *W. Theuer.*
[212] DRP 752677 (1940), IG Farbenindustrie, Inv. *B. Wendt.*
[213] DBP 1119646 (1959), Du Pont, Inv. *J. Gessner* and *R. C. Seyler.*
[214] DBP 814901 (1947), ICI, Inv. *R. H. Wilson*; DBP 859313 (1948), GAF, Inv. *W. W. Williams* and *W. E. Wallace*; DBP 870263 (1951), Ciba, Inv. *F. Ackermann.*
[215] DBP 1090168 (1957), Bayer, Inv. *J. Hegemann, A. Mitrowsky*, and *H. Roos.*
[216] Jap. Pat. 5505983 (1955), Nisso Chem. Ind., Inv. *G. Hayakawa.*
[217] Cf., *e.g.*, DOS 2430624 (1973), Sandoz, Inv. *F. Fleck* and *H. R. Schmid.*
[218] DBP 1250830 (1965), Bayer, Inv. *H. Gold* and *E. A. Kleinheidt.*
[219] Brit. Pat. 1174631 (1967), Bayer, Inv. *H. Gold* and *E. A. Kleinheidt.*
[220] DBP 1096909 (1957), Geigy, Inv. *H. Häusermann*; DBP 1274063 (1964), Bayer, Inv. *O. Berendes, H. Gold*, and *C.-W. Schellhammer*; US-Pat. 3429880 (1965), Geigy, Inv. *H. Häusermann*; US-Pat. 3518266 (1967), Geigy, Inv. *H. Häusermann* and *E. Troxler.*
[221] DBP 1249211 (1961), Bayer, Inv. *E. Siegel* and *H. Gold.*
[222] DAS 1294922 (1964), Ciba, Inv. *A. E. Siegrist et al.*
[223] DBP 1273479 (1961), ICI, Inv. *J. R. Atkinson* and *S. Hartley.*
[224] *K.-D. Bode*, Tenside Deterg. *12*, 69 (1975).
[225] *H. Hefti*, Textilveredlung *4*, 94 (1969).
[226] MVC-Report 2: Fluorescent Whitening Agents. Stockholm 1973; cf. also *F. Coulston, F. Korre, R. Anliker*, and *G. Müller*: Environmental Quality and Safety, Suppl. Vol. 3. Thieme, Stuttgart, in press.

Detection of Fragment Genesis in the Mass Spectrometer: DADI Mass Spectrometry as an Aid in the Structure Analysis of Organic Compounds

New analytical methods (3)

By Urs Peter Schlunegger[*]

"*D*irect *A*nalysis of *D*aughter *I*ons" (DADI) can be carried out with commercial mass spectrometers embodying the Nier-Johnson inverse geometry. DADI measurements permit experimental detection of the consecutive formation of molecule fragments (fragment genesis). Knowledge of fragment genesis enables the chemist to clarify the fragmentation processes of molecule-ions and provides information on the structure of fragments formed in the mass spectrometer. In combination with classical mass spectrometry such information makes it easier to determine the structure of compounds, to analyze mixtures, to determine the sequence in periodically constructed molecules, for example oligopeptides, and to study rearrangement reactions occurring in the mass spectrometer.

1. Introduction

*D*irect *A*nalysis of *D*aughter *I*ons (DADI) was first put forward by *Maurer et al.* in May 1971[1]. In November of that year *Beynon* and *Cooks* published the same method under the abbreviated name MAIKES (*M*ass *A*nalyzed *I*on *K*inetic *E*nergy *S*pectrometry)[2]. Both designations attempt to characterize the basis of the method, *Beynon*'s more from the theoretical standpoint. The abbreviation DADI seems to be more readily understood by the practical chemist and will therefore be used here. Since DADI mass spectrometry is relatively young and may not be too well known to chemists, its potential utilization will first be demonstrated for the case of 3-methyl-4-phenyl-2-butanone (Fig. 1). The classical mass spectrum (Fig. 2a) of this compound is reproduced as a typical example in a widely used textbook of organic chemistry[4]. In the discussion of the relationships between structure and mass spectra the fragment ion at $m/e = 147$ ($M^+ - 15$) is there described as the product of removal of the methyl group α to the carbonyl group (Fig. 1: cleavage site a). On closer consideration the question arises whether this ($M - 15$) fragment may not also arise partially by cleavage of the methyl group from position 3 (Fig. 1: cleavage b, β-cleavage relative to the carbonyl group).

Classical mass spectrometry, now used widely as a method of structure determination in organic compounds, can give no definite answer in this case, because it is always isolated

[*] Priv.-Doz. Dr. U. P. Schlunegger
Organisch-chemisches Institut der Universität
CH-3000 Bern 9, Freiestrasse 3 (Switzerland)

molecule fragments that are measured in classical mass spectrometry. Only one thing is primarily common to all these fragments, namely their origin from the molecule considered or from the sample under examination. The classical mass

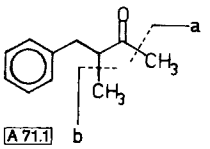


Fig. 1. 3-Methyl-4-phenyl-2-butanone. a, b: Possible cleavage sites for the generation of the (M − 15) fragment.

spectrum generally says little or nothing about the genetic relationships between the ions formed. The mass spectroscopist often has to solve the difficult problem of putting together the puzzles presented by the molecule fragments into one reasonable whole by means of known fragmentation mechanisms and his own experience.

"Metastable peaks" are sometimes observed in classical mass spectra (cf. Section 3). These may give some indications of the genetic relationships between ions, but unambiguous results are seldom obtained. The same can be said of the data from accurate mass determinations (*e. g.* "peak matching") of individual ions for the calculation of their elemental compositions. Particular difficulties always arise when, as in the above example of 3-methyl-4-phenyl-2-butanone, two isomeric ions (of the same elemental composition) can be formed by removal of one methyl radical. Any "metastable peak" that may arise in the classical sense means, at best, that the ($M^+ - CH_3$) ions originate from the molecular ion. The same is fundamentally true of the results obtained by the Barber-Elliott defocusing technique[3], which is a procedure for seeking precursor ions ("mother ions").

The decision which of the two possible types of ion is formed in the example discussed above (Fig. 1) is thus possible with the classical mass-spectrometric procedure only after labeling with heavy isotopes. The compound labeled in position 1, namely 1,1,1-trideuterio-3-methyl-4-phenyl-2-butanone[5], then gave the mass spectrum reproduced in Fig. 2b. As expected, the molecule-ion is shifted with respect to the unlabeled molecule-ion by three mass units, namely from $m/e = 162$ to $m/e = 165$. Cleavage, postulated in the textbook[4] (Fig. 1: a), of the trideuteriomethyl group in the α-position to the carbonyl group leads to the ion at $m/e = 147$ (M − 18); alongside this, however, there is also a peak at $m/e = 150$ which, as M − 15, can only be interpreted as due to removal of the other, unlabeled, methyl group (Fig. 1: b).

In contrast to this method of detection, a procedure for seeking daughter ions, namely *D*irect *A*nalysis of *D*aughter *I*ons (DADI mass spectrometry), provides experimental data for the nondeuteriated ketone that clearly show that both of the theoretically possible methyl cleavages occur.

By systematic DADI analysis it could be proved that the fragments $m/e = 119$ (determination of accurate mass: C_9H_{11}) and $m/e = 105$ (C_8H_9) are formed from the ($M - CH_3$) ions at $m/e = 147$. Provided that no intramolecular rearrangement occurs, according to the generally known rules of fragmentation these two ions cannot originate from a single type of ion (at $m/e = 147$). However, assumption of the two alternative methyl cleavages from the molecular ion allows the formation

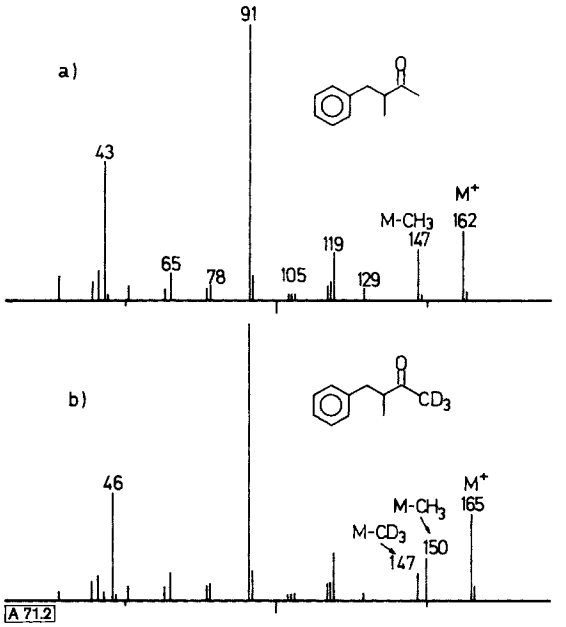


Fig. 2. Classical mass spectra of: a) 3-methyl-4-phenyl-2-butanone and b) 1,1,1-trideuterio-3-methyl-4-phenyl-2-butanone for the detection of the two possible cleavages of a methyl group.

of the ions at $m/e = 119$ and 105 to be unconstrainedly explained (Fig. 3).

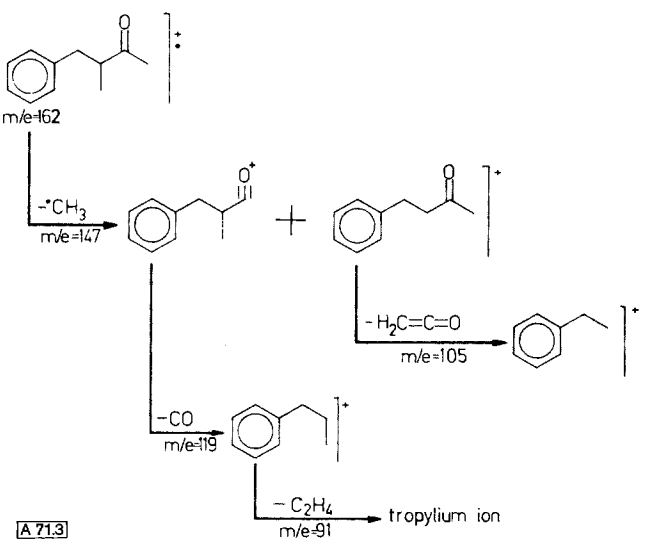


Fig. 3. Transitions demonstrated by DADI for fragmentation of 3-methyl-4-phenyl-2-butanone.

This example thus shows that by means of DADI mass spectrometry new structural data can be obtained not only of molecules but in addition of any interesting molecule fragments. This provides a new possibility for the determination of the structure of organic molecules, and the following Sections therefore present in greater detail the principles and the applications of DADI mass spectrometry.

2. Fundamentals

2.1. General

The nonspecialized user of mass spectrometry often considers the ionization and fragmentation of organic molecules to take place exclusively in the ion source.

Only on closer consideration does he recall the existence of metastable ions and realizes that fragmentation processes occur during a certain time or over a part of the path of flight within the mass spectrometer. The corresponding time relationships can be easily estimated from the ion velocity (v) for each mass spectrometer. This relation is:

$$v = \sqrt{\frac{2eU}{m}} = \sqrt{\frac{2 \times \text{charge} \times \text{accelerating potential}}{\text{mass}}} \quad (1)$$

In a mass spectrometer with an acceleration potential of 3000 V a particle of around 100 mass units thus attains a velocity of some $7 \cdot 10^4$ m/sec. The path from the ion source to the ion detector (*e.g.* electron multiplier) is about 1.5 m in a double-focusing instrument such as the Varian MAT-CH5-DF. This length is flown by the mass in question in *ca.* 10^{-5} s. Ions with a mean lifetime of this order can therefore decompose during their journey through the mass spectrometer: these are described as metastable. The kinetic energy ($mv^2/2$) of the primary particle (the mother ion) achieved during acceleration in the ion source is then divided between the resulting products (the daughter ion and the neutral particle). These continue their journey from the primary ion in different ways, in accordance with their mass or kinetic energy, which means that the daughter ions formed pass through the mass spectrometer to the detector under conditions different from those affecting the primary mother ion.

Not all the individuals of a given species of such metastable primary particles decompose simultaneously within an infinitely short time; the decomposition is generally spread over a certain interval. Thus, the daughter products are not all formed within a narrowly delimited space.

If the origins are in the region of an electrical or magnetic field, the field influences the flightpath of the subsequent products—the daughter ions—to different extents, depending on their different origins. Therefore such ions cannot be focussed and do not give an evaluable peak in the detector. If, however, the origin of a specific type of particle is in a field-free region all of them are similarly influenced by the next field. The new focusing thus effected produces at the detector a peak somewhat imprecisely called a "metastable peak" (it is in fact due not to the metastable species itself but to the products of its decomposition). Such peaks can, as is well known, often be found in the spectra produced by instruments embodying the usual geometry. However, in double-focussing instruments such as the Varian MAT-CH5-DF the second field (electrostatic field, energy filter) focuses out these metastable particles so that normally they cannot be observed.

2.2. The Principle of "DADI Metastables"

In principle a metastable ion may decompose not only in the first field-free space (between the acceleration field and the first deflection field), but also anywhere on its path within the mass spectrometer, particularly in the second field-free region of a double-focusing instrument (Fig. 4). In this case the daughter products from these metastable ions can be focused on the detector by decoupling and alteration of the second deflection field, and so measured. Here there is an appreciable difference from the processes in the first field-free region: the second field-free region does not contain all the ions formed and accelerated in the ion source, but only those that have already passed the first deflection field. All the other particles are deflected to the wall of the apparatus and are there discharged. Thus, if decomposition of metastable particles is observed in the second field-free space, they must necessarily originate only from ions that were "selected" by the first deflection field.

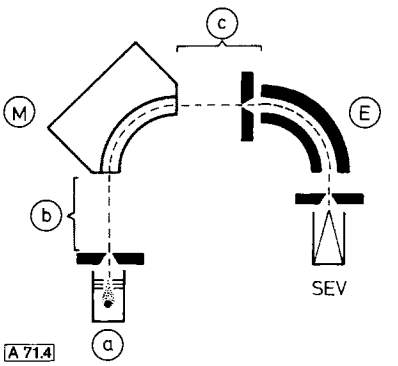


Fig. 4. Schematic structure of a DADI mass spectrometer (inverse Nier-Johnson geometry). a: Ion source; g: first field-free space; M: magnetic analyzer; c: second field-free space, DADI region; E: electrostatic analyzer (energy filter); SEV: detector.

If it is possible to select only a single ionic species by means of the first deflection field, then the assignment of the products of decomposition in the second field-free region is relatively simple and clear. However, the most widely used double-focusing mass spectrometers are built with Herzog-Mattauch or Nier-Johnson geometry. This means that after acceleration the ions pass first through an electrostatic field (energy filter), to be subsequently separated according to their masses in the downstream magnetic field. In the (second) field-free region of these machines—between the electrostatic and the magnetic field—ions are found that have relatively little energy scatter but any possible mass, and if they decompose there, the genetic assignment of the subsequent products presents considerable difficulties.

Very different conditions are set up on reversal of the field arrangements, for example in an inverse Nier-Johnson geometry such as is realized in practice in the Varian-MAT CH5-DF, 311 or 112. There the mass separation is achieved already in the first field, so that only ions having a mass "set" by the magnet reach the second field-free region. Decomposition of this species generates daughter ions whose origin is characterized physically. In other words, the genetic connection between the precursor ion "set" by the magnet and its daughter products is guaranteed. With such considerations in mind *Maurer et al.*[1] designated this measuring procedure as "DADI" (*D*irect *A*nalysis of *D*aughter *I*ons).

In a search for the daughter ions the electric field of the "DADI" mass spectrometer is decoupled and varied. At the primary setting—the potential U_1 of the electrostatic field—the precursor ion passes through this field with kinetic energy $M_1v^2/2$. When a decomposition occurs, the kinetic energy becomes divided between the daughter ion and a neutral particle. The daughter ion (and also the neutral particle) retains the velocity of the precursor ion almost completely, but its kinetic energy is now smaller because of its smaller mass. Thus, it cannot pass the analyzing electric field (the energy filter) under the same conditions as the precursor ion, but only at a lower field strength corresponding to its smaller mass. In practice, therefore, the primary deflection potential

U_1 is successively reduced and, on the appearance of a peak at the detector, the corresponding potential U_2 of the electric field is measured. By scanning of the whole energy region all the daughter ions formed from one mother ion in the second field-free region can thus be found. The mass of the daughter ions can be calculated from the relation:

$$M_{\text{daughter ion}} = M_{\text{mother ion}} \cdot \frac{U_2}{U_1} = f \cdot U_2 \qquad (2)$$

where $U_{1(2)}$ is the potential at the deflection condenser at which the mother ion (daughter ion) is focused on the detector.

With commercial instruments (*e.g.* MAT CH5-DF, 311, 112) the deflection potential can be decreased automatically.

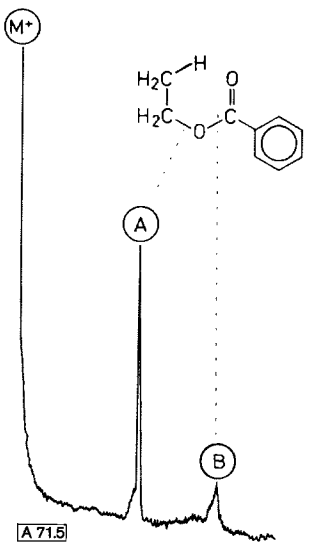


Fig. 5. DADI spectrum of ethyl benzoate (numerical values in Table 1).

In practice one proceeds by first "setting" the interesting mother ion with normal operation of the mass spectrometer. After decoupling of the deflection potential the whole potential region is scanned and the SEV signals are simultaneously recorded. An example of such a DADI spectrum is reproduced in Fig. 5 and the corresponding numerical values are given in Table 1[5].

Table 1. Potentials measured at the electrostatic deflection field (ESD potential) of the DADI spectrum of ethyl benzoate (see Fig. 5).

Peak	ESD potential [V]	$m/e_{calc.}$	Assignment
M^+	506.55	150	Starting ion (mother ion)
A	411.95	122	$M^+ - C_2H_4$ (McLafferty)
B	354.9	105	Benzoyl cation

3. Definitions and Presentation of DADI Results

From what has been said above it follows that the ion masses are determined by DADI spectrometry just as in classical mass spectrometry, but that in addition data on the genetic relationships between the ions are obtained. Clear presentation of these relationships is not difficult in the case of single measurements, but in a comprehensive systematic DADI analysis of one molecule so much data may be collected that their presentation may present great difficulties. In the course of routine DADI analyses we therefore developed a method of presentation that permits the genetic relationships between the ions and the results of the accurate mass determinations to be easily recognized.

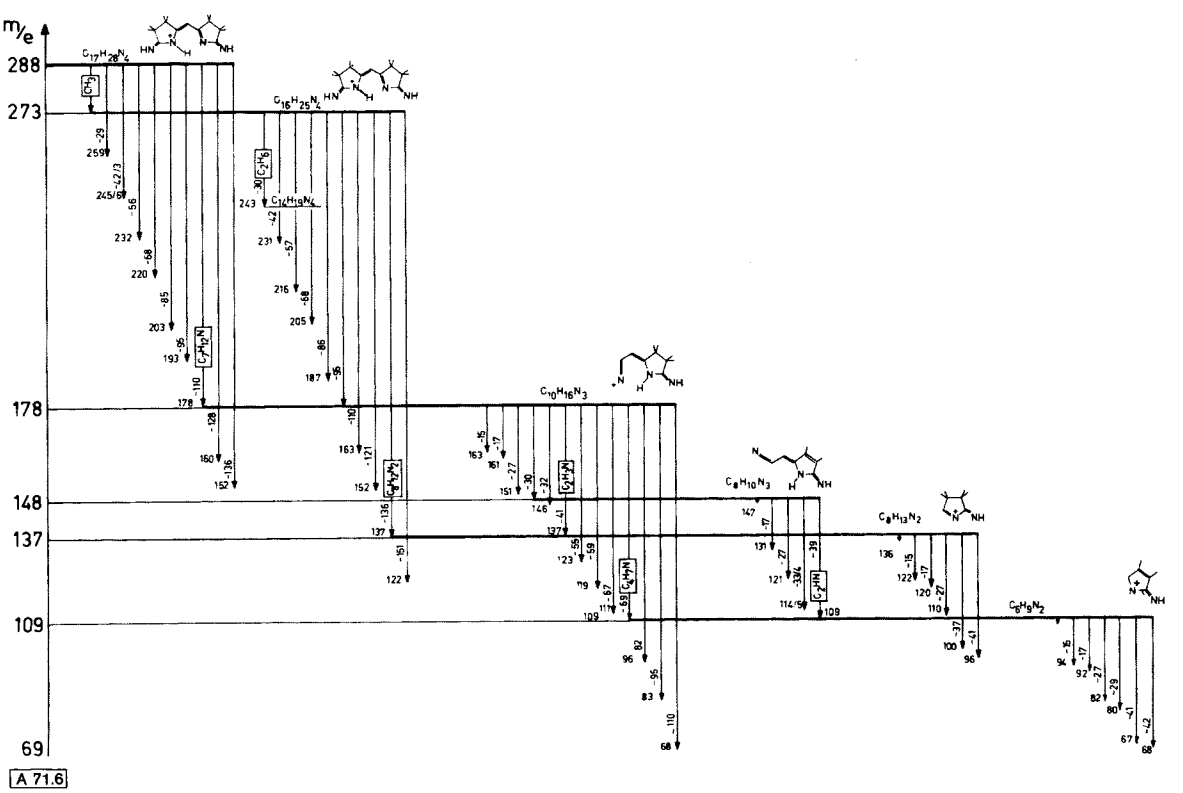


Fig. 6. Presentation of DADI data (part from the DADI spectrum of bisamidine [7]).

The simplest form of presentation selected above in Fig. 3 was applied in the complicated case of "bisamidine" which is an intermediate in the synthesis of hexahydroporphins[7]. An extract from the DADI spectrum of this compound is reproduced in Fig. 6. There the transitions, measured by the DADI method, of all ionic species from their own mass level to the daughter ions formed are drawn as a collection of vertical, downward-pointing arrows. In addition, the results of accurate mass determination, mass numbers, and structural elements can be entered horizontally at the appropriate mass level. Furthermore, there is space in the scheme to enter the defocusing data by the Barber-Elliott method[3] in analogous form (example in [7]). The mass differences often useful for interpretation are, however, added vertically to the appropriate transitions. In this way it is made relatively easy for the reader to discover the relationships from the drawing.

All the daughter ions formed directly from one type of ion constitute one "ion generation". For example, it can be clearly seen that the ion at $m/e=178$ can arise directly from the molecule-ion M^+ at $m/e=288$. Removal of the 110 mass units corresponds to a loss of $C_7H_{12}N$, obtained as the difference between corresponding values of the accurate mass determination. It can also be seen that the ion at $m/e=178$ is also generated by a two-stage process—a "fragmentation series"—first by transition from $m/e=288$ to $m/e=273$ with the loss of a methyl radical and then by transition from $m/e=273$ to $m/e=178$.

For the description of the genetic ionic relationships derived from the numerical data we propose the following method of presentation:

An arrow, pointing to the right, leads from the mass number of the mother ion to the collection of direct daughter ions enclosed in square brackets, *i.e.* all the ions belonging to one generation are collected inside one set of brackets; an example from Fig. 6 is: $m/e=288\rightarrow$[273, 259, 245/6, 232, 220, 203, 193, 178, 160, 152].

Mass numbers corresponding to the ions of a fragmentation series and thus belonging to different generations are naturally separated by arrows pointing to the right; an example from Fig. 6 is: $m/e=288\rightarrow273\rightarrow137\rightarrow96$.

4. Applications in Organic Chemistry

Newly discovered methods are usually first tested to see whether they have any advantages over previous methods. Only then are attempts made to apply the new technical possibilities to the study of unsolved problems. This trend can also be seen in the case of DADI mass spectroscopy, as the following examples may show.

4.1. Structure Elucidation of Molecules and Molecular Fragments

Experience has shown that "metastable peaks" cannot always be detected in a normal mass spectrum. If, however, such a peak does appear, an attempt is made to find the corresponding transition or fragmentation. After an initial failure to recognize its potential this method of evaluation has today become a much used routine. Nevertheless, the appearance and the recognition of these "metastable peaks" are governed by chance, and in addition it is not always possible to assign the corresponding fragmentation unambiguously.

DADI measurements provide a fundamental improvement in this situation. On the one hand, in our experience DADI-measurable ionic species occur more frequently than do "metastable peaks" in the normal mass spectrum, although with present day instruments only a relatively small region of the total ion lifetime is accessible to us (through a relatively small "observation window" provided through the second field-free region in CH5-DF, MAT 311, and MAT 112). On the other hand, as explained above, assignment of the DADI-measurable ions is provided by the mode of construction of the instruments, which defines the genetic relationships by physical means. It thus appeared possible to replace or at least to supplement the normal mass spectrum by DADI measurements, and this will be illustrated below by examples from the literature.

Thus, *Richter*, *Liehr*, and *Schulze*[8] have shown that under the conditions of electron impact ionization 2,3-dihydro-1-benzoxepin underwent ring contraction with the formation of a methyl group (Fig. 7). Proof of the postulated exocyclic methyl group could be provided by DADI measurements, which demonstrated that the (M − 15) peak originated from the molecule.

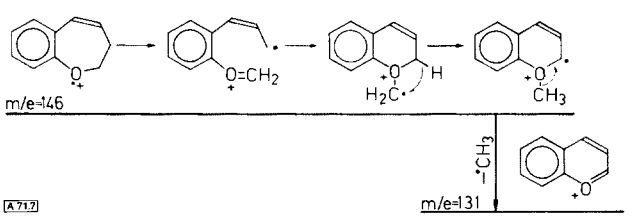


Fig. 7. Detection of ring contraction of 2,3-dihydro-1-benzoxepin after impact ionization [8] (removal of a methyl group demonstrated by DADI data).

The known removal of 29 mass units from the parent ion of nicotine could also be clarified by DADI measurements[9]. According to that work the elimination of 29 mass units should be regarded as a two-stage process (Fig. 8). Ethylene is lost in the first step, and it is clear that only after rearrangement of the (M − 28) ion is an H atom driven out of the molecule, since according to DADI $(M-29)^+$ is formed from $(M-28)^+$.

Not only ring contraction (Fig. 7) and ring formation (Fig. 8) but also ring expansion could be established by DADI

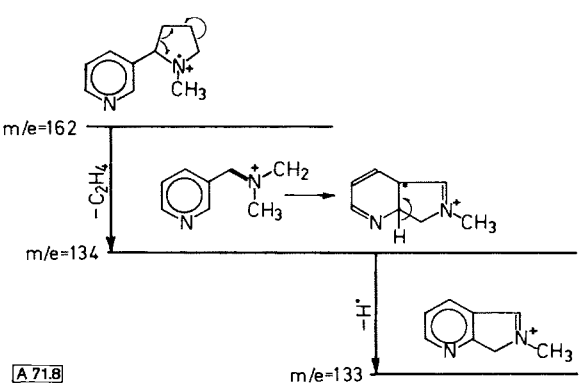


Fig. 8. Two-stage fragmentation of nicotine with rearrangement, demonstrated by DADI (M^+ 162→134→133).

measurements. The findings by DADI measurements concerning dialkyl spiro[cyclopropane-1,9'-fluorene]-2,3-dicarboxylates agreed with the results obtained from the classical "metastable peaks"[10].

Heimgartner, Weibel, and *Hesse*[11] used DADI analyses in combination with classical "metastable peaks". Combining their results with those from high-resolution mass spectrometry and deuteration experiments, they were able to show that mass-spectrometric decomposition of 1-tetralol derivatives was only partly in line with the previously assumed retro-Diels-Alder mechanism.

4.2. Determination of Fragmentation Series

The above examples show that DADI spectra can be measured for parent ions as well as for fragment ions. If the decomposition of consecutive ions is followed throughout the generations the fragmentation series of the molecule concerned or of its fragments is obtained directly, which means that the sequence of measurements provides a direct determination of the daughter ions of the second or higher generation. This can be explained for the example of a nickel complex with a porphinoid ligand system[12]: We are here concerned with a planoid nickel compound containing two axial methoxy groups in the *cis*-position to one another (Fig. 9). From the

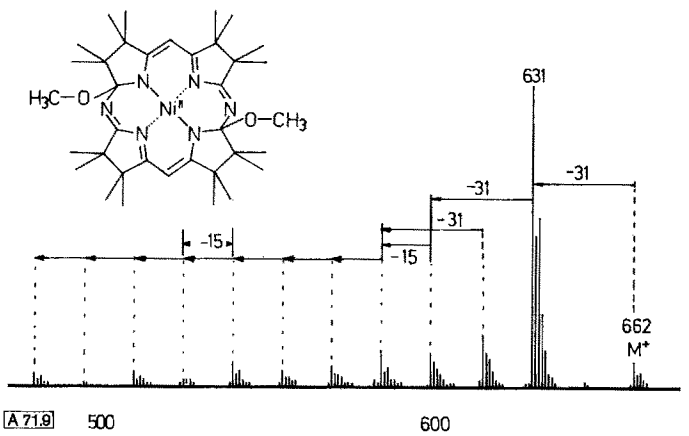


Fig. 9. Fragmentation series of a planoid nickel complex: consecutive removal of methyl radicals demonstrated by DADI.

normal mass spectrum the conclusion seemed to be that several fragments were split off in radical form one after the other, but it could not be unambiguously proved that no other type of fragmentation would lead to the ions observed. DADI analysis of these consecutive ions, however, proved that after the loss of the two methoxy groups the nickel complex actually split off methyl radicals in succession—which was a rather unusual behavior. In Fig. 9 the measured transitions are entered on the classical mass spectrum.

Fragmentation series established by DADI data combined with results of accurate mass determinations and defocusing experiments by the Barber-Elliott method[3] have also served for the determination of the structure of the key ion in the mass spectrum of bisamidine, an intermediate in the synthesis of hexahydroporphins[7].

Fragmentation series determined with the aid of DADI data were also applied to explain the rearrangements of prolinol derivatives. Analysis of ions of various generations established the structures of the *N*-alkoxyprolinyl esters investigated[13]. The same procedure was used for structure determination of nitrated anticonvulsants[14].

4.3. Tests for Purity and Analysis of Mixtures

DADI mass spectrometry can provide valuable service in testing of purity and in the study of mixtures of substances, particularly in combination with high-resolution mass spectrometry (cf. 3-methyl-4-phenyl-2-butanone). If, after an analysis of the classical mass spectrum, the presence of two or more compounds in one sample is suspected, the procedure is to follow the fragmentations or fragmentation series (cf. Section 4) of the suspected ions by DADI mass spectrometry and to observe whether all of them are derived from one type of parent ion. If this is not the case, a mixture of parent ions must be assumed. Analysis of a mixture is similarly possible by means of fragment ions. In this connection it should be recalled that fragments of the same mass but different structure can often be formed from one homogeneous type of molecule (cf. the example of 3-methyl-4-phenyl-2-butanone); in that case the mixture analysis is applied to the ion types under study.

This procedure was used in the case of the *N*-tosylprolinyl acetates for the determination of homogeneity[15]. The classical mass spectrum of the *N*-tosylprolinol (Fig. 10) was readily interpretable.

However, the *O*-acetylated compound showed a group of peaks around $m/e = 173$, whose origin could not be immediately explained. Since accurate measurements have shown the absence of sulfur and oxygen in the species at $m/e = 173$, an impurity in the preparation first had to be considered. In further work analysis showed that $m/e = 173$ was formed from the acetylated molecules (297 $(M^+) \rightarrow$ 237 $(M^+ - CH_3COOH) \rightarrow$ [222, 183, 173 $(237 - SO_2)$, ...]), but not from the free tosylprolinol (255 $(M^+) \rightarrow$ 237 $(M^+ - H_2O) \rightarrow$ [183, 155, 82]) (cf. Fig. 11). In an extended investigation $m/e = 237$ was

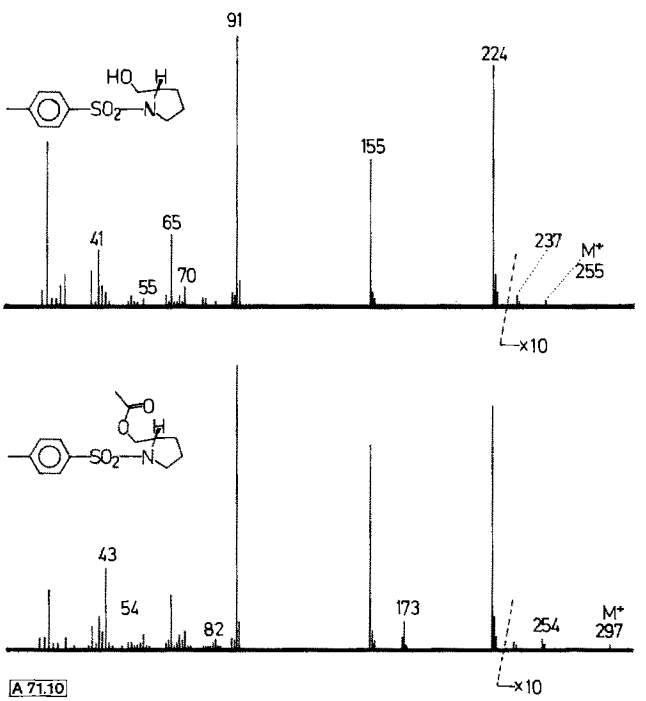


Fig. 10. Mass spectra of *N*-tosylprolinol and *N*-tosylprolinyl acetate; an ion is formed unexpectedly at $m/e = 173$ from the acetylated compound.

established as the last possible mother ion, which interestingly enough occurred also in the spectrum of unesterified *N*-tosylprolinol but clearly did not possess the structure of the McLafferty rearrangement product expected for the ester. Together with the demonstration that our esterified prolinol derivative was pure, proof was thus provided that ions at $m/e=237$ had different structure in spite of the same elementary composition.

DADI analysis of a pristane fraction (2,6,10,14-tetramethylpentadecane) may be put forward as another example of a test for purity[5]. The DADI spectrum of the parent ion at $m/e=268$ ($C_{19}H_{40}$) can be explained without difficulty by the theoretically expected fragmentation of pristane, as Fig. 12 shows. The intensities of the DADI peaks also correspond to a great extent with theoretical expectations, in that, for example, the energetically favored cleavage at the branch points of the molecule is strongly expressed. Only the (M^+-29) peak cannot be at once brought into agreement with the assumed structure. On the assumption that no rearrangement occurs, it must therefore be concluded that the pristane analyzed was not quite pure. The occurrence of the peak (M^+-29) ($M-C_2H_5$) therefore indicates clearly the presence of a trace of an isomer with a terminal ethyl group (*e.g.* 2,6,10,13-tetramethylpentadecane).

DADI results were applied by *Brent* and *Rouse*[16] to the analysis of a mixture in connection with a procedure in a patent application. The mixture was one of mono-, di-, tri- and tetramethyl homologs produced in the methylation of a pyrimidinone derivative I (Fig. 13) with methyl iodide in the presence of a base. The point under discussion was the position at which the methyl group of the monomethyl derivative had entered the molecule.

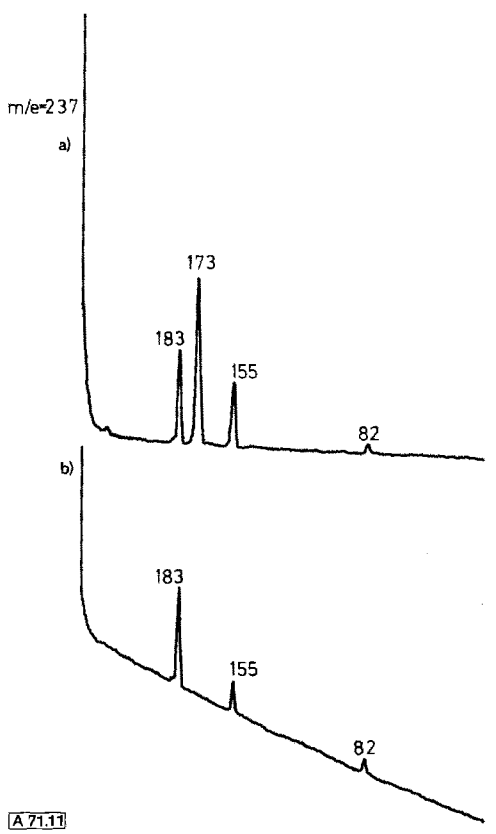


Fig. 11. DADI spectra of: a) *N*-tosylprolinyl acetate and b) *N*-tosylprolinol. (The sloping zero line does not disturb the evaluation).

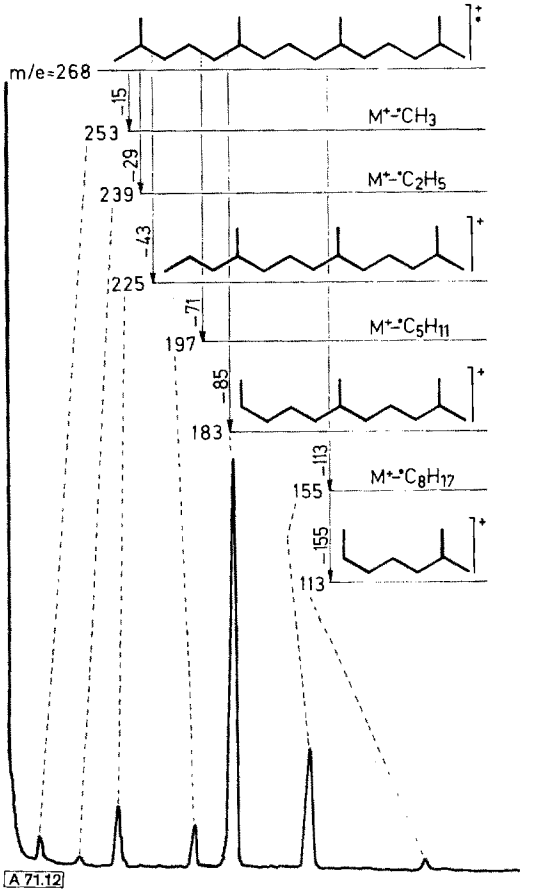


Fig. 12. Pristane fraction: assignment of fragmentation sites to the DADI spectrum.

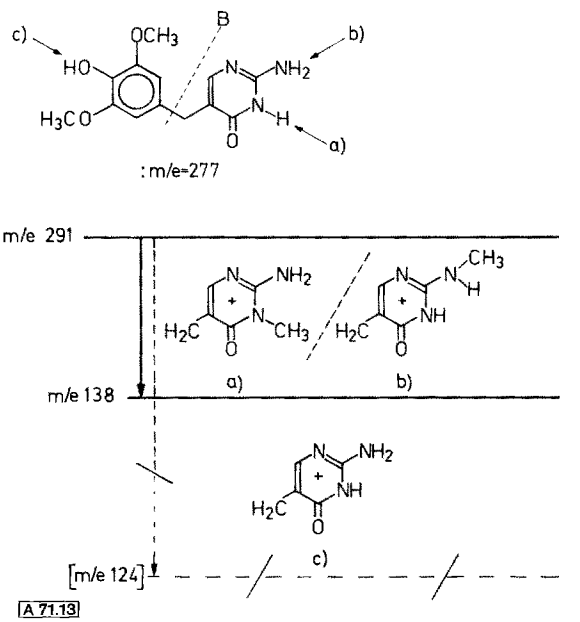


Fig. 13. Detection of the site of the methyl group in monomethyl derivatives of 2-amino-5-(4-hydroxy-3,5-dimethoxybenzyl)-4(3*H*)-pyrimidinone (the DADI measurement was effected on a mixture of mono-, di-, tri- and tetramethyl derivatives, starting from the molecule-ion at $m/e=291$ of the monomethyl derivative). a: Favored site of cleavage on impact ionization; a, b, c: possible sites of methylation.

Since all the monomethyl derivatives must have mass 291 (277 + 14 for the inserted methylene group), DADI analysis of the mixture was started at $m/e=291$. Since cleavage of the parent ion in the mass spectrometer occurs preferentially between the arene and the bridging methylene group (Fig.

13: cleavage point B), a fragment should appear at $m/e = 138$ (124 + 14 for the CH_2 group inserted) if there is a single methylation of the pyrimidine system, whereas the fragment should remain at $m/e = 124$ if there is methylation in the phenolic portion of the molecule. The DADI results showed a transition $m/e = 291 \rightarrow 138$, but not $m/e = 291 \rightarrow 124$ (Fig. 13). It was thus concluded that the monomethylation products contain the additional methyl group in the pyrimidine portion.

The possibility, described in the last paragraph, of differentiating ion structures, has also been demonstrated systematically by *Smith, Djerassi, Maurer*, and *Rapp*[17] on examples from steroid chemistry. For a mixture of estrone (M^+ at $m/e = 270$), estradiol (M^+ at $m/e = 272$) and estriol (M^+ at $m/e = 288$) they showed that the DADI spectra of the three parent ions correspond to a great extent to the simplified classical mass spectra of the pure substances; the DADI values observed remained unaltered by the admixture in this simple case. The DADI spectrum also provided valuable information in the more complicated case of mixtures of isomeric ions (same elementary composition); the spectrum then contains additively the peaks of all the ionic species, as shown above in the introductory example of 3-methyl-4-phenyl-2-butanone. This fact was used by *Levsen, Wipf*, and *McLafferty*[18] to differentiate, for example, between leucine and isoleucine residues in peptides. Analysis of peptide mixtures presents a problem that is interesting in this connection. Our own group[19] has been able to differentiate, and to analyze the sequence in three isomeric tripeptides, even in a mixture of the three components.

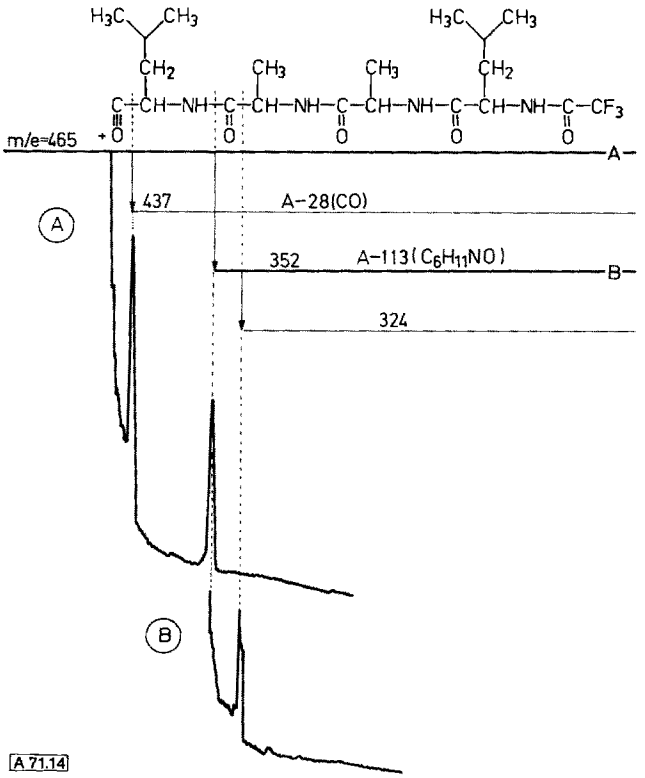


Fig. 14. Stepwise analysis of different ion generations for species from an oligopeptide derivative. A: First magnetic field setting ($m/e = 465$) gave DADI spectrum Ⓐ; B: second magnetic field setting ($m/e = 352$) gave DADI spectrum Ⓑ.

4.4. Analyses of the Sequences in Oligomers

The DADI technique makes it possible not only to clarify fragmentation series but also simultaneously to determine the component sequence in oligomers. Experience has taught that "metastable" ions are formed very frequently from amino acid derivatives and peptides, and this led us to consider determination of the amino-acid sequence of oligopeptides by DADI mass spectrometry. We first analyzed some *N*-trifluoroacetylpeptide esters that we happened to have at hand.

The fundamental procedure is presented schematically in Fig. 14. After the selection of an ionic species A (here $m/e = 465$) by means of the magnetic field the DADI analysis (Fig. 14: A) afforded the direct daughter ions at $m/e = 437$ and $m/e = 352$. Finally, the mass B ($m/e = 352$) corresponding to the second generation was "set" by the magnetic field and again a search was made for the relevant daughter ions (third generation). In this example (Fig. 14: B) there was no difficulty in detecting $m/e = 324$ corresponding to the removal of CO. The procedure was followed logically further, by searching from a recognized daughter ion for the daughter ions of the next higher generation[19, 20, 6].

Experience has shown that this stepwise procedure is not always necessary. Occasionally such a large number of daughter ions could be recognized that almost the complete amino-acid sequence could be derived in one step. This is illustrated in Fig. 15 for the case of a hexapeptide; there the sequence of several amino acids could be derived from a single DADI spectrum. Optimization of the procedure will undoubtedly lead to still more sophisticated results.

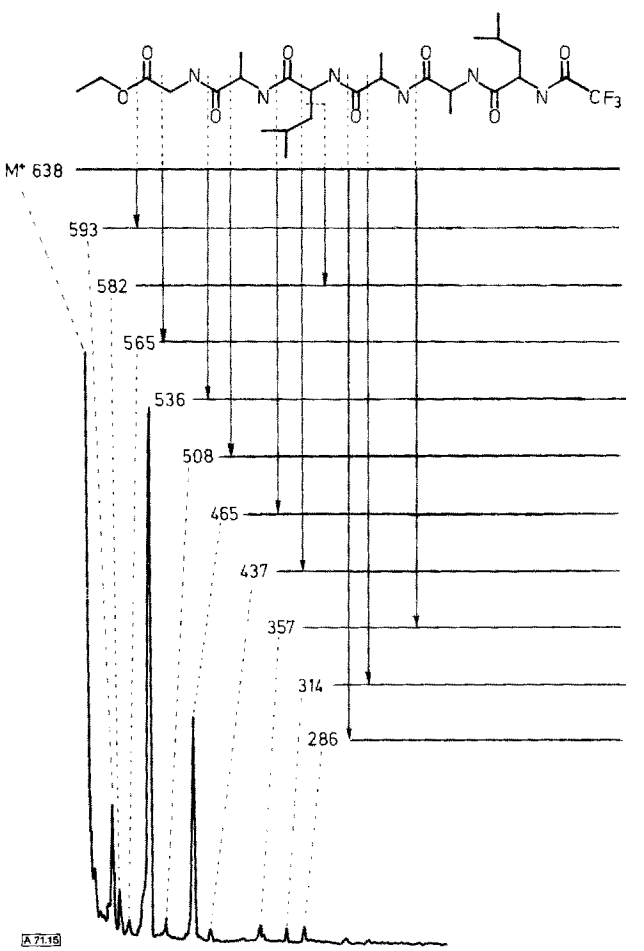


Fig. 15. Evaluation of the DADI spectrum of a hexapeptide (except for $m/e = 582$ all the DADI ions are sequence-characteristic).

4.5. Determination of the Structure of Mass-Spectrometrically Generated Fragments and Rearrangement Products

Analysis of daughter ions of higher generations not only makes it possible to determine fragmentation series and component sequences but also permits indications to be elegantly obtained about the structure of mass-spectrometrically generated fragments and rearrangement products. Analysis of the rearrangement fragment at $m/e=173$ in the spectrum of *N*-tosylprolinyl acetate[15] will serve as an example. As described above (Fig. 11), it could be shown by DADI that $m/e=173$ was formed from the McLafferty product at $m/e=237$ by the elimination of SO_2. This raised the question of the structure of this sulfur-free product, which must undoubtedly be due to a rearrangement. The DADI results for $m/e=173$ afforded the structural units, as demonstrated schematically in Fig. 16.

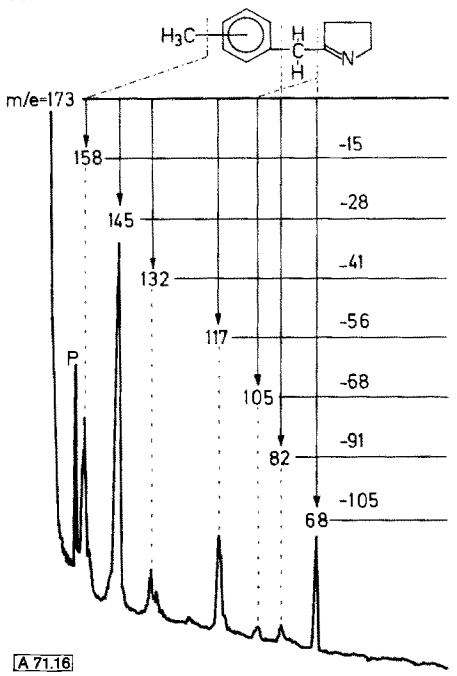


Fig. 16. Provision of structural evidence for a rearrangement product generated by DADI in the mass spectrometer from *N*-tosylprolinyl acetate. (P: often observable "phantom peak" of unknown genesis, presumably not substance-dependent).

The postulated structure is confirmed by the appearance of fragments $m/e=105$ and $m/e=68$. If the loss of SO_2 had led to reunion of the toluene portion to the pyrrolidine nitrogen, the daughter ion at $m/e=105$ should not have been formed, but at the most the tropylium ion at $m/e=91$.

There is no need here to discuss the other daughter ions from $m/e=173$, as they are all easily explained by fragmentation of the pyrrolidine group.

Here again it should be noted that the explicit fragmentation sequence could hardly have been elucidated by classical mass spectrometry: the corresponding ionic intensities are very low in the normal spectrum, being of the order of maximally, a few percent[15].

5. Current Technical Limitations of DADI Mass Spectrometry

DADI measurements can be carried out today using, for example, the Varian MAT instruments CH5-DF, 311, and 112 and are limited by the properties of these instruments.

The relatively large amount of material required for this type of mass spectrometry (of the order of 1—5 milligrams) is a minor disadvantage, but this amount could be reduced if, by means of an on-line computer, the sites of the signals and the corresponding potentials at the electrostatic field could be determined more quickly and recalculated into mass units, so that time required for analysis (the evaporation time) could be shortened.

A second limitation is due to the relatively low resolving power of the electrostatic deflection field in the commercial instruments named above. It could be maximally 200—300 (10% valley), and difficulties can then be expected in the determination of (X−1) peaks for the larger ions; however, this is unlikely to be an insuperable hindrance to the questions usually posed in structure analysis.

A further limitation of the method is that we can observe only a relatively small portion of the ion lifetime. At a velocity of about 7×10^4 m/s, for example, an ion of mass 100 passes through the second field-free region of about 0.25 m in only *ca.* 3×10^{-6} s. As we have seen above, the corresponding total flight time is about 10^{-5} s. Thus, with the present instruments at the most about one-quarter of the ion flight time can be observed. The observation space can be extended to some extent by lowering the acceleration potential U; in accordance with eq. (1), the ionic velocity can thus be reduced so that the flight time increases, but only by a factor of $\sqrt{U}$. A further increase in the "observation window" can be achieved only by alterations to the apparatus. Yet another problem is due to the relatively limited sensitivity, and an ion source with a higher ion output would be a welcome improvement.

In conclusion, it can be claimed that in spite of the drawbacks DADI mass spectrometry offers a new and valuable aid in the elucidation of the structure of compounds.

This work was supported by the Swiss Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project No. 2.8850.73).

Received: May 10, 1974;
revised: December 23, 1974 [A 71 IF]
German version: Angew. Chem. *87*, 731 (1975)
Translated by Express Translation Service, London

[1] Lecture given by *K. H. Maurer, C. Brunnée, G. Kappus, K. Habfast, U. Schröder*, and *P. Schulze* (Varian MAT, Bremen), 19th Annual Conference on Mass Spectrometry and Allied Topics, Atlanta (USA), May 1971.
[2] *J. H. Beynon* and *R. G. Cooks*, Res. Dev. *22*, 26 (1971).
[3] *J. H. Beynon*, Anal. Chem. *42*, 97A (1970).
[4] *J. B. Hendrickson, D. J. Cram*, and *G. S. Hammond*: Organic Chemistry, 3rd Ed. McGraw-Hill, New York 1970. p. 283ff.
[5] *U. P. Schlunegger*, unpublished work.
[6] *H. von Felten*, Licentiatsarbeit, Universität Bern 1972.
[7] *U. P. Schlunegger, S. Leutwyler, F. Friedli*, and *R. Scheffold*, Helv. Chim. Acta *58*, 65 (1975).
[8] *W. J. Richter, J. G. Liehr*, and *P. Schulze*, Tetrahedron Lett. *1972*, 4503.
[9] *J. G. Liehr, P. Schulze*, and *W. J. Richter*, Org. Mass Spectrom. *7*, 45 (1973).
[10] *W. J. Richter* and *A. M. Braun*, Helv. Chim. Acta *56*, 569 (1973).
[11] *H. Heimgartner, P. A. Weibel*, and *M. Hesse*, Helv. Chim. Acta *57*, 1510 (1974).
[12] *R. Scheffold* and *J. Löliger*, private communication.
[13] *W. Wiegrebe, E. G. Herrmann, U. P. Schlunegger*, and *H. Budzikiewicz*, Helv. Chim. Acta *57*, 301 (1974).
[14] *W. Wiegrebe, L. Wehrhahn*, and *U. P. Schlunegger*, Pharm. Acta Helv. *49*, 253 (1974).

[15] *W. Wiegrebe, U. P. Schlunegger*, and *E. G. Herrmann*, Pharm. Acta Helv., in press.
[16] *D. Brent* and *D. Rouse*, Application Note No. 12, Varian MAT 1973.
[17] *D. H. Smith, C. Djerassi, K. H. Maurer*, and *U. Rapp*, J. Am. Chem. Soc. *96*, 3482 (1974); *U. Rapp*, Lecture, Meeting of the Arbeitsgemeinschaft Massenspektrometrie GDCh, München/Martinsried (Germany), June 1973.
[18] *K. Levsen, H. K. Wipf*, and *F. W. McLafferty*, Org. Mass Spectrom. *8*, 117 (1974).
[19] *U. P. Schlunegger*, Lecture, Meeting of the Arbeitsgemeinschaft Massenspektrometrie GDCh, Marburg/Lahn (Germany) October 1974.
[20] *U. P. Schlunegger*, Lecture, Meeting of the Arbeitsgemeinschaft Massenspektrometrie GDCh, München/Martinsried (Germany) June 1973.

Optical Properties of Pigments—Objective Methods for Testing and Evaluation

By Hans G. Völz[*]

Although man has used pigments to impart color to his surroundings since prehistoric times, it is only in the 20th century that methods for objective testing and evaluation of their optical properties have become available. Colorimetry and color-order systems based on principles of color perception, in particular the Adams-Nickerson system, which form the basis of these methods are described, and are followed by a discussion of the theories of light absorption and light scattering, in particular of the Kubelka-Munk theory. Of the important optical pigment properties chromaticity and color difference, tinting strength and lightening power (of white pigments), and the hiding power of colored and uncolored coatings are discussed on the basis of the testing methods. Sweeping developments in computer technology during recent years have contributed significantly to the present advanced status of testing practice; further progress in testing methods may be expected in the future as our understanding of the visual process improves.

1. Introduction

Imparting color using natural pigments is one of the oldest and most venerable of the cultural activities of mankind. This was a familiar facet of knowledge even before the discovery of the cave paintings of Altamira. Investigations of Greek vase painting[1] have unveiled a picture of highly advanced technique, namely the use of synthetic chromatic pigments as ceramic coloring materials. It is easily overlooked that despite a marked artistic expressiveness and skilled craftsmanship only inadequate materials and inadequate knowledge of fundamentals were available; viewed in this light the results achieved appear all the more admirable.

In the past authorities on the esthetic aspects of art sometimes stated the view that supreme artistic achievements are the result of optimum materials and of an advanced state of knowledge. Thus, among others, the unrepeatable nature of masterpieces of creative art (*e.g.*, Ancient Egyptian mosaics, classical oil paintings) was explained by ascribing to their creators pigments that could no longer be produced in the same quality—partly because the know-how has been lost and partly because the raw materials of those days are no longer available. Apart from the fact that masterpieces of such status require no justification of this kind, the basic premise of the argument is unsound. At no time in history has man had such a range of high quality synthetic pigments available as today, and at no other time has so much been known about the optical properties of pigments as at the present.

Tables 1 and 2 survey important inorganic and organic synthetic pigments[2].

[*] Dr. H. G. Völz
Bayer AG
415 Krefeld-Uerdingen (Germany)

Manufacture of pigments has become an important branch of trade. Annual world production substantially exceeds four million tons, of which about 96% constitute inorganic pigments. Titanium dioxide pigments alone, which did not exist 60 years ago, account for more than half of world production. The high level of technology is due not least to elucidation of the principles governing the optical properties of pigments and hence to advances in objective testing and evaluation methods[3]. Continued development of such methods is necessary for the following reasons:
development of novel pigments and the improvement of products currently being manufactured;
production control;
understanding between manufacturers and users.

The last two points include computer-controlled colorant formulation calculations for paints and plastics.

2. Fundamentals

2.1. Colorimetry; CIE System

There are excellent publications describing the theoretical foundations of colorimetry (*e.g.* refs.[4–6], which contain further literature references). Here only a brief and very general description can be given.

Colors are sensory impressions—a statement that can hardly be denied. How can one measure sensory impressions objectively? *Newton* took the decisive step[7] by creating the essential basis for all scientific understanding of color phenomena in splitting sunlight into its spectral components and correctly interpreting this process. Since the converse also applies, *i.e.* every color stimulus can be synthesized from the spectrum colors, there is thus a spectral distribution $\varphi(\lambda)$ which, since the days of *Young*[8], can be measured with a

Table 1. Survey of the principal inorganic pigments (after [2]).

Chemical class	White	Black	Yellow	Red	Blue	Green
Sulfides Selenides	Zinc sulfides		Cadmium sulfide	Cadmium selenide	Ultramarine	
Oxides	Titanium dioxides	Iron oxide black	Nickel titanium yellow Iron oxide yellow	Iron oxide red	Cobalt blue	Chromium oxide Hydrated chromium oxide
Chromates			Chromate pigments			Mixed greens
Carbon		Carbon blacks				

Table 2. Survey of the principal organic pigments (after [2]).

Chemical pigment class	Yellow	Red	Violet	Blue	Green
Azo pigments	® Hansa yellow Benzidine yellow Nickel green gold Azo condensation pigments	Toluidine red ® Lithol red ® Naphthol AS red			
Phthalocyanines				Phthalocyanine blue	Phthalocyanine green
Polycyclic pigments					
(a) forming vat dyestuffs	Anthrapyrimidine	Thioindigo Perylenes	Isoviolanthrone	® Indanthrene blue	
(b) not forming vat dyestuffs	Isoindolinone	Quinacridones	Dioxazine		

spectrograph. If we call the color sensation recorded by the eye the "psychophysical color" and denote it by $\mathfrak{F}$, then there must be a relation between $\varphi(\lambda)$ and $\mathfrak{F}$. What is the nature of this relation?

An answer to the above question requires knowledge of a certain physiological fact, in addition to those of a purely physical nature, which was discovered empirically by *Young* in the last century and formulated by *Grassmann*[9] ("*Grassmann*'s laws"); it may be described as follows: if we choose *three* suitable spectral distributions we can accurately simulate the other color stimuli by additive mixing of these three "reference stimuli" (also called primary colors). In each case, the desired result is obtained with only one mixing ratio. It should be added that the mixing described here always involves the mixing of light (additive color mixture), in contrast to the series arrangement of optical filters with various transmittances (subtractive color mixture). If *addition* of colors is defined as their mixing, then *multiplication* of a color by a number is also defined (*e.g.* doubling on the addition of two identical colors). On this basis, *Grassmann*'s laws may be written:

$$\mathfrak{F} = X \cdot \mathfrak{X} + Y \cdot \mathfrak{Y} + Z \cdot \mathfrak{Z}$$

or $\mathfrak{F} = m(x \cdot \mathfrak{X} + y \cdot \mathfrak{Y} + z \cdot \mathfrak{Z})$

where $m = X + Y + Z$ and $X = X/m$, *etc.*

X, Y, Z are called "tristimulus values", x, y, z "chromaticity coordinates", m is a physical intensity factor, and $\mathfrak{X}$, $\mathfrak{Y}$, $\mathfrak{Z}$ are the reference stimuli: It also follows from the above definition of addition that transformation to three other reference stimuli $\mathfrak{X}'$, $\mathfrak{Y}'$, $\mathfrak{Z}'$ must be linear (affine transformation).

The task of color measurement consists in determining m, x, y (z need not be determined because $x+y+z=1$). On account of the threefold variety of the colorimetric numbers there is an obvious analogy with the three dimensions of spatial geometry, and indeed, $\mathfrak{X}$, $\mathfrak{Y}$, $\mathfrak{Z}$ may be interpreted by reason of the addition rule as vectors in whose "tripod" the color is a resultant vector $\mathfrak{F} = \{X,Y,Z\}$. The above equations further reveal that only X, Y, Z (or x, y, z) are representatives of the wavelength-dependence of $\mathfrak{F}$, because the reference stimuli are fixed colors. The spectrum colors form a unidimensional set and therefore lie on a space curve whose points can be characterized by the associated wavelength λ ("spectrum color curve"). However, since every color $\mathfrak{F} = \{X,Y,Z\}$ can be mixed from spectrum colors because of the intensity distribution $\varphi(\lambda)$, the summation over the spectral curve must yield the tristimulus values. With sufficiently small steps the sums become integrals, leading to the relationships:

$$X = \int \varphi(\lambda)\bar{x}(\lambda)\mathrm{d}\lambda \quad \textit{etc.}$$

(The values $\bar{x}(\lambda)$, $\bar{y}(\lambda)$, $\bar{z}(\lambda)$ are the X, Y, Z values of the spectrum colors.) For dry colors, $\varphi(\lambda)=\beta(\lambda)$ is the spectral luminance factor, which is obtained on illumination with (equal-energy) white light. Illumination with light of a different spectral distribution $S(\lambda)$ gives reflected light of distribution $\beta(\lambda)S(\lambda)$; in the above integrals $\varphi(\lambda)$ must be replaced by this product. $\bar{x}(\lambda)$, $\bar{y}(\lambda)$, $\bar{z}(\lambda)$ can be determined experimentally by making observers produce the individual spectrum colors, each having an intensity $m=1$, on a visual colorimeter by mixing from the reference stimuli $\mathfrak{X}$, $\mathfrak{Y}$, $\mathfrak{Z}$ and determine their relative mixing ratios for each value of λ.

It should be mentioned that this Young-Helmholtz trichromatic theory has meanwhile received excellent confirmation from physiological research: three and only three macular pigments have been found in the human eye, their chemical constitution has been elucidated (rhodopsins), and their spectrum sensibility curves have been measured. Furthermore, there are three types of color vision receptor cells (cones), each of which contains only one such macular pigment[10].

Although the relationships outlined above were already recognized by *Helmholtz*[11], it was not until 1931 that the primary colors were specified. At that time the Commission Internationale de l'Eclairage (CIE, International Commission on Illumination), following the first useful experimental investigations of $\bar{x}(\lambda)$, $\bar{y}(\lambda)$, $\bar{z}(\lambda)$ by *Wright*[12] and *Guild*[13], decided to propose worldwide adoption of such primary colors. The curves determined by several observers were averaged; the result is the "CIE Standard Colorimetric Observer". In order to be able to embrace all possible colors, ("virtual") coordinates lying outside the spectrum color curve were introduced as reference stimuli $\mathfrak{X}$, $\mathfrak{Y}$, $\mathfrak{Z}$; these three reference stimuli were obtained by an affine transformation from the primary colors (three spectrum colors). The CIE principles are described in the standard DIN 5033; X, Y, Z are called CIE tristimulus values, x, y, z are called CIE chromaticity coordinates, and $\bar{x}(\lambda)$, $\bar{y}(\lambda)$, $\bar{z}(\lambda)$ are termed CIE spectral tristimulus values. Selection of the reference stimuli is such that the system has the following properties (Fig. 1):

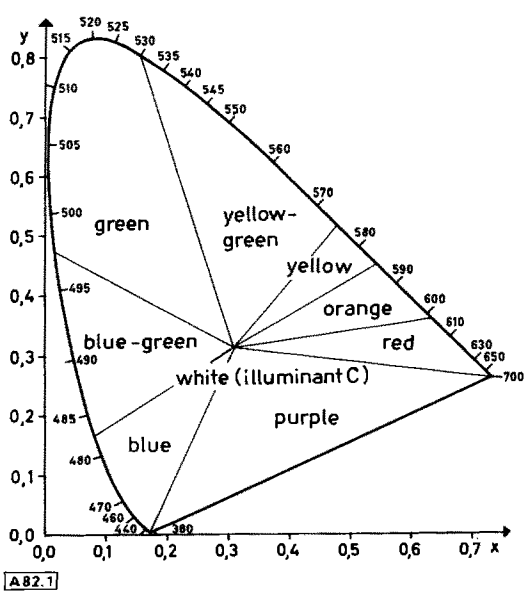


Fig. 1. CIE chromaticity diagram (after [6]).

in the x,y chromaticity diagram, the additive mixture of two colors lies on the rectilinear join of the components according to the center of gravity rule

the shoesole-shaped spectrum color curve in the x,y plane is limited by the purple boundary at the bottom (the colors lying on it do not exist in the spectrum but are mixtures of red and violet):

with equal-energy illumination the achromatic locus (white point) lies at $x_w=y_w=1/3$;

the CIE spectral tristimulus value function $\bar{y}(\lambda)$ corresponds to the luminous efficiency curve $V(\lambda)$ of the human eye specified by the CIE as early as 1924; in place of m the lightness measure $Y=m\times y$ is given as the third colorimetric number in addition to x and y.

At this point a further physiological fact of interest is worth mentioning. It follows from the above presentation that there may be very many different spectral distributions $\varphi(\lambda)$ belonging to one and the same color $\mathfrak{F}$ ("metameric color stimuli"). Since the eye can discriminate something like 100 spectral colors and approximately as many degrees of lightness, it ought to be possible to produce the highly respectable number of 100^{100} spectral distribution mixtures which the human eye is able to discriminate. In fact, however, because of the trichromatic principle, the eye only discriminates 100^3 colors. There is thus an enormous reduction of the offered information in the eye and the series-connected organs. In cybernetic terms the huge supply of information constituting a single color stimulus (information content 600 to 700 bits), which cannot be processed in practice in a sufficiently short time, is sensibly reduced to about 20 bits. This is an information quantity readily processed by the brain in one second, as is known from comparisons with other sense organs[14].

2.2. Color-Order Systems Based on Principles of Color Perception; the Adams-Nickerson (AN) System

The CIE system has permitted mutual understanding of colors throughout the world. The receiver of a communication can accurately locate the point in question in the chromaticity diagram with the aid of the three numerical values x, y, Y (and a few additional data; *e.g.* details of the measuring geometry of the colorimeter used, whether gloss was included, the CIE standard illuminant used) without having seen the relevant color. Since the advent of the system its unrestricted applicability for all technical uses of color has been demonstrated, including its use for color television[15].

However, for assessing pigments and pigmented systems some wishes remain unfulfilled; only the two most important ones will be named here:

the CIE system is not quite plain;

it is not appropriate for determining color differences perceived.

Concerning the first point: While the x,y,Y data do permit a color-order system, it is difficult to conceive the nature of the color from the coordinates themselves. *Helmholtz* had formerly made a useful remedial proposal based on the fact that the colors can be divided up and classified according to a different "triunity" and one can come to an agreement with others. These are:

the brightness (colors can be classified as either "clearer" or "darker");

the tone (which is oriented according to the spectrum colors in some fashion yet to be specified);
the saturation (in which each color is thought of as a mixture of the "saturated" tone and white; the color is the more saturated the smaller the portion of white it contains).

While this adds to the obviousness of the system the second desire—a method for determining color differences—remains unfulfilled. That the CIE chromaticity diagram cannot be physiologically equispaced is revealed by Figure 1. The green colors (from blue-green to yellow-green) occupy more than half of the area enclosed by the curve, while all other colors must be content with what is left over. And yet a determination of color differences is so important in practice that it must be regarded as one of the principal tasks of colorimetry. How can one arrive at an objective determination of color differences?

It is appropriate to begin with a concept in which color physiology plays a part. This is the "absolute color space" which is interpreted as the spatial arrangement of chromatic values such that the differences between two colors in any spatial direction correspond to the differences perceived. However, such a color space cannot be derived purely theoretically, because it must correctly reproduce the results of color matching experiments on samples with small color differences. In accord with what has been said above, a space of this kind can be established with the aid of the color qualities brightness, tone, and saturation in an arrangement such as is shown in Figure 2.

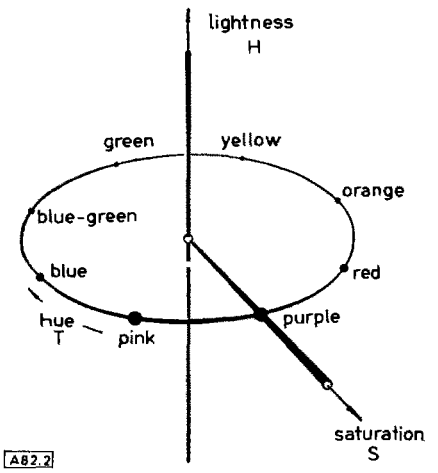


Fig. 2. Color classification according to hue, saturation, and lightness (after [16]).

The starting point is a substantial number of dye samples which are to be classified by hue, saturation, and finally brightness in psychologically equispaced steps. (For details see ref.[16].) An onion-shaped solid of irregular outline is obtained (*e.g.* there are more distinct dark-blue tones than light-red ones), whose vertical axis is the gray scale (cf. Fig. 7). A horizontal section furnishes a color plane as in Figure 2, the "onion rings" are loci of equal saturation. There are several systems built up in this manner; the system presumably most widespread in the world is the Munsell system, which is available in the form of an atlas[17]. In the Munsell system brightness, tone and saturation, are called value, hue, and chroma.

To determine color differences by *calculation* the transformation rules between the CIE system (in which the color measurement has to be performed) and the color-order system based on color perception is determined; when this has been accomplished color differences can be calculated in the latter. In the course of time—generally owing to the needs of industrial color testing—a large number of color-difference systems have arisen, for example, the "DIN Farbenkarte" (DIN Color Atlas, DIN 6164)[18]. For testing pigments the Deutscher Normenausschuß (German Standards Committee) has proposed (DIN 6174) the trial use of the Adams-Nickerson system (AN System[19, 20]), which has been well known all over the world for decades and which is derived from the Munsell system. The three spatial coordinates are denoted by A_1 as the red-green axis, A_2 as the yellow-blue axis, and A_L as the brightness axis; in Fig. 2 the A_1 axis lies approximately in the line joining red to blue-green, A_2 in the line joining yellow to violet, and A_L is the vertical axis. To calculate the AN coordinates the X, Y, Z are first transformed into the value functions V_x, V_y, V_z. This operation is performed using a relationship like the logarithmic function which accommodates the physiologically equispaced brightness steps somewhat in the manner familiar from *Weber*'s law. A_1, A_2, A_L are obtained from V_x, V_y, V_z by the relationships:

$$A_1 = 40(V_x - V_y), \quad A_2 = 16(V_y - V_z), \quad A_L = 9.2\,V_y$$

This apparently rather odd formulation of differences is also well founded physiologically. In the retina the primary excitation of the cones is processed further in six types of nerve cells, of which four operate in antiparallel sense and the other two in parallel spectral sense. The latter build up a black-and-white system, the ones active in the antiparallel sense the chromatic color system[21].

Picturing two colors measured on pigmented layers as radius vectors in the AN color space, for test specimen $\mathfrak{A}_P = \{A_{1P}, A_{2P}, A_{LP}\}$ and for the color standard $\mathfrak{A}_B = \{A_{1B}, A_{2B}, A_{LB}\}$, then $\Delta E_{AN} = |\mathfrak{A}_P - \mathfrak{A}_B|$, the color difference in the AN space, measured in AN units (ANU). A significant advantage of the AN system is that it is possible to split up the color difference found into individual differences in various ways as desired. This is shown in Figure 3 by way of a model.

Following separation of the AN value difference $\Delta A_L = A_{LP} - A_{LB}$ there remains the AN chromaticity difference $\Delta A_C = |\mathfrak{A}'_P - \mathfrak{A}'_B|$ in the equal-brightness plane, with the dashed vectors arising by projection of $\mathfrak{A}_P$, $\mathfrak{A}_B$ into the A_1/A_2 plane. The chromaticity difference ΔA_c may be broken down further in two ways: firstly, manifestly into its two rectangular coordinates $\Delta A_1 = A_{1P} - A_{1B}$ and $\Delta A_2 = A_{2P} - A_{2B}$ (red-green or yellow-blue values), so that $\Delta A_c^2 = \Delta A_1^2 + \Delta A_2^2$; secondly, into the AN chroma difference $\Delta A_S = |\mathfrak{A}'_P| - |\mathfrak{A}'_B|$ and the AN hue difference ΔA_T, which is defined so that $\frac{1}{2}\Delta A_T^2 = |\mathfrak{A}'_P||\mathfrak{A}'_B| - (\mathfrak{A}'_P, \mathfrak{A}'_B)$ equal to the difference between magnitude product and scalar product. By virtue of this definition the second break-down of ΔA_c is also Euclidean: $\Delta A_C^2 = \Delta A_S^2 + \Delta A_T^2$. To identify the turning direction of the change of shade, ΔA_T is given the sign of the A_L component of the vector product $[\mathfrak{A}'_P, \mathfrak{A}'_B]_L$, *i.e.* the hue difference is positive when a clockwise rotation along the shortest path leads from reference to sample in the color plane, and *vice versa* (see DIN 6174 and ref.[22]).

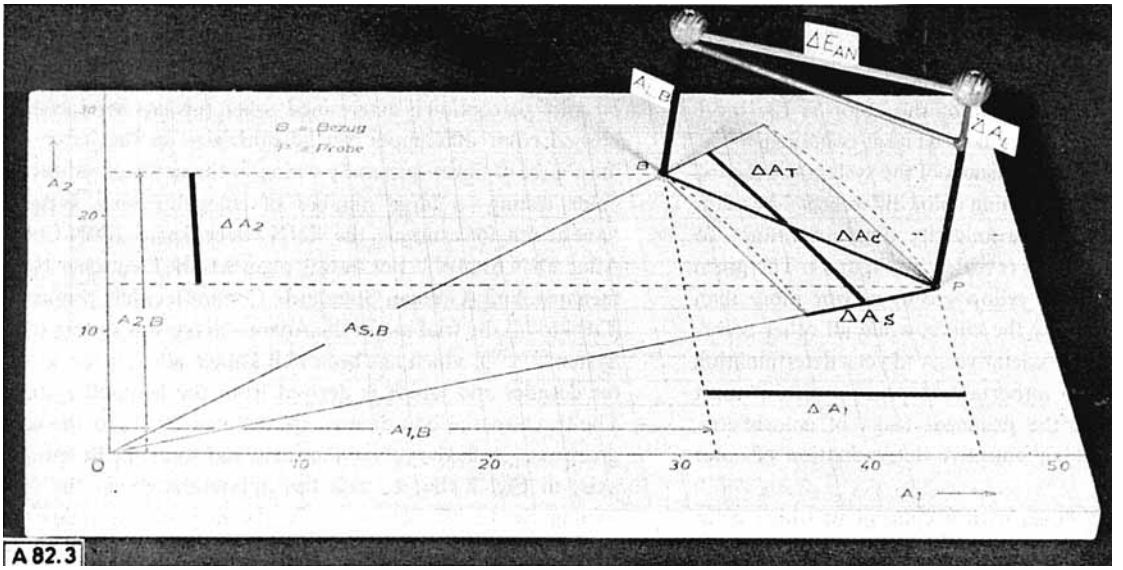


Fig. 3. Break-down of color differences into individual differences in the AN system (see text; the vectors $\mathfrak{A}'_B$, $\mathfrak{A}'_P$ correspond to the distances $\overline{OB}$, $\overline{OP}$). Key: Bezug = reference; Probe = test sample.

The introduction of the AN system ended a state of uncertainty and lack of comparability in pigment testing. Initial reports describing the experience gained[23] give a favorable picture.

2.3. Absorption and Scattering Theories; Kubelka-Munk Theory

When a light quantum enters a pigmented layer one of the following three processes determines its further fate:
it strikes a pigment particle and is absorbed;
it strikes a pigment particle and is scattered;
it passes through unhindered (assuming a nonabsorbing binder).

The essential physico-optical properties of the pigments are accordingly their absorbing power and scattering power. When absorption is very small compared with scattering, the pigment is white; when it is very large in comparison with scattering over the entire visible region, it is black; when the absorption is selective we have a chromatic pigment. How does the spectral luminance factor $\beta(\lambda)$ mentioned in Section 2.1 arise quantitatively?

The pigment tester is nowadays in the enviable position of being able to reduce $\beta(\lambda)$, and hence the optical properties of the pigment, almost entirely to basic physical quantities. He thus profits by being able to work with familiar physical laws. The schematic survey of Figure 4 illustrates the relationships in question.

The essential physical properties are listed at bottom left, while important technical properties are given at the top on the left-hand side. Substantial data are given in between: they represent the theoretical concepts relating technical and physical properties. The relationships are as follows:
colorimetry reduces the tristimulus value back to the luminous reflectance spectrum $\beta(\lambda)$;
the Kubelka-Munk theory reduces $\beta(\lambda)$ to scattering and absorption as well as to the layer thickness (scattering coefficient s and absorption coefficient k, film thickness h);
the theory of dependent scattering reduces s to the pigment concentration c and the scattering cross section Q_S of the primary particles (k is linearly proportional to the absorption cross section Q_A and the concentration c);
the *Mie* theory, finally, relates Q_S and Q_A to the particle size D, the wavelength λ, and the photometric characteristics of materials, *i.e.* refractive index n and absorption index $\varkappa$.

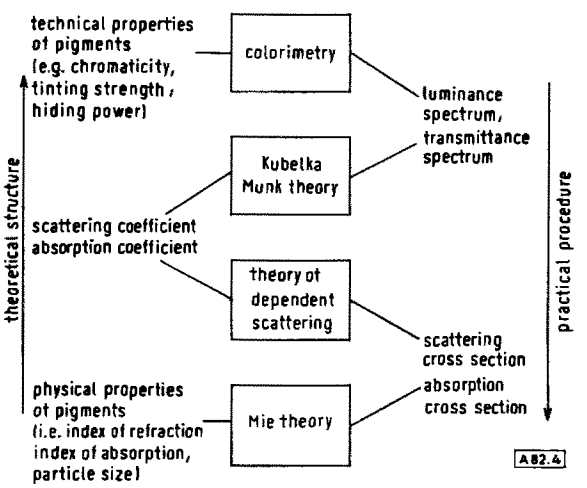


Fig. 4. Schematic representation of the relationships between optical pigment properties and their theoretical bases.

Among the phenomenological theories which establish the relationship between the spectral luminance factor on the one hand and the absorption and scattering coefficients on the other hand, it is the theory of *Kubelka* and *Munk*[24, 25], dating back to 1931, that has long been accepted for practical applications in the treatment of coloristic and dyeing problems on account of its simplicity and suitability. It is applicable to layers which not only absorb light but also scatter it and, consequently, it is even more comprehensive, especially for luminous reflectance, than is *Lambert*'s law for transmittance. This theory is therefore much more important for practical work than *Mie*'s theory, and so its basic features will be described here.

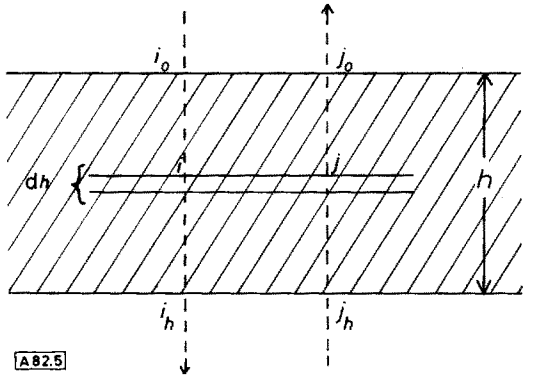


Fig. 5. Model illustrating the Kubelka-Munk theory (see text).

The Kubelka-Munk theory is based on the concept that the optical behavior of an absorbing and scattering layer can be described by only two constants, namely the absorption coefficient k and the scattering coefficient s. In a daring simplification the radiant flux of diffuse incident light is represented by a single beam i and the flux of light scattered opposite to the direction of incidence by a beam j. Each beam is attenuated by absorption and scattering losses, but is intensified by the scattering losses of the opposite beam (see Fig. 5). These losses are steered quantitatively by the two constants k and s. A simple system of two coupled differential equations can be set up, which can be solved for the relevant boundary conditions (i_0 and j_0 on the incidence side, i_h and j_h on the far side). The integrals provide solutions for the transmittance $\tau(k,s,h)=i_h/i_0$ and the luminance factor $\beta(k,s,h)=j_0/i_0$ as a function of k, s, and the layer thickness h, in special cases also with the inclusion of a desired background having luminous reflectance β_0. The quantity in the Kubelka-Munk theory that is used most widely, the luminance factor β_∞ of the opaque ("infinitely thick") layer, is particularly important. Its connection with s and k is described by a very simple equation:

$$k/s = (1-\beta_\infty)^2/(2\beta_\infty)$$

This expression ("the Kubelka-Munk function") shows that β_∞ depends only on the absorption coefficient-to-scattering coefficient ratio and not on their individual values over the sphere of validity of the theory. Tabulated values of the equation are available; it has found very wide application wherever information concerning absorption and scattering based on luminance factor measurements is desired[26] (*e.g.*, in dyeworks, thin-layer chromatography, and IR spectroscopy).

The Kubelka-Munk theory is a special case of a more general phenomenological theory based on radiative transfer equations[27]. Therefore, it must not be overlooked that it is based on quite a simple model which sometimes does not truly represent the practical conditions: it applies, strictly speaking, only to idealized diffuse light (*i.e.*, light whose radiation has no preferential direction), but which is rarely encountered in everyday practice. In addition, it does not allow for the generally present leap in refractive index at the layer surface or for surface gloss. Consequently, further theories have been formulated which allow for the above deviations but which necessarily are more complicated[28, 29]. So far only a single improvement has gained support, namely, the computational elimination of optical surface phenomena such as gloss, surface reflection, and internal reflection. These are allowed for by a subsequent correction of the luminance factor; formulas are available for this purpose[30].

In general, a pigment collective is not monodisperse but polydisperse, *i.e.* it has a particle-size distribution. The distribution is suitably described as the volume distribution of the diameters $v(D)$ (see Sheet 1 of DIN 53206). What is also of interest is the concentration dependence of k and s. As statement of the concentration an adequate measure was defined, namely, the pigment volume portion $c=v_P/V$, *i.e.* the pigment volume v_P divided by the total volume V. (In paint technology the pigment volume concentration PVC$=100c$ in % is generally used.) While k obeys *Beer*'s law up to high concentrations, *i.e.* varies linearly with c, the c *versus* s relationship gives rise to difficulties. Since the distance between the particles becomes smaller with rising concentration, typical disturbances with and obstructions of the scattering of individual particles appear; s thus follows a linear course only for small values of c (Beer region) but falls behind the linear course for higher values of c (cf. the two curves in Fig. 9). Quantitative description of the $s(c)$ relationship requires a theory of dependent scattering; however, there is as yet no closed theory in a form suitable for practical use. Formulas of phenomenological type are therefore used as an aid[31].

In conclusion, *Mie*'s theory will be briefly touched upon because it bridges the gap between the scattering and absorption properties of the individual particles and the physical constants and particle size. Our knowledge of the relationships between, on the one hand, absorption and scattering and, on the other hand, the particle size D, refractive index n, absorption index $\varkappa$, and wavelength λ is based substantially on information furnished by this theory[32]. *Mie* applied the Maxwell equations to a model in which a plane wave front strikes an optically isotropic sphere having a refractive index n and an absorption index $\varkappa$. The quantities resulting from integration (absorption cross section Q_A, scattering cross section Q_S) are dimensionless numbers; they give the ratio of the optically effective cross section to the geometric cross section of the particle.

The theory has provided a valuable insight into the effect of particle size on the coloristic properties of pigments[33, 34]. This last link in the chain has accomplished the desired aim: the optical pigment properties have been referred back to the complex refractive index $n^*=n-i\varkappa$ and the particle size D. As a result, it has become possible to calculate the spectral luminance factor of an unknown pigment and hence its coloristic properties in advance from given complex refractive index, concentration, and particle-size distribution.

3. Pigment Properties

3.1. Color Measurement and Color Differences

Many of the methods of testing technically important optical properties of pigments are available as DIN standards[35, 36], and some have also appeared as Proposals of the International Organization for Standardization (ISO).

It was shown in Section 2.1 that the problem of *color measurement* can be reduced to a determination of x, y, Y; according to the equations given this amounts to a measurement of the CIE tristimulus values X, Y, Z (see DIN 5033).

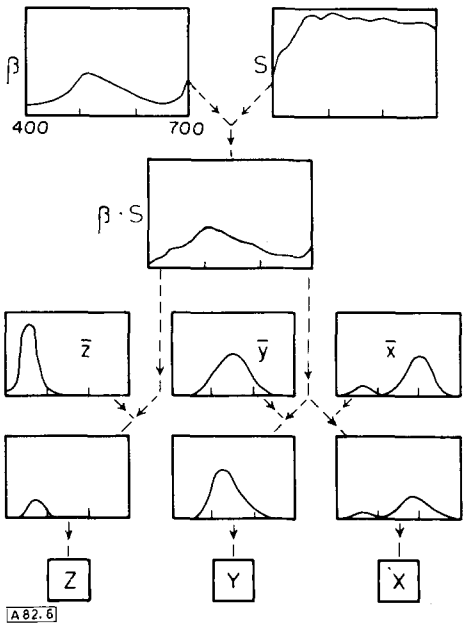


Fig. 6. Schematic representation of color measurement (after [37]).

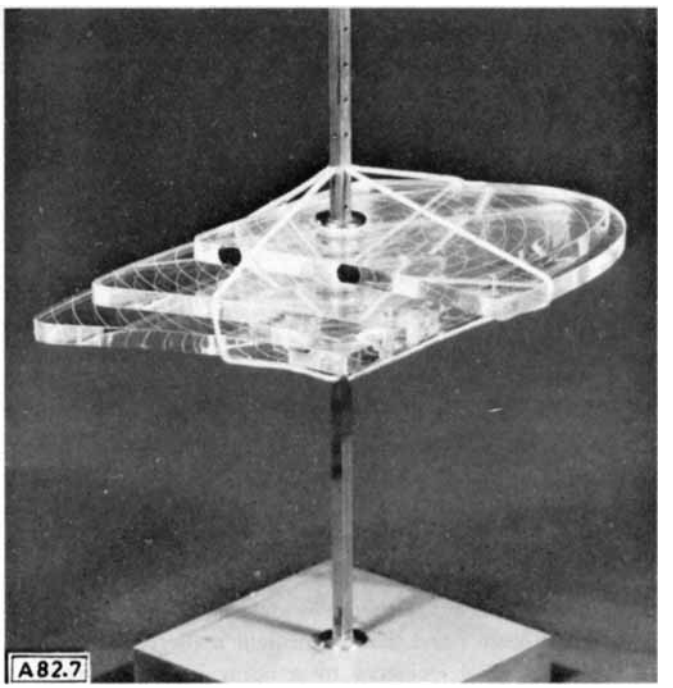


Fig. 7. Model of the AN color space.

For measuring color it is necessary to multiply the product $\beta \cdot S$ by the CIE spectrum tristimulus values, $\bar{x}$, $\bar{y}$, $\bar{z}$ to obtain the three curves of the bottom line in Figure 6 giving areas equal to X, Y, Z. These areas correspond to the above-described integrals, and since these allow two different interpretations there are two different types of instruments. These instruments utilize:

the tristimulus method ("three-filter colorimeters"). The transmittance curves of optical filters together with the lamp spectrum and the receiver sensitivity correspond to $S \cdot \bar{x}$, *etc.*, so that the measured intensities give X, Y, Z directly;

the spectrum method ("spectrophotometer"). The β-curve is recorded by a spectrograph. Multiplication by $\bar{x}$, $\bar{y}$, $\bar{z}$ and the subsequent integrations are performed by built-in analog computers or by internal or external digital computers.

The two types of instruments are used for color measurement; instrument manufacturers have developed suitable photometers and have perfected them during the last few years[6].

After color measurements on sample and reference pigment the X, Y, Z values are transformed into the AN system for calculating the color differences. Figure 7 shows a model of the AN color space (cf. ref.[22]). The crossed bands locate the position of the A_1/A_2 axis cross; the band extending from the front left-hand side to the rear right-hand side lies in the plane of the A_1-axis (red is at the front, left; $A_1 > 0$) the band extending from right to left lies in the plane of the A_2-axis (yellow is on the right; $A_2 > 0$). The circles marked on the plates are spaced at a distance of 10 ANU from one another. The similarity with the Munsell color solid system is clearly revealed: a typical feature is the great number of distinct dark violet and pale yellow shades (cf. Fig. 2).

For a moderate effort, the formalism of the AN system is readily programable on a larger-type desk computer, which may be in on-line connection with the colorimeter. Figure 8 shows the printout of a commercial desk computer by way of example; after the CIE tristimulus values it states the loci of the reference pigment and sample on the AN color diagram (two iron oxide yellow pigments) and, finally, the color difference ΔE with its break-down (see Section 2.2).

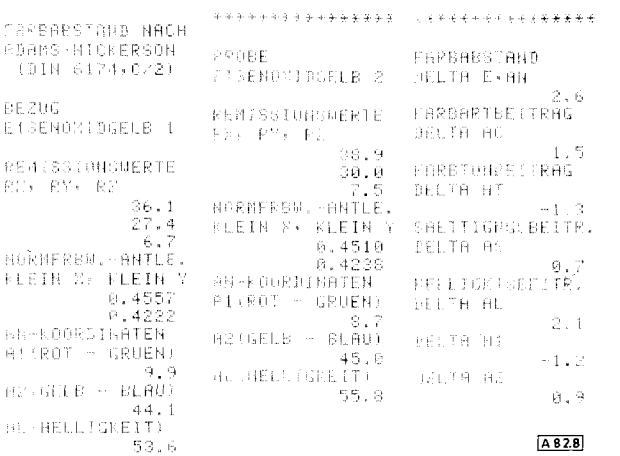


Fig. 8. Color difference between two iron oxide yellow pigments (desk computer printout). Key:

Adams-Nickerson Color Difference DIN 6174, (C/2)	Sample Iron Oxide Yellow 2	Color Difference Delta E, AN 2.6
Reference Iron Oxide Yellow 1	Luminous Reflectances RX, RY, RZ 38.9 30.0 7.5	AN Chromaticity Difference Delta AC 1.5 AN Hue Difference Delta AT −1.3
Luminous Reflectances RX, RY, RZ 36.1 27.4 6.7	CIE Chromaticity Coordinates x, y 0.4510 0.4238	AN Chroma Difference 0.7
CIE Chromaticity Coordinates x, y 0.4557 0.4222	AN Coordinates A1 (Red-Green) 8.7	Lightness Difference Delta AL 2.1
AN Coordinates A1 (Red-Green) 9.9	A2 (Yellow-Blue) 45.0	Delta A1 −1.2
A2 (Yellow-Blue) 44.1	AL (Lightness) 55.8	Delta A2 0.9
AL (Lightness) 53.6		

Color measurement on white pigments is somewhat simpler regarding statement of results because such measurements amount to a determination of the relative color cast. For this purpose the surroundings of the reference pigment are divided into eight sectors which are given the names of the colors from red to violet. By computation that octant is looked for in which the color of the sample lies (DIN 55981). The distance between sample and reference pigment is called intensity of the color cast. When a machine with an α-printer is available the name of the color can be printed out directly instead of the octant number.

If we recall that in the past color differences found in pigment testing have had to be expressed verbally (*e.g.* "a little lighter and yellower") it becomes clear how much progress has been made. Nevertheless, a further improvement of the AN system and of the other color difference systems should be aimed at; this refers both to the manipulation (ease of interpretation of the results, mathematical formalism) and to compatibility with visual color matching. A factor which gives rise to difficulties is that our knowledge of the process of color vision is still limited—especially the information processing by the nervous system and brain connected after the eye[10].

3.2. Tinting Strength, Lightening Power

Tinting strength is a measure of the ability of a colored pigment to impart its color to other light-scattering substances (*e.g.* pigmented coatings). The lightening power is so to speak the tinting strength of white pigments; it is the power to increase the luminance factor of a *per se* black or colored binder. Tinting strength and lightening power state the percentage weight ratio which enables the sample (weight m_P) to replace the reference pigment (weight m_B) for adjusting to the same color quality (color depth) in a white system or, respectively, with the same lightening, in a colored system. Accordingly, tinting stength and lightening power are defined by the equation

$$F = 100(m_B/m_P)_{\beta_\infty = \text{const.}}$$

where $\beta_\infty = \text{const}$, denoting the adjustment. Both are true properties of yield, because twice the color strength means, for example, that only half the weight of this pigment is required. In order to express the economic effects of higher color strengths, the reciprocal color strength multiplied by 10^4 ("color equivalent") is sometimes quoted to characterize this property.

In addition to scattering power, the lightening power is the most important property of white pigments; its value depends practically only on the scattering coefficient. Since the latter changes little with the wavelength over the visible region—as with most pigments—for white pigments a single measurement in the middle of the visible spectrum is sufficient.

In the past the lightening power was determined as follows. The weight of the pigment to be tested was varied until the lightness of a blue or black paste was equal to the lightness value of a standard rubbing as established visually. This procedure is tedious because in testing of entirely unknown pigments it can happen that four or five rubbings are required until adjustment is obtained. Rationalization was therefore attempted at an early stage. Also, it was desirable to replace the visual assessment by an objective photometric procedure. Since 1960 a test specification has been available which meets these requirements (DIN 53192). It is based essentially on two fundamental findings. The first is the linear course of the scattering coefficient over the region of low pigment volume portions c, *i.e.* over the Beer region[38]. The second is the realization of the linear course of the logarithm of the inverse Kubelka-Munk function in the luminance factor between 0.2 and 0.6[33]. This holds because the scattering coefficient is proportional to the inverse Kubelka-Munk function s/k, k being almost wholly determined by the blue or black pigment in the paste; it may therefore be regarded as constant. These two conditions enable one to construct a calibration straight line[39].

Typically for the novel procedure:
only one rubbing of the pigment need be prepared;
the optical assessment is left to a photometer (one measurement at one wavelength is adequate, see above);
a theoretically based—generally colorimetric—criterion is used for the comparison (here the equality of the k/s values);
a computational aid is used for obtaining the result (here the calibration curve or an appropriately programmed computer).

These features are quite generally characteristic for the development of rational objective methods; we shall encounter them again in the case of tinting strength and hiding power. The photometer and the calibration curve here "simulate" the laboratory assistant performing the old procedure, who had to prepare rubbings until matching of the reference pigment was accomplished.

Nevertheless, this attractive and elegant technique has one drawback. For the reasons stated in Section 2.3, the procedure allows a determination of the lightening power of white pigments only over the region of low pigment volume portions c. Since, however, in practice information is often desired at higher values of c as well, the makeshift remedy at present is to determine the scattering power at the concentrations of interest and to draw conclusions about the yield from the results obtained (DIN 53164 and 53165). As Figure 9 shows, this procedure is not permissible outside the Beer region.

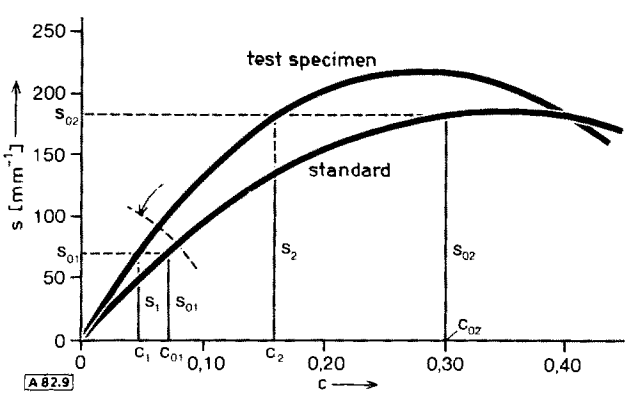


Fig. 9. Aid to the explanation of lightening power (see text). The arrow points to the limit of the Beer region. While $c_1 : c_{01} = s_1 : s_{01}$; but: $c_2 : c_{02} \neq s_2 : s_{02}$.

For the determination of *tinting strength* a simple visual matching procedure is available that was developed from practical working. Here too, the progress to rationalization

was inevitable; the next step was a photometric evaluation technique which already uses the Kubelka-Munk theory (DIN 53234). The basis is the linear dependence of the absorption coefficient k on the pigment volume concentration (PVC); Figure 10 shows some experimental values obtained with iron oxide red pigments. The value of the Kubelka-Munk function is shown plotted directly against the PVC. This technique is justified because the scattering coefficient s in the reducing white is determined by the titanium dioxide pigment present in excess and is therefore practically constant. The procedure relies on matching the absorption maximum of the pigments being compared, but in some instances adjustment of the absorption maximum is in poor agreement with visual matching. A further problem is to decide on the criterion applicable for adjusting the reference pigment and sample

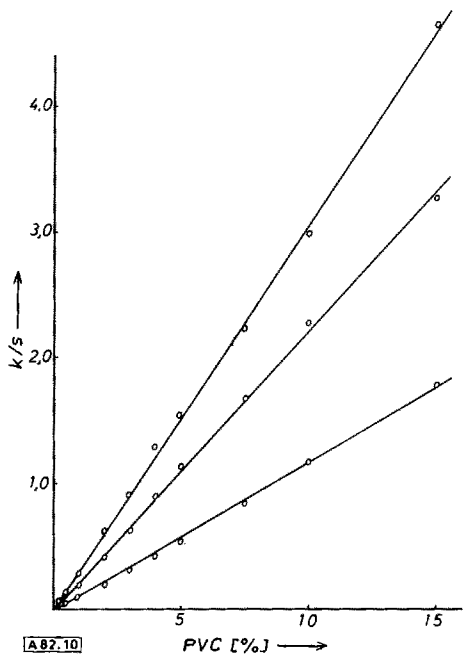


Fig. 10. Kubelka-Munk function k/s *versus* pigment volume concentration (PVC) of three iron oxide red pigments (for $\lambda = 530$ nm).

when, with differing spectra, a complete match between the colors cannot be obtained. Visual matching provided such a criterion (color depth), which set out to enable the tinting strength to be assessed even in the absence of shade identity; in addition, a computer program has been developed which enables the color strength to be determined rationally[40]. It is based on a principle ("spectral principle") utilizing the wavelength-dependent Kubelka-Munk constants $s(\lambda)$ and $k(\lambda)$ for calculating the match; this is discussed in Section 3.3.

Tinting strength in the wider sense is also one of the fundamentals in paint formulations. It is taken to mean the mixing ratio of the pigment components required for preparation of a desired shade. Colorant formulation calculation and computer correction of formulas on a colorimetric basis are today important special fields in coloristic technology[6, 41]

3.3. Hiding Power

Here too, we shall begin with white pigments for sake of simplicity, *i.e.* the definition and method of determination of the hiding power of achromatic coatings will be explained first. While lightening power can be defined from a knowledge of the scattering coefficient s, a determination of hiding power additionally requires a knowledge of the absorption coefficient k. The definition makes use of a black-and-white contrast background on which the coating film is applied. Determination of the hiding power then consists in finding the coating layer thickness that just causes the contrast background to disappear. The layer thickness that fulfills this condition is called the "covering layer" (in mm). Its inverse value, the hiding power (in $mm^{-1} = m^2/l$), like the color strength, is a yield property, because it gives the area in square meters which can be coated with 1 liter of paint to give an opaque film.

This definition at once suggests a possible method of determination. Layers of various thickness are prepared on a defined black-and-white background until the eye just fails to perceive the contrast. Such a procedure occupies much time and the situation is therefore analogous to that used for measuring the lightening power and tinting strength. A method is desirable which allows the determination to be made by photometric measurement on a single paint coating. It is precisely this technique that constitutes the procedure introduced in 1967 (DIN 53162) on the basis of the Kubelka-Munk theory.

The principle of the determination is explained in Figure 11; the covering layer is found at the point at which the ratio of the luminance factor over black and white $\beta_B/\beta_W = 0.98$. This ratio represents the hiding power criterion of the "just noticeable lightness difference" between black and white while allowing for a discrimination threshold of the human eye of 2%. Since β_B and β_W can be obtained from the Kubelka-Munk theory, the determination can be carried out purely by computation when only k and s have been determined experimentally, by measuring a noncovering layer over black and white.

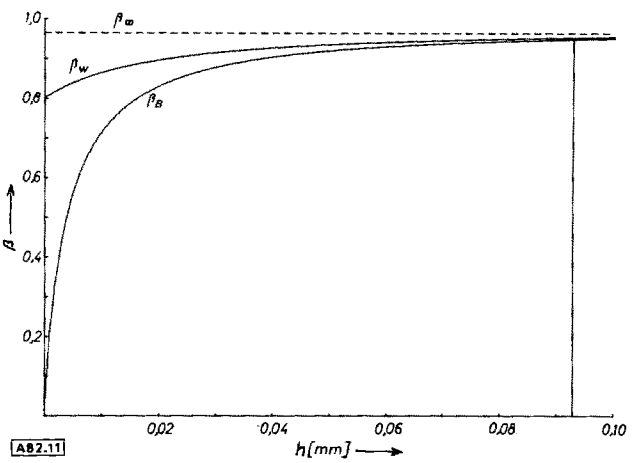


Fig. 11. Aid to the definition of hiding power (see text). The arrow points to the covering layer for $\beta_B/\beta_W = 0.98$. h is the layer thickness.

Meanwhile, it has been found that the procedure needs to be improved in certain respects. In our laboratory we are at present carrying out this determination by the following modifications:

replacement of the black-and-white card by black glass plates;

measurement of β_∞ on a covering layer and of β_B on a noncov-

ering layer on top of the black glass plate; k and s are calculated according to *Kubelka* and *Munk*[42],
correction of the luminance factors β to allow for optical surface phenomena[30],
determination of the layer thickness h by pneumatic measurement[43] instead of the gravimetric determination,
carrying out of the calculations with an electronic computer.

These measures enhance the accuracy appreciably[44] and, in addition, save time.

Figure 12 illustrates the principle of the hiding power determination.

There is as yet no standard test specification for determining the hiding power of chromatic coatings. The above old-established trying procedure was improved by once again working with a photometer and using a colorimetric criterion for determining the hiding layer (*e.g.* 1 ANU between black and white). However, the procedure can be rationalized: here too preparation of only one paint layer is the desired objective.

1. Preparation of paints with pigment volume concentrations of about 3%, 8%, 13%, 20%, 30%, and 40%.
2. Application of paint films onto black glass plates (paint spinner)
(a) "infinitely thick" layer,
(b) layer thickness chosen such that $0.02 < \beta_x - \beta_B < 0.06$.
3. Drying of the paint film.
4. Determination of the layer thickness h of the paint film (pneumatic measurement).
5. Measurement of luminance factors β_x and β_B.
6. Calculation of hiding power (computer).
7. Plotting of the diagram of hiding power *versus* pigment volume concentration.

Fig. 12. Scheme for the determination of the hiding power of white pigments.

The development of a procedure analogous to that used for the "achromatic hiding power" was initially hindered by the following obstacle. The Kubelka-Munk theory, which is after all an important basis of rationalizing a method of determination, is applicable only to spectral luminance factors. This is an insignificant restriction in the case of achromatic coatings, but with chromatic paint films the choice of the wavelength at which the measurement and calculation are to be carried out poses a problem. Should one not embrace the entire luminance spectrum in the calculation, and what method of evaluation is then offered? These questions were answered by the discovery of a principle that was first reported in 1964[45].

The entire luminance spectrum is measured. From the results and after measuring the layer thickness, the spectral scattering and absorption coefficients $s(\lambda)$ and $k(\lambda)$ are measured at different wavelengths, for example, at intervals of 10 nm, using the Kubelka-Munk method. Where these values are known it is possible to predict the luminance factors over black and white at the chosen wavelengths of the spectrum for any layer thickness. The CIE standard colorimetric system is then used to calculate the lightness Y displayed by a color having the just determined spectrum.

This procedure provided the means of determining by iteration the layer thickness for which the hiding power criterion $Y_B/Y_W = 0.98$ is fulfilled. This "spectral principle" is the key to the treatment of testing methods depending on the visual assessment of a match of two paint films (cf. the tinting strength determination in Section 3.2). During the period which followed improvements were effected, especially by introducing a just tolerable color difference (*e.g.* 1 ANU) as the hiding power criterion and by the use of computers[46].

4. Conclusion

An attempt has been made to represent the optical properties of pigments on the basis of theoretical fundamentals and the methods used to test them, and to show which problems have not yet been solved satisfactorily despite the considerable successes during the past decade. Nevertheless, it seems justified to conclude that thanks to the CIE system, the AN system, and the Kubelka-Munk theory considerable advances have been made. The concepts underlying the modern methods of testing possess a considerable degree of difficulty owing to the complex: light source/sample/eye/brain system that has to be simulated by the methods of determination. The necessity of simulating this complex system leads one to appreciate that further advances will be attainable in the future only if problems of even higher degrees of difficulty have been tackled. The "simple" methods of determination reported in the literature from time to time are not likely to yield solutions to these problems. The solutions will rather come from an improvement in our knowledge of an insight into the cybernetic and physicochemical principles involved in the perception of optical stimuli by the eye and the associated organs. The occasional objection to the novel methods and further developments, that the computational outlay is too extensive, is without foundation, since economically priced high-performance desk computers effecting the calculation in a matter of seconds have become available. In this way, an essential condition for advances in this field is established, *i.e.* the remarkable development in the field of computer techniques during recent years. It alone enables a color measurement and testing laboratory in the form encountered today to objectivize test problems of this degree of complexity and to carry out testing of the described kind rationally and in reasonable time.

Received: July 2, 1975 [A 82 IE]
German version: Angew. Chem. 87, 721 (1975)
Translated by Express Translation Services, London

[1] *W. Noll, R. Holm,* and *L. Born,* Angew. Chem. 87, 639 (1975); Angew. Chem. internat. Edit. 14, 602 (1975).
[2] *G. Lincke,* Farbe + Lack 75, 632 (1969).
[3] *H. G. Völz:* XI. Fatipec-Kongress 1972. Ariminum, Mailand 1972, p. 43.
[4] *E. Schrödinger,* Ann. Phys. (Leipzig) 63, 397, 427, 481 (1920); *M. Born,* Naturwissenschaften 50, No. 2, 3 (1963).
[5] *W. Schultze:* Farbenlehre und Farbenmessung. 7th Edit. Springer, Berlin 1966.
[6] *A. Berger* and *A. Brockes,* Bayer-Farben-Revue, Sonderheft 3/1 (1971).
[7] *I. Newton:* Opticks. Innys, London 1704—1730 (New edition, McGraw Hill, New York 1931).
[8] *T. Young,* Phil. Trans. Roy. Soc. London 92, 12 (1802).
[9] *H. Grassmann,* Ann. Phys. (Leipzig) 89, 69 (1853).
[10] *G. Wald,* Angew. Chem. 80, 857 (1968).
[11] *H. v. Helmholtz:* Handbuch der physiologischen Optik. Voss, Leipzig 1911.
[12] *W. D. Wright,* Trans. Opt. Soc. London 30, 141 (1928/29).
[13] *H. Guild,* Phil. Trans. Roy. Soc. London *A 230,* 149 (1931/32).
[14] *K. Steinbuch:* Automat und Mensch. Springer, Berlin 1971 1971, 4th edit., pp. 200ff.
[15] *N. Mayer,* Farbe, in press.
[16] *G. Wyszecki,* Farbsysteme, Musterschmidt, Göttingen 1960, pp. 81ff.
[17] *A. H. Munsell:* Atlas of the Munsell Color System. Wadsworth-Howland, Boston 1915.
[18] *M. Richter,* Farbe 1, 85 (1953).
[19] *E. Q. Adams,* J. Opt. Soc. Am. 32, 168 (1942).
[20] *D. Nickerson* and *K. F. Stultz,* J. Opt. Soc. Am. 34, 550 (1944).
[21] *R. L. de Valois,* Internat. Farbtagung "Color 69", Tagungsbericht. Musterschmidt, Göttingen 1970, Vol. 1, p. 29.
[22] *A. Reule,* Farbe 23, 17 (1974).
[23] *L. Gall,* Farbe + Lack 79, 279 (1973).
[24] *P. Kubelka* and *F. Munk,* Z. Tech. Phys. 12, 539 (1931).

[25] *P. Kubelka*, J. Opt. Soc. Am. *38*, 448 (1948).
[26] *G. Kortüm*: Reflexionsspektroskopie. Springer, Berlin 1969.
[27] *H. G. Völz*: VI. Fatipec Congress 1962. Congress Book. Verlag Chemie, Weinheim 1962, p. 98.
[28] *S. Chandrasekhar*: Radiative Transfer, Clarendon Press, Oxford 1950.
[29] *P. S. Mudgett* and *L. W. Richards*, J. Paint Technol. *45*, 586 (1973).
[30] *A. Brockes*, Farbe *9*, 53 (1960).
[31] *H. G. Völz*, Ber. Bunsenges. Phys. Chem. *71*, 326 (1967).
[32] *G. Mie*, Ann. Phys. *25*, 377 (1907).
[33] *W. Jaenicke*, Z. Elektrochem. *60*, 163 (1956).
[34] *A. Brockes*, Optik (Stuttgart) *21*, 550 (1964).
[35] *E. Fritzsche*, Farbe + Lack *80*, 731 (1974).
[36] *H. G. Völz*, Farbe, in press.
[37] *D. L. MacAdam*, TAPPI *38*, 78 (1955).
[38] *W. Grassmann* and *H. Clausen*, Dtsch. Farben-Z. *7*, 211 (1953).
[39] *A. Berger* and *H. H. Weber*, Farbe + Lack *65*, 228 (1959).
[40] *L. Gall*: IX. Fatipec Congress 1968. Congress Book. Chimie des Peintures, Brussels 1968, Sect. 1, p. 34.
[41] *L. Gall*: Internat. Color Conference Colour 73. Hilger, London 1973, p. 153.
[42] *H. Rechmann* and *F. Vial*, Farbe + Lack *74*, 233 (1968).
[43] *G. Kämpf* and *H. G. Völz*, Farbe + Lack *77*, 629 (1971).
[44] *H. G. Völz*, Farbe *19*, 231 (1970).
[45] *H. G. Völz*: VII. Fatipec Congress 1964, Congress Book. Verlag Chemie, Weinheim 366; Farbe + Lack *71*, 725 (1965).
[46] *L. Gall*, Farbe + Lack *72*, 955, 1073 (1966).

COMMUNICATIONS

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

Dichlorofluoromethanesulfenyl Isothiocyanate

By *Engelbert Kühle*, *Hermann Hagemann*, and *Linthard Oehlmann*[*]

Dedicated to Professor Siegfried Petersen on the occasion of his 65th birthday

To our knowledge, sulfenyl isothiocyanates, unlike acyl, imidoyl, phosphoryl, and sulfonyl isothiocyanates, have not hitherto been prepared. While reaction of acyl chlorides with the salts of thiocyanic acid generally affords acylated isothiocyanates, this method fails with sulfonyl and sulfenyl chlorides. These acyl chlorides react with thiocyanates *via* S—S coupling to give sulfonyl and sulfenyl thiocyanates.

Sulfonyl isothiocyanates have become readily accessible by initial formation of a SO_2—N—C linkage and its subsequent conversion into an SO_2—NCS grouping[1].

The synthesis of dichlorofluoromethanesulfenyl isothiocyanate *(3)* starts with addition of cyanogen chloride to dichlorofluoromethanesulfenyl chloride *(1)* to give dichlorofluoromethanesulfenyl isocyanide dichloride *(2)*[2].

$$\underset{(1)}{Cl_2FC{-}S{-}Cl} \xrightarrow{ClCN} \underset{(2)}{Cl_2FC{-}S{-}N{=}CCl_2} \xrightarrow{P_2S_5} \underset{(3)}{Cl_2FC{-}S{-}N{=}C{=}S}$$

[*] Dr. E. Kühle [+], Dr. H. Hagemann, and Dr. L. Oehlmann
Bayer AG, Zentrale Forschung WHL
509 Leverkusen (Germany)
[+] To whom correspondence should be addressed.

Compound *(2)* and P_2S_5 are heated in boiling xylene until dissolution of the P_2S_5 is complete (*ca.* 24 h). Distillation affords a fraction of b. p. 64—66 °C/12 torr—approximately 50 % of the initial amount of *(2)*—which is shown by coupled GC/MS to have the following composition: xylene (4 %), *(2)* (81 %), *(3)* (10 %), $Cl_2FC{-}S{-}S{-}CFCl_2$ (2 %).

The IR spectrum of the pure compound *(3)* isolated by preparative GC exhibits a broad strong NCS band at 1940 cm^{-1} (dichlorofluoromethanesulfenyl thiocyanate: medium strength sharp band at 2251 cm^{-1}).

Received: April 7, 1975 [Z 231 IE]
German version: Angew. Chem. *87*, 707 (1975)
Publication delayed at authors' request
CAS Registry numbers: *(1)*, 2712-93-8; *(2)*, 39202-34-1; *(3)*, 55701-56-9

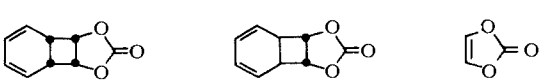
[1] *K. Dickoré* and *E. Kühle*, Angew. Chem. *77*, 429 (1965); Angew. Chem. internat. Edit. *4*, 430 (1965).
[2] *H. Hagemann*, DOS 2126540 (1971), Bayer AG.

Photochemical Cycloaddition of Benzene to Vinylene Carbonate

By *Hans-Georg Heine* and *Willy Hartmann*[*]

Dedicated to Professor Siegfried Petersen on the occasion of his 65th birthday

In connection with our studies on *cis*-1,2-cyclobutanediols and bicyclo[4.2.0]octane derivatives we have been interested in the two carbonates *(1)* and *(2)* and have investigated the photoaddition of benzene to vinylene carbonate *(3)* as



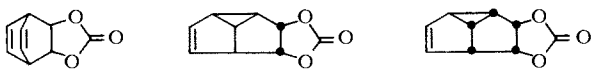
(1) *(2)* *(3)*

a direct route to these, as yet, undescribed compounds. Singlet excited benzene reacts with olefins to give 1,2-, 1,3-, and to a lesser extent 1,4-addition products. Since functionally substituted olefins[1] afford predominantly, or exclusively, bicy-

[*] Dr. H.-G. Heine and Dr. W. Hartmann
Zentralbereich Forschung, Wissenschaftliches Hauptlaboratorium der Bayer AG
4150 Krefeld-Uerdingen (Germany)

clo[4.2.0]octa-2,4-diene derivatives one could expect 1,2-addition to be the favored process also in the photoreaction of benzene with *(3)*.

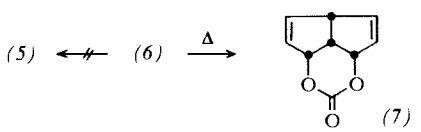
However, irradiation[2] of a 1.0 M solution of *(3)* in benzene (*ca.* 10% conversion) affords a 1:1:5 mixture of the 1:1 adducts *(4)* (m.p. 113—115 °C), *(5)* (m.p. 78—79 °C), and *(6)* (m.p. 79—81 °C) in 70—80% total yield.



(4) *(5)* *(6)*

Catalytic hydrogenation of *(4)* with uptake of two mol equivalents of H_2 and subsequent hydrolysis affords bicyclo[2.2.2]octane-*cis*-2,3-diol. Complete assignment of structure and configuration of the two dihydrosemibullvalene derivatives *(5)* and *(6)* follows unequivocally from the ^{13}C- and ^1H-NMR spectroscopic data[3].

The two 1,3-cycloadducts *(5)* and *(6)* behave differently on thermolysis. Whereas the *exo*-isomer *(5)* remains unchanged on heating to 150 °C/N_2[4], the *endo*-isomer *(6)* rearranges under the same conditions to give the six-membered ring carbonate *(7)* (m.p. 124—125 °C) in 70—80% yield. *endo*→*exo*-Isomerization does not take place. The structure of *(7)* is clearly evident from the ^1H-NMR spectrum (AA'BB'CC'XY type)[3].



(5) ⇄ *(6)* —Δ→ *(7)*

The valence isomerization of dihydrosemibullvalenes to bicyclo[3.3.0]octa-2,7-dienes with migration of a hydrogen atom or an alkyl group has already been described[5, 6]. To the best of our knowledge the rearrangement *(6)*→*(7)* represents the first example of a 1,5-sigmatropic shift of a functional substituent in this class of compounds. Since such 1,5-sigmatropic rearrangements proceed suprafacially it is understandable that *(5)* and *(6)* exhibit different thermal behavior.

The preferred 1,3-addition in the reaction of electronically excited benzene with *(3)* is surprising in view of the already mentioned results with other functionally substituted olefins. Our findings are also inconsistent with the recently reported concept[1] of the factors governing the selectivity of photochemical benzene cycloadditions. According to this concept the 1,2-addition ought to dominate over the 1,3-addition if the following condition is fulfilled:

$$9.6\,eV < I.P._{olefin} < 8.65\,eV$$

Accordingly *(3)*, which has a relatively high ionization potential (*I.P.*) of 10.08 eV[7], should give predominantly *(1)* and/or *(2)*.

Orientating experiments show that irradiation of substituted arenes, such as anisole or *p*-xylene, and *(3)* likewise leads predominantly to 1,3-cycloadducts. This provides a simple route to preparatively interesting starting compounds for reactions in the tricyclo[3.3.0.0^{2,8}]octene series, for example for the synthesis of substituted semibullvalenes.

Received: June 9, 1975 [Z 277 IE]
German version: Angew. Chem. *87*, 708 (1975)

CAS Registry numbers:
(3), 872-36-6; *(4)*, 32342-24-8; *(5)*, 56030-39-8; *(6)*, 56086-20-5; *(7)*, 56030-40-1; benzene, 71-43-2

[1] *D. Bryce-Smith, A. Gilbert, B. Orger*, and *H. Tyrrell*, J. C. S. Chem. Comm. *1974*, 334.
[2] Low-pressure mercury lamp (70 W), Gräntzel, Karlsruhe; N_2, 35 °C.
[3] A complete discussion of the NMR spectra, for the recording of which we wish to thank Dr. *D. Wendisch*, will be published in a later communication.
[4] On heating to 200—250 °C, *(5)* undergoes uncontrolled pyrolysis.
[5] *W. R. Roth* and *B. Peltzer*, Liebigs Ann. Chem. *685*, 56 (1965).
[6] *R. Srinivasan*, Tetrahedron Lett. *1971*, 4551.
[7] Determined from the PE spectrum, for the recording of which we wish to thank Professor Dr. *H. Bock*.

Preparation of $[SiCl_2bipy_2](ClO_4)_2$ by Oxidation of $SiCl_2bipy_2$[1]

By *Dieter Kummer* and *Tarimala Seshadri*[*]

We obtained the first cationic bis(2,2'-bipyridine) complex of silicon $[Si(OCH_3)_2bipy_2]Cl_2$ by treatment of $SiCl_2bipy_2$ with methanol[2]. Its properties, and in particular its solvolytic stability, make a knowledge of further members of this class of compound desirable.

By treating $SiCl_2bipy_2$ (the green isomer)[3] with chlorine we have now prepared $[SiCl_2bipy_2]Cl_2$. This compound, which is also unusually stable against solvolysis, can be transformed in methanolic solution by ion exchange into the sparingly soluble $[SiCl_2bipy_2](ClO_4)_2$ *(1)* which is isolable as colorless crystals. Its elemental analysis accords with the calculated values. Its conductivity and the molecular weight determinations (cryoscopic) prove the ionic structure and the presence of a 1:2 electrolyte in methanol and water[4]. Chloride cannot be detected in fresh solutions but instead the expected amount of perchlorate appears. ClO_4^- ions also exist in the solid substance (IR spectrum). The compound thus consists of the $[SiCl_2bipy_2]^{2+}$ cation and ClO_4^- anions. An octahedral structure of the cation with the two chlorine atoms in the *cis*-positions follows from the ^1H-NMR spectrum (cf. Ref. [2]). The structure of the complex is important because of the structure of green $SiCl_2bipy_2$ which was unknown until recently. Since chlorination of the latter being a simple electron transfer reaction should not alter the positions of the atoms the structure of $[SiCl_2bipy_2]^{2+}$ leads to the conclusion that $SiCl_2bipy_2$ is also a *cis*-octahedral complex. This has meanwhile been confirmed by X-ray structure analysis of the green $SiCl_2bipy_2$[5].

The solvolytic stability of the cation of *(1)* is remarkable, including that of the SiCl groups: solutions in methanol are stable for weeks at 25 °C; only in months is $[Si(OMe)_2bipy_2]^{2+}$ formed (cf.[2]). An increase in temperature hastens this process.

In aqueous solution observable formation of $[Si(OH)_2bipy]^{2+}$ occurs only within a few hours[2], but complete conversion requires several days.

In acid solution *(1)* behaves in the same way, but OH^- ions in excess (>2 equivalents) at once liberate bipy. With an equivalent amount of base, *e.g.* $NaOCH_3$, replacement of the SiCl groups can be achieved with retention of the complex cation.

Experimental:

Chlorine (0.5 g, 6.6 mmol) is condensed on to a slurry of green $SiCl_2bipy_2$ (1.54 g, 3.74 mmol; from Si_2Cl_6 + 3 bipy[6]) in CH_2Cl_2. When the solution is warmed to room temperature with stirring, the color fades gradually to provide a yellowish product; after several hours' stirring the CH_2Cl_2 is evaporated and the product ($[SiCl_2bipy_2]Cl_2$) is dissolved in methanol and placed on a column of perchlorate ion-exchanger (Merck Lewatit MP 5080). Thereafter thin colorless crystals of *(1)*

[*] Prof. Dr. D. Kummer and Dr. T. Seshadri
Institut für Anorganische Chemie der Universität
75 Karlsruhe 1, Englerstr. 11 (Germany)

are precipitated from the methanol solution by means of ether. They decompose at 184 °C; their solubility in methanol is *ca.* 3 g/l.

Received: May 14, 1975 [Z 258 IE]
German version: Angew. Chem. 87, 742 (1975)

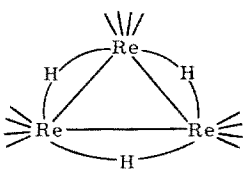
CAS Registry numbers:
$SiCl_2bipy_2$, 55853-11-7; $[SiCl_2bipy_2]Cl_2$, 55923-77-8; $[SiCl_2bipy_2](ClO_4)_2$, 55925-19-4; $[Si(OMe)_2bipy_2]^{2+}$, 55853-12-8; $[Si(OH)_2bipy_2]^{2+}$, 55853-13-9

[1] Part 6 of The Chemistry of Halosilane Adducts. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 5: *D. Kummer* and *H. Köster*, Z. Anorg. Allg. Chem. *402*, 297 (1973).
[2] *D. Kummer* and *H. Köster*, Z. Anorg. Allg. Chem. *398*, 279 (1973).
[3] *S. Herzog* and *F. Krebs*, Z. Chem. *8*, 149 (1968).
[4] MW (in H_2O): exp. 221; calc. 610.27; $\Lambda_c = 117.8$ cm^2/Ω·mol (20 °C), $c = 2.93 \times 10^{-3}$ mol/l in methanol.
[5] *A. G. MacDiarmid*, personal communication.
[6] *D. Kummer* and *H. Köster*, Angew. Chem. *81*, 897 (1969); Angew. Chem. internat. Edit. *8*, 878 (1969).

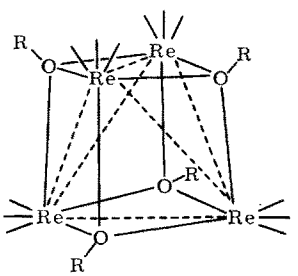
Carbonylrhenium Clusters by Photoreaction of $Re_2(CO)_{10}$ with Water[**]

By *Max Herberhold* and *Georg Süss*[*]

Decacarbonyldirhenium, $Re_2(CO)_{10}$ *(1)*, is stable towards water even under drastic conditions; nor is it attacked by dilute acids or bases[1]. A "base reaction" can only be achieved with methanolic potassium hydroxide, whereupon a dinuclear complex $K[Re_2(CO)_8O_2H]$ is formed[2]. We have now found that *(1)* reacts smoothly with H_2O in aqueous ether under photolytic conditions: the solution initially contains both the known[3] trinuclear hydrido complex $[Re(CO)_4H]_3$ *(2)* and an apparently tetranuclear hydroxo complex $[Re(CO)_3(OH)]_4$ *(3)*. Species *(2)* is transformed into *(3)* under the reaction conditions so that *(3)* is obtained exclusively if irradiation is continued for a sufficient time.



$[Re(CO)_4H]_3$
(2)



$[Re(CO)_3(OR)]_4$
(3), R = H
(4), R = D
(5), R = OCH_3

The new hydroxo complex *(3)* is colorless, air-stable, and nonvolatile in a high vacuum. The simple IR spectrum suggests a highly symmetrical structure; in addition to the absorption bands of a tricarbonyl group (ν(C≡O) 2021 (s) and 1919 (vs) cm^{-1} in THF), a sharp double band (ν(O—H) 3550 cm^{-1} in KBr) is observed. In the ^{1}H-NMR spectrum (diamagnetic) just *one* broad singlet at δ = 6.50 ppm in $[D_6]$acetone is found which corresponds to the hydroxy protons and slowly disappears in the case of solutions of *(3)* in deuterated solvents (H/D exchange). The ^{13}C-NMR spectrum[4] likewise exhibits only *one* signal (δ = 196.67 ppm in $[D_8]$THF) which does not split when the temperature is lowered to −80 °C. This means that all the C atoms in *(3)* are equivalent.

The hydrogen atoms in $[Re(CO)_3(OH)]_4$ *(3)* can be reversibly replaced by deuterium with D_2O, the reaction product being $[Re(CO)_3(OD)]_4$ *(4)* (ν(O—D) 2575 cm^{-1} in KBr). Reaction with diazomethane affords $[Re(CO)_3(OCH_3)]_4$ *(5)* which, in contrast to *(3)*, is sufficiently volatile for recording a mass spectrum. This spectrum exhibits a molecular peak somewhat above *m/e* 1200 (calc. 1200—1208) and a stepwise loss of CO, CH_3O, and CH_3 fragments[5].

While the relative molecular mass of *(3)* could not be unequivocally determined[6], the mass spectrum of *(5)* indicates a tetrameric molecule. All findings are in accord with the assumption that *(3)*, *(4)*, and *(5)* have the structure of tetranuclear, tetrahedral tricarbonylrhenium complexes (distorted cubane structure).

According to studies on the photolysis of $Re_2(CO)_{10}$ *(1)* in CCl_4[7] the initial step of the photoreaction appears to be homolysis to give radicals $Re(CO)_5$. These reactive fragments probably then react with H_2O, either directly or after loss of CO groups, to form polynuclear carbonylrhenium complexes.

Procedure[8]:

Water (10 ml) is added to a solution of $Re_2(CO)_{10}$ *(1)* (0.33 g, 0.5 mmol) in diethyl ether (200 ml) and the stirred mixture irradiated for 15 h with a high pressure mercury arc (Hanovia S-200 W). The residue obtained from the ethereal phase is washed with pentane to remove *(1)* and chromatographed in ether on acidic alumina. The colorless eluate affords $[Re(CO)_3(OH)]_4$ *(3)* which is recrystallized from ether/pentane (1:2) and dried at 80 °C in a high vacuum: yield 0.16 g (53 %); dark coloration >160 °C, decomposition ≈350 °C.

Received: June 16, 1975 [Z 271 IE]
German version: Angew. Chem. 87, 710 (1975)

CAS Registry numbers:
(1), 14285-68-8; *(3)*, 56553-73-2; *(5)*, 56553-72-1

[1] *W. Hieber* and *H. Fuchs*, Z. Anorg. Allg. Chem. *248*, 256 (1941).
[2] *W. Hieber* and *L. Schuster*, Z. Anorg. Allg. Chem. *285*, 205 (1956).
[3] *D. K. Huggins*, *W. Fellmann*, *J. M. Smith*, and *H. D. Kaesz*, J. Am. Chem. Soc. *86*, 4841 (1964).
[4] Bruker HFX 90; measurements by Dr. *C. G. Kreiter*.
[5] Atlas CH4, ion source TO4; measurements by Dr. *J. Müller*.
[6] Osmometric measurements lead to contradictory results for complexes of similar type; they also fail in the case of *(3)* because of its insufficient solubility. The method according to *Rast* (camphor) likewise failed to give unambiguous results.
[7] *M. Wrighton* and *D. Bredesen*, J. Organometal. Chem. *50*, C35 (1973).
[8] All operations carried out under N_2.

[*] Doz. Dr. M. Herberhold and Dipl.-Chem. G. Süss
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. *G. S.* is indebted to the Studienstiftung des Deutschen Volkes for a postgraduate grant.

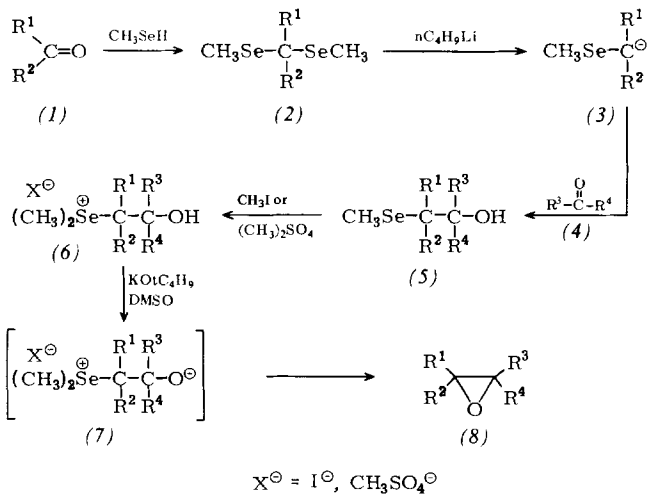
A New Route to Epoxides

By *D. Van Ende*, *Willy Dumont*, and *Alain Krief*[*]

We recently described a synthon which allows the epoxide synthesis from phenyl selenoacetals and carbonyl compounds[1]. Further investigations have demonstrated that the use of methyl selenoacetals offers several advantages (Scheme 1), the main ones are listed below:

[*] Dipl.-Chem. D. Van Ende, Dr. W. Dumont, and
Prof. Dr. A. Krief [**]
Department de Chimie, Facultes Universitaires de Namur
61, rue de Bruxelles, B-500 Namur (Belgium)

[**] On leave from CNRS (France).



Scheme 1.

1. The previously unknown methyl selenoacetals *(2)* of carbonyl compounds, even of aldehydes, can be prepared in high yields (Table 1).

Table 1. Dimethyl selenoacetals prepared from carbonyl compounds *(1)* and methaneselenol *(2)*.

R^1	R^2	Yield [%]	B. p. [°C/torr]
H	H	80 [a]	80/15
H	CH_3	80	72/15
H	nC_6H_{13}	70	140/18
CH_3	CH_3	90	85/25
CH_3	C_2H_5	90	54/0.8
$-(CH_2)_5-$		80	86/0.7

[a] Prepared from diiodomethane and potassium methyl selenate.

2. The nucleophilicity of α-methyl selenocarbanions *(3)*, even of the highly substituted ones, is so high that they can react with a large variety of carbonyl compounds *(4)*, including enolizable or hindered ones such as deoxybenzoin or 2,2,6,6-tetramethylcyclohexanone (Table 2).

3. The nucleophilicity of the selenium atom in the β-hydroxy methyl selenides *(5)* is higher than in the phenyl analogs and allows the synthesis of the corresponding selenonium salts *(6)* with methyl iodide or methyl sulfate (expensive silver tetrafluoroborate is not needed[11]) without concomitant rearrangement[1].

The potentiality of the method is increased by the volatility of the by-products[2] encountered during the synthesis and by the availability of the reagents[3].

When the intermediates *(5)* and *(6)* are not purified, the epoxide *(8)* is generally obtained in pure form in the range of 60—80% overall yield from the carbonyl compound *(4)*.

In some cases, when β-hydroxy selenides *(5)* contain a cyclohexyl directly attached to the selenium atom, we were unable to isolate the corresponding salt (from methyl iodide or methyl sulfate) and in contrast with the process previously described, an olefin is formed: for instance, heptylidenecyclohexane[4] is obtained in 90% yield from *(5n)* and methyl iodide. Nevertheless, the desired epoxide *(8f)* is obtained from 1,1-bis(methylseleno)heptane and cyclohexanone.

Finally, it is interesting to note that the carbanions *(3)* do not equilibrate under the experimental conditions.

Experimental:

Dimethyl selenoacetals (2): These are conveniently prepared by passing HCl gas through a mixture of the carbonyl compound *(1)* (28 mmol) and methaneselenol (63 mmol) at 0 °C for 30 min. After stirring for 1 h, the solution is neutralized (Na_2CO_3/H_2O), extracted, dried and distilled. All the reactions must be done in a hood.

β-Hydroxy selenide synthesis (5): *n*-Butyllithium (5.25 mmol) (2 N in hexane, Merck) is slowly added at −78 °C under nitrogen to a solution of selenoacetal *(2)* (5.5 mmol) in anhydrous THF (10 ml). After 1 h (−78 °C), the carbonyl compound *(4)* (5 mmol) in THF (5 ml) is added and the resulting solution is stirred for 2 h at −78 °C and 1 h at 25 °C, hydrolyzed, extracted, and dried. Compound *(5)* is generally obtained quite pure after evaporation of butyl methyl selenide (b. p. 141 °C/760 torr, 0 °C/1 torr). It can be purified chromatographically (SiO_2 2 mm, Merck, ether/pentane 2:8, $R_f = 0.2$).

Selenonium salt (6): *(5)* (2 mmol) is stirred with methyl iodide or methyl sulfate (4 mmol) for 2 h at 25 °C. The mixture (which becomes rapidly crystalline in the case of iodide) is washed three times with dry ether in order to remove the unreacted selenide *(5)* and if necessary the unreacted carbonyl compound *(4)*.

Epoxide (8): Potassium *tert*-butoxide (2.3 mmol) and the salt *(6)* (2 mmol) are stirred in DMSO (10 ml) at 25 °C for

Table 2. β-Hydroxy selenides *(5)*, -selenonium iodides *(6)*, and epoxides *(8)* prepared according to Scheme 1.

	R^1	R^2	R^3	R^4	*(5)* Yield [%]	*(6)* Yield [%]	*(8)* Yield [%] calc. from *(6)*	*(8)* Yield [%] calc. from *(4)*
a	H	H	H	C_6H_5	87	90	90	69
b	H	CH_3	H	C_6H_5	90	88	97	78
c	H	CH_3	$-(CH_2)_5-$		94	93	87	76
d	H	CH_3	$-(CH_3)_2C-(CH_2)_3-C(CH_3)_2-$		82	82	83	56
e	H	CH_3	C_6H_5	$CH_2C_6H_5$	88	73	98	63(60) [a, b]
f	H	nC_6H_{13}	$-(CH_2)_5-$		60	90	72	39
g	CH_3	CH_3	H	C_6H_5	88	92	80	65(90) [a]
h	CH_3	CH_3	C_6H_5	$CH_2C_6H_5$				(84) [a]
i	CH_3	CH_3	$-(CH_2)_2-CHC(CH_3)_3-(CH_2)_2-$					(60) [a]
j	CH_3	C_2H_5	H	C_6H_5	81	90	90	66(55) [a, b]
k	CH_3	C_2H_5	$-(CH_2)_5-$		60	100	86	52
l	CH_3	C_2H_5	H	nC_6H_{13}	82	90	66	49
m	$-(CH_2)_5-$		H	C_6H_5	85	67	93	53
n	$-(CH_2)_5-$		H	nC_6H_{13}	76			
o	$-(CH_2)_5-$		$-(CH_2)_5-$		41			

[a] Without purification of the intermediates *(5)* and *(6)*.
[b] With dimethyl sulfate as alkylating agent for *(5)*.

30 min. After hydrolysis, the product is extracted and dried. Solvent removal leads to the nearly pure epoxide which can be purified chromatographically (SiO_2 Merck, ether/pentane).

Received: May 2, 1975;
revised: June 9, 1975 [Z 275 IE]
German version: Angew. Chem. 87, 709 (1975)

CAS Registry numbers:
(2), $R^1=R^2=H$, 56051-03-7; *(2)*, $R^1=H$, $R^2=CH_3$, 56051-04-8; *(2)*, $R^1=H$, $R^2=nC_6H_{13}$, 56051-05-9; *(2)*, $R^1=R^2=CH_3$, 56051-06-0; *(2)*, $R_1=CH_3$, $R^2=C_2H_5$, 56051-07-1; *(2)*, $R^1R^2=-(CH_2)_5-$, 56051-08-2; *(5a)*, 56051-09-3; *(5b)*, 56051-10-6; *(5c)*, 56051-11-7; *(5d)*, 56051-12-8; *(5e)*, 56051-13-9; *(5f)*, 56051-14-0; *(5g)*, 56051-15-1; *(5j)*, 56051-16-2; *(5k)*, 56051-17-3; *(5l)*, 56051-18-4; *(5m)*, 56051-19-5; *(5n)*, 56051-20-8; *(5o)*, 56114-35-3; *(6a)*, 56144-90-2; *(6b)*, 56144-91-3; *(6c)*, 56144-92-4; *(6d)*, 56144-93-5; *(6e)*, 56144-94-6; *(6f)*, 56144-95-7; *(6g)*, 56144-96-8; *(6j)*, 56144-97-9; *(6l)*, 56144-99-1; *(6m)*, 56145-00-7; *(8a)*, 96-09-3; *(8b)*, 4436-22-0; *(8c)*, 17328-74-4; *(8d)*, 56051-21-9; *(8e)*, 56051-22-0; *(8f)*, 56051-23-1; *(8g)*, 10152-58-6; *(8h)*, 56051-24-2; *(8i)*, 56051-25-3; *(8j)*, 56051-26-4; *(8k)*, 37545-92-9; *(8l)*, 56051-27-5; *(8m)*, 53898-16-1; *(1)*, $R^1=R^2=H$, 500-00-0; *(1)*, $R^1=H$, $R^2=CH_3$, 75-07-0; *(1)*, $R^1=H$, $R^2=n$-C_6H_{13}, 66-25-1; *(1)*, $R^1=CH_3$, $R^2=CH_3$, 67-64-1; *(1)*, $R^1=CH_3$, $R^2=C_2H_5$, 78-93-3; *(1)*, $R^1R^2=-(CH_2)_5-$, 108-94-1; methaneselenol, 6486-05-1

[1] *W. Dumont* and *A. Krief*, Angew. Chem. *87*, 347 (1975); Angew. Chem. internat. Edit. *14*, 350 (1975).
[2] Methyl butyl selenide: b.p. 0 °C/1 torr. Dimethyl selenide: b.p. 58 °C/760 torr.
[3] *G. E. Coates*, J. Chem. Soc. *1953*, 2839.
[4] VPC, IR, NMR, mass spectra are identical with an authentic sample prepared from heptylidenetriphenylphosphorane and cyclohexanone.

Influence of the Distance of the Proline Carbonyl from the β and γ Carbon on the ^{13}C Chemical Shifts

By *Ignacy Z. Siemion*, *Theodor Wieland*, and *Karl-Heinz Pook*[*]

^{13}C-NMR spectroscopy can supply useful information about the *cis-trans* isomerism of the acyl residue (X) bound to nitrogen in proline-containing peptides, since the signals of the β-C and γ-C atoms are more separated in *cis*-XPro than in *trans*-XPro[1]. Information can also be obtained, of course, from the effect of the proline carbonyl orientation on the chemical shift of the β-C resonance[1].

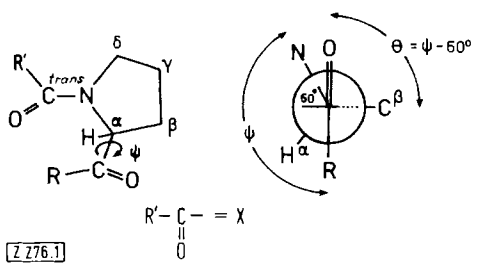


Fig. 1. Dihedral angle ψ and $\theta=(\psi-60°)=O{=}C{-}C^{\alpha}{-}C^{\beta}$ in proline peptides.

[*] Prof. Dr. I. Z. Siemion [+] (Alexander-von-Humboldt Fellow)
Chemisches Institut der Universität
Wroclaw (Poland)
Prof. Dr. Th. Wieland
Chemisches Institut für medizinische Forschung, Abteilung Naturstoff-Chemie
69 Heidelberg (Germany)
Dr. K.-H. Pook
Analytisches Laboratorium der Fa. C. H. Boehringer Sohn
6507 Ingelheim (Germany)
[+] Author to whom all correspondence should be addressed.

We have studied this "proximity effect" systematically by measuring the ^{13}C-NMR spectra of a few conformationally well-defined cyclic peptides of proline[2] including data already available in the literature. While the coplanar acyl-proline bond is usually *trans*, but in cyclic and polyproline peptides is also present in the *cis* conformation, no energy barriers exist for the geometry of the structural element $C^{\beta}{-}C^{\gamma}{-}C{=}O$, so that the distance between C=O and C-β described by the dihedral angle θ[3] (see Fig. 1) can be of varying size.

As shown in Figure 2 the chemical shift difference of the γ and β carbon resonances of proline, $\Delta\delta_{\gamma\beta}$, at least between 0 and *ca.* 100° is a linear function of the absolute value of θ.

There is a distinct difference between the slopes of the curves for the *cis*- and the *trans*-XPro peptides. Whether the linear relationship continues up to $\theta=180°$ will be tested on further rigid proline derivatives. The equations of the curves, calculated by the method of least squares, are:
for the *cis*-series: $\Delta\delta_{\beta\gamma}=0.081\,|\theta|+2.47$,
and
for the *trans*-series: $\Delta\delta_{\beta\gamma}=0.036\,|\theta|+0.73$

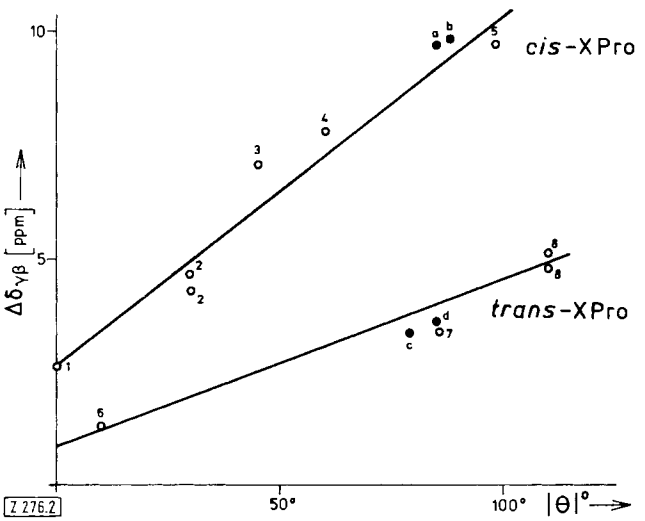


Fig. 2. Linear dependence of the difference in chemical shifts of the ^{13}C-NMR signals of β-C and γ-C of proline ($\Delta\delta_{\gamma\beta}$) with dihedral angle $\theta=(\psi-60°)$. For explanation see text.

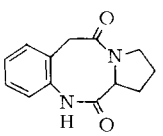
The θ-values in the compounds *(1)* to *(4)* were measured on Dreiding models constructed with the aid of data from the literature[4, 5]. The values for polyproline I *(5)*[6], polyproline II *(7)*[7], cyclo(Gly-L-Pro)$_3$ *(6)*[8] and gramicidin S-A *(8)*[9] were calculated from published data. The points a, b, c, and d in Figure 2 refer to ^{13}C-NMR values measured on antamanide-Na^+ in CD_3OD and are in good agreement with *Patel*'s[10] measurements in CD_3CN. Of the previously unassigned signals for the γ-C atoms of the four proline rings it could be concluded that the two occurring at high field (23.39 and 23.91 ppm) are due to the Pro-8 and Pro-3 moieties, since, according to X-ray structure analysis[11], these are *cis*-XPro residues in which the γ-C signals occur at higher field than in *trans*-XPro (see Refs. [1, 12]). Accordingly, the resonances at 25.87 and 26.29 ppm must be due to the two *trans* moieties Pro-7 and Pro-2. Of the four β-C signals at 29.46, 29.64, 33.10, and 33.74 those at higher field correspond to the *trans*-XPro moieties Pro-7 and Pro-2, the lower ones to Pro-3 and Pro-8. The $\Delta\delta_{\beta\gamma}$-values of the four proline residues are listed in Table 1 together with the θ-values measured by X-ray structure analysis on the antamanide Li^+-complex[13].

Table 1. Chemical shifts δ of the ^{13}C-NMR signals (in ppm, rel. to TMS) of the β- and γ-carbons of proline and the dihedral angle θ of a few conformationally defined peptides of proline. a—d see text.

No.	Compound	Solvent	δC^{β}	δC^{γ}	$\Delta\delta_{\gamma\beta}$	θ [°]
					cis-Series	
(1)	cyclo-Anthranoyl-L-prolyl [a]	CD_3OD/D_6-DMSO (1:1)	26.78	24.15	2.63	0
(2)	cyclo-L-Prolyl-L-prolyl	CD_3OD D_6-DMSO (1:1)	28.39	23.86	4.53	− 30
		D_2O			4.61	
		DMSO [1]			4.30	
(3)	cyclo-Tri-L-prolyl	CD_3OD/D_6-DMSO (1:1)	29.70	22.65	7.05	ca. 45
(4)	cyclo-L-Prolyl-D-prolyl	CD_3OD/D_6-DMSO (1:1)	30.11	22.32	7.79	− 60 (L-Pro-)
(5)	Polyproline I	H_2O [1]			9.70	98
	Antamanide-Na^+					
	a Pro-8	CD_3OD	33.10	23.39	9.71	85 [11]
	b Pro-3	CD_3OD	33.74	23.91	9.83	88 [11]
					trans-Series	
	c Pro-2	CD_3OD	29.64	26.29	3.35	79 [11]
	d Pro-7	CD_3OD	29.46	25.87	3.59	85 [11]
(6)	cyclo-(Gly-L-Pro)$_3$	$CD_3CN/CDCl_3$ [8] (1:1)			1.30	10
(7)	Polyproline II	H_2O [1]			3.30	86
(8)	Gramicidin S-A	DMSO [9]			5.10	− 100
		CH_3OH [9]			4.80	
					cis-Series	
(9)	cyclo-Homoanthranoylprolyl	CD_3OD/DMSO (1:1)	31.41	23.16	8.25	75–80

[a] New compound; m.p. 209—211 °C; $C_{12}H_{12}N_2O_2$ (216.23), obs. $m/e = 216$ (M^+).

We have used the above observed relationship for determining the conformation of the previously undescribed cyclohomoanthranoyl-L-prolyl *(9)* (m.p. 260—261 °C; $C_{13}H_{14}N_2O_2$ (230.25), observed $m/e = 230$ (M^+)). Compound *(9)* can be constructed with the aid of Dreiding models in two stable conformations, one with $\theta = 30°$, the other with θ between



(9)

70 and 100°. We found $\Delta\delta_{\gamma\beta} = 8.25$ and therefore, using the plot for *cis*-XPro in Figure 2, we assign a value of $\theta = 75$—80° to the cyclic peptide *(9)*.

Received: July 16, 1975 [Z 276 IE]
German version: Angew. Chem. 87, 712 (1975)

CAS Registry numbers
(1), 18877-34-4; *(2)*, 19943-27-2; *(3)*, 2277-82-9; *(4)*, 53990-72-0; *(5)*, 25191-13-3; *(6)*, 56144-84-4; *(7)*, 25213-33-6; *(8)*, 113-73-5; *(9)*, 56144-85-5; antamanide-Na^+, 34344-26-8

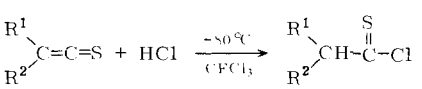
[1] See *e.g. D. E. Dorman* and *F. A. Bovey*, J. Org. Chem. *38*, 2379 (1973), and literature cited therein.
[2] The measurements were carried out by *W. Pryss* in Dr. *K.-H. Pook*'s laboratory. We wish to thank him for his excellent work.
[3] For a definition of the spatial parameters of the peptide chain see the IUPAC-IUP Recommendation in Biochemistry 9, 3471 (1970).
[4] *I. Z. Siemion*, Liebigs Ann. Chem. *748*, 88 (1971).
[5] *Ch. M. Deber, D. A. Torchia*, and *E. R. Blout*, J. Am. Chem. Soc. *93*, 4893 (1971).
[6] *W. Traub* and *U. Shmueli*, Nature *198*, 1165 (1963).
[7] *P. M. Cowan* and *S. McGavin*, Nature *176*, 561 (1953).
[8] *V. Madison, M. Atreyi, C. M. Deber*, and *E. R. Blout*, J. Am. Chem. Soc. 96, 6725 (1974).
[9] *W. A. Gibbons, J. A. Sogn, A. Stern, L. C. Craig*, and *L. F. Johnson*, Nature *227*, 840 (1970).
[10] *D. J. Patel*, Biochemistry *12*, 667 (1973).
[11] *I. L. Karle*, J. Am. Chem. Soc. *96*, 4000 (1974).
[12] *G. R. Bedford* and *P. J. Sadler*, Biochim. Biophys. Acta *343*, 656 (1974).
[13] The values obtained on X-ray structure analysis of the Na^+-complex are in complete agreement with those obtained with the Li^+-complex.

Aliphatic Thioacyl Chlorides. Preparation and Properties

By *Günther Seybold*[*]

Thioacyl halides *(2)* are of great importance in preparative organic chemistry as thioacylating agents. While the aromatic compounds have been described in numerous publications, all previous attempts to synthesize the aliphatic representatives of type R—CS—Cl have so far failed. Only a few perfluorinated compounds have been prepared[1].

We have found that addition of hydrogen chloride to the, now, readily accessible thioketenes[2] provides a simple and direct route to this class of compounds.

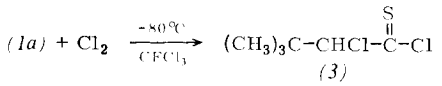


(1a)–(1c) *(2a)–(2c)*

(a), $R^1 = C(CH_3)_3$, $R^2 = H$; *(b)*, $R^1 = C_6H_5$, $R^2 = CH_3$; *(c)*, $R^1 = R^2 = CH_3$

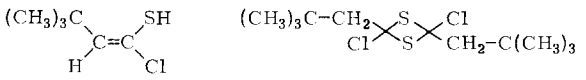
When hydrogen chloride is passed into solutions of the thioketenes *(1a)–(1c)* at −80 °C the violet thioketene color disappears within a few seconds and yellow to orange-red solutions of the thioacyl chlorides *(2a)–(2c)* are formed. *(1a)* also adds chlorine under the same conditions with quantitative formation of the 2-chloro-3,3-dimethylthiobutyryl chloride *(3)*.

[*] Dr. G. Seybold
Institut für Organische Chemie der Universität
8 München 2, Karlstr. 23 (Germany)
Present address:
BASF AG, Farbenforschung
6700 Ludwigshafen (Germany)



Compounds *(2a)*–*(2c)* and *(3)* have strong thioacylating properties similarly to the corresponding thioketenes, but they are thermally much more stable. However, *(2b)*, *(2c)*, and *(3)* can be handled only in solution; on attempting to isolate them in substance they undergo decomposition. 3,3-Dimethylthiobutyryl chloride *(2a)*, on the other hand, can be obtained analytically pure in yields of >90% by distillation. It is an orange-red, pungent oil, which can be stored indefinitely at −40 °C but slowly decomposes at room temperature. The structure of *(2a)* follows from elemental analysis and from its physical properties.

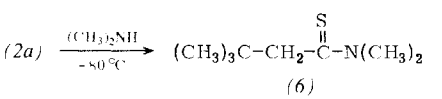
The ^{1}H-NMR spectrum of *(2a)* (in $CFCl_3$) shows two singlets at δ = 1.12 (9H) and δ = 3.17 (2H). Thus, a possible tautomeric form *(4)* can be ruled out. In the IR spectrum (2960, 1470,

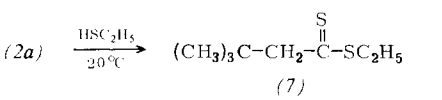


(4) *(5)*

1365, 1230, 1215, 940, 920, 850 cm^{-1}) the intense double band at 1215/1230 cm^{-1} can be assigned to the CS stretching vibration[3]. The mass spectroscopic fragmentation of *(2a)* resembles that of a carbonyl chloride. No molecular ion is observed even at an ionization energie of 20 eV; the most intense peak occurs at $m/e = 115 \triangleq M^+ - Cl$. The UV spectrum (in cyclohexane), λ_{max} (log ε): 480 (1.08), 304 (2.24), 257 (3.74), 207 (4.10), agrees remarkably well with that previously predicted for thioacetyl chloride[4]. The ^{13}C-NMR spectrum contains signals (in ppm rel. to TMS) for *C*S at 215.0, for CH_2 at 69.9, for *C* at 33.3, and for CH_3 at 29.6[5]. It can therefore be ruled out that *(2a)* is present as the symmetrical dithietane *(5)* since the ring carbon atoms in dithietanes exhibit relatively small chemical shifts (*e.g.* 74 ppm rel. to TMS in tetrachlorodithietane[5]).

The chemical properties of *(2a)* are also in agreement with the above structural assignment.

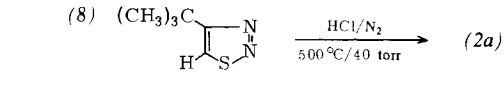




Even at −80 °C it reacts spontaneously and quantitatively with dimethylamine to give the thioamide *(6)*. On reaction with ethanethiol at room temperature it affords the dithioester *(7)* in 73% yield[6]. *(2b)*, *(2c)*, and *(3)* behave similarly. On prolonged standing at room temperature *(2a)*–*(2c)* and *(3)* polymerize with concomitant elimination of hydrogen chloride to give undefined resinous products.

The synthesis of *(2a)* can also be accomplished, albeit in lower yields, under conditions in which *(1a)* occurs only as intermediate: when the thiadiazole *(8)* is pyrolyzed at 500 °C/40 torr in a stream of hydrogen chloride/nitrogen, *(2a)* is obtained in yields of 40–50%. A simple apparatus can be used for the pyrolysis, as is usually employed for carrying out ester pyrolyses.

The preparatively most simple route to *(2a)* is the reaction of potassium 3,3-dimethyl-1-butynethiolate *(9)* with hydrogen



chloride. Compound *(9)* is readily accessible by reaction of *(8)* with potassium ethoxide in dioxane[7].

3,3-Dimethylthiobutyryl chloride (2a)

A stream of dry hydrogen chloride is passed through a vigorously stirred suspension of well-dried and finely powdered *(9)* (1.0 g) in *n*-pentane (80 ml) at −80 °C. The temperature of the mixture is allowed to increase to −10 °C over a period of four hours; after decantation and subsequent removal of solvent in vacuum, distillation of the residue at room temperature and 10^{-3} torr in a water-cooled condenser affords *(2a)* as an orange-red oil, $n_D^{23} = 1.5130$ (yield: 0.49 g ≙ 49%).

Received: June 23, 1975 [Z 278 IE]
German version: Angew. Chem. 87, 710 (1975)

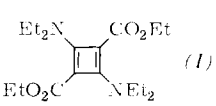
CAS Registry numbers:
(1a), 54191-76-3; *(1b)*, 54191-77-4; *(1c)*, 44158-23-8; 56008-74-3; *(2b)*, 56008-75-4; *(2c)*, 56008-76-5; *(3)*, 56008-77-6; *(6)*, 54191-81-0; *(7)*, 13831-14-6; *(8)*, 40753-16-0; *(9)*, 56008-78-7

[1] *K. T. Potts* and *C. Sapino* in *S. Patai:* The Chemistry of Acylhalides. Interscience, London 1972, p. 349.
[2] *G. Seybold*, Tetrahedron Lett. *1974*, 555; *G. Seybold* and *Ch. Heibl*, Angew. Chem. *87*, 171 (1975); Angew. Chem. internat. Edit. *14*, 248 (1975).
[3] *R. Mayer* and *S. Scheithauer*, J. Prakt. Chem. [4] *21*, 214 (1963).
[4] *J. Fabian*, *H. Fiola*, and *R. Mayer*, Tetrahedron *23*, 4323 (1967).
[5] We thank Dr. *J. Firl* for recording the ^{13}C-NMR spectra.
[6] The structure of the reaction products was confirmed by elemental analysis and comparison with authentic samples.
[7] *A. Shafiee* and *I. Lalezari*, J. Heterocycl. Chem. *10*, 11 (1973).

New Stable Cyclobutadienes

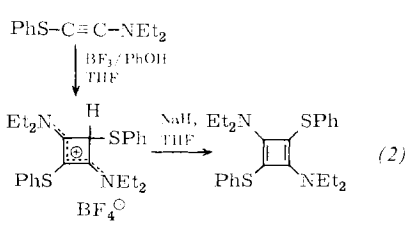
By *Rudolf Gompper*, *Siegfried Mensch*, and *Günther Seybold*[*]

The unusual properties of the cyclobutadiene derivative *(1)*[1] (dimerization only above 120 °C, almost square ring[1b])



(1)

induced us to look for other combinations of substituents that would lead to stabilization of the antiaromatic four-membered ring and might give information about the nature of the stabilizing effect.



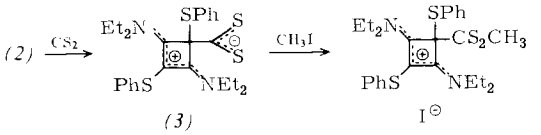
(2)

We were able to synthesize the cyclobutadiene derivative *N,N,N',N'*-tetraethyl-2,4-bis(phenylthio)cyclobutadiene-1,3-diamine *(2)* [orange crystals; IR (CCl_4): 1635, 1580, 1475,

[*] Prof. Dr. R. Gompper, Dr. S. Mensch, and Dr. G. Seybold
Institut für Organische Chemie der Universität
8 München 2, Karlstrasse 23 (Germany)

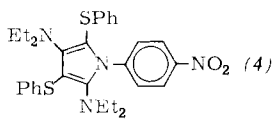
[**] Estimated from the 65 to 75% yield of recrystallized product of reaction of *(6)* with methyl iodide.

1438, 1375, 1278 cm^{-1}; UV (THF): 370, 301 nm]. This remains unchanged for more than 48 h in the solid state at room temperature. At 60 °C it decomposes with darkening, but dimerization, as for *(1)*, could not be observed. The reactions of *(2)* with HX, methyl iodide, bromine or acetylenedicarboxylic esters correspond to those of *(1)*[1a].



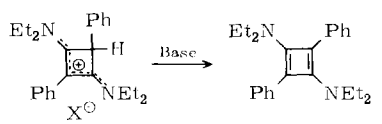
(3) $I^{\ominus}$

New observations are the formation of *(3)* from *(2)* and carbon disulfide as well as the production of the pyrrole *(4)* from *(2)* and *p*-nitrophenyl azide. Apparently *(2)*, unlike *(1)* can also react in accord with a 1,3-dipolar cycloaddition.



(4)

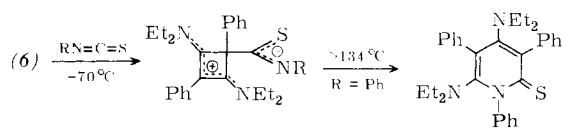
Although *(2)* can be fitted at least formally into the donor-acceptor scheme[1], this interpretation is inapplicable to *(6)*. Deprotonation of the cyanine salt *(5)*[2] can be effected by NaH in dioxane or THF, by $NaNH_2$ in THF, by KH in THF or by Li diisopropylamide/tetramethylethylenediamine in THF. By the last method *(6)* can be isolated as a light brown crystalline substance containing as impurity maximally 30 %[**] of the complex of Li perchlorate and tetramethylethylenediamine [the other methods afford solutions of *(6)*]. *(6)* is stable for at least 1 h in the solid state at room temperature.



(5) *(6)*

X = Cl, BF_4, ClO_4

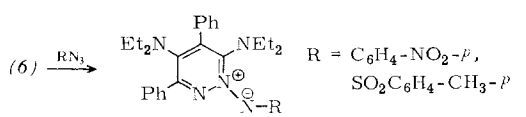
The reactions of *(6)* with methyl iodide, acetylenedicarboxylic esters, propiolic esters and water correspond to those of *(1)* and *(2)*. Zwitterionic products *(7)* are formed from *(6)* and isothiocyanates; when heated, *(7a)* is transformed into



(7a), R = Ph
(7b), R = SO_2Ph

(8)

the thiopyridone *(8)*. The action of *p*-nitrophenyl or *p*-toluenesulfonyl azide on *(6)* affords 1:1 adducts which are probably the pyridazine-*N*-imides *(9)* rather than the triazepines[3].



(9)

Received: June 30, 1975 [Z 281 IE]
German version: Angew. Chem. 87, 711 (1975)

CAS Registry numbers:
(2), 56008-79-8; *(3)*, 56008-80-1; *(4)*, 56008-81-2; *(5)* (X = ClO_4), 56008-82-3; *(5)* (X = Cl), 56008-83-4; *(5)* (X = BF_4), 15005-77-3; *(6)*, 56008-84-5; *(7a)*, 56008-85-6; *(7b)*, 56008-86-7; *(8)*, 56008-87-8; *(9)* (R = $SO_2C_6H_4$—CH_3—*p*), 56008-88-9; *(9)* (R = C_6H_4—NO_2—*p*), 56008-89-0

[1] a) *R. Gompper* and *G. Seybold* in *E. D. Bergmann* and *B. Pullmann*: Aromaticity, Pseudo-Aromaticity, Anti-Aromaticity. Israel Academy of Sciences and Humanities, Jerusalem 1971, p. 215; b) *R. Gompper, J. Kroner, G. Seybold*, and *H.-U. Wagner*, Tetrahedron, in the press.
[2] a) *J. Ficini* and *C. Barbara*, Tetrahedron Lett. *1966*, 6425; b) *L. Ghosez, B. Haveaux*, and *H. G. Viehe*, Angew. Chem. *81*, 468 (1969); Angew. Chem. internat. Edit. *8*, 454 (1969).
[3] Cf. *C. W. Rees, S. F. Gair*, and *R. C. Storr*, Chem. Commun. *1971*, 1545; *C. W. Rees, S. F. Gait, M. J. Rance*, and *R. C. Storr*, J. C. S. Chem. Comm. *1972*, 688. We thank Prof. *Rees* for valuable advice.

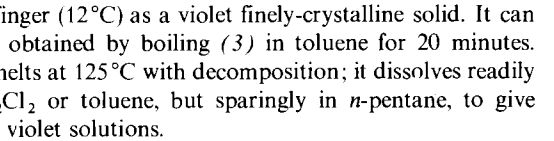
$C_6H_5P[Mn(CO)_2C_5H_5]_2$: A Phosphinidene Complex with Trigonal Planar Coordinated Phosphorus(I)[**]

By *Gottfried Huttner, Hans-Dieter Müller, Albin Frank*, and *Hans Lorenz*[*]

We recently reported on the synthesis and structure of the arsinidene complex $C_6H_5As[Cr(CO)_5]_2$ *(1)*[1], in which phenylarsanediyl, C_6H_5As, is stabilized as a bridging ligand with trigonal planar coordinated arsenic(I).

While the occurrence of phenylarsinidenes was first established by the detection of *(1)*, the occurrence of phosphinidene intermediates was demonstrated—especially by *U. Schmidt*'s[2] work—by means of trapping reactions. We have now found that phenylphosphinidene, C_6H_5P, can, like phenylarsinidene, also be stabilized as a ligand in transition metal complexes.

The phosphinidene complex *(4)* is formed in the thermolysis of tris(cyclopentadienyldicarbonylmanganese)triphenylcyclotriphosphane *(3)*, which is obtained by delithiation of cyclopentadienyldicarbonylmanganesedilithiophenylphosphane *(2)*[3].



(2) *(3)* *(4)*

On warming *(3)* to 110 °C at 10^{-2} torr *(4)* collects at a cool finger (12 °C) as a violet finely-crystalline solid. It can also be obtained by boiling *(3)* in toluene for 20 minutes.

(4) melts at 125 °C with decomposition; it dissolves readily in CH_2Cl_2 or toluene, but sparingly in *n*-pentane, to give reddish violet solutions.

Its ^{1}H-NMR spectrum shows two signals in the intensity ratio 1:2, which are assigned to the phenyl- and the cyclopentadienylprotons [$\delta(C_6H_5) = 6.9$, $\delta(C_5H_5) = 4.15$ ppm, internal TMS].

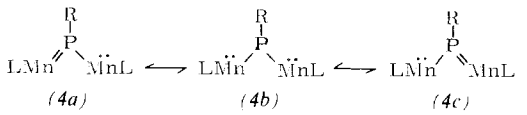
In the IR spectrum of *(4)* six bands are observed for the CO stretching vibrations [1992 (s), 1972 (s), 1938 (vs), 1912 (vs), 1883 (s) cm^{-1} in toluene]. From the number of bands it can be concluded that rotameric forms are present; the band positions would indicate that the phosphinidene ligand has good electron-acceptor properties.

[*] Doz. Dr. G. Huttner, Dipl.-Chem. H.-D. Müller, Dipl.-Chem. A. Frank, and Dr. H. Lorenz
Anorganisch-chemisches Laboratorium der Technischen Universität
8 München 2, Arcisstr. 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Leibniz Rechenzentrum der Bayerischen Akademie der Wissenschaften.

The mass spectrum of *(4)* shows the molecular ion at $m/e = 460$ and peaks for the $(M-2CO)$ and $(M-4CO)$ fragments. Additional signals are observed for the $C_5H_5(CO)_2MnP(C_6H_5)^+$, $C_5H_5MnP(C_6H_5)^+$, and $P(C_6H_5)^+$ ions.

The electronic spectrum of *(4)* shows an intense absorption at 19600 cm^{-1} ($\varepsilon = 7000$ l mol^{-1} cm^{-1}), which does not occur in complexes of the type $C_5H_5(CO)_2MnL$ (L = phosphane, amine). As in the case of the arsinidene complex *(1)*[4], we ascribe this band to an electronic transition in the three-center, four π-electron system *(4a)* to *(4c)*.



(4a) *(4b)* *(4c)*

L = $C_5H_5(CO)_2$; R = C_6H_5

The formulas indicate that four electrons from filled manganese d-orbitals are used to complete the octet of the sextet ligand $C_6H_5-\ddot{P}:$.

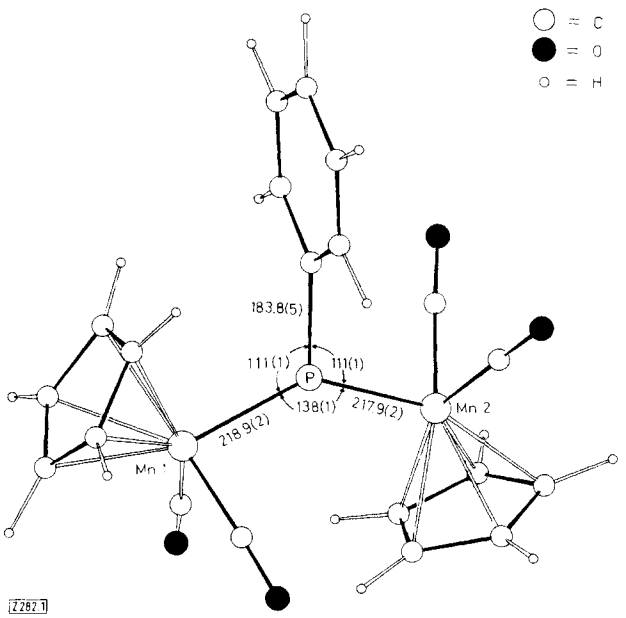


Fig. 1. Structure of $C_6H_5P[Mn(CO)_2C_5H_5]_2$.

In full agreement with this the X-ray structure analysis of *(4)* (Fig. 1)[5] shows that the phosphorus atom lies in a plane with its three substituent atoms (Mn, Mn, and C_{phenyl}) and that the Mn—P bond lengths are unusually short. They have a length of 218.4 ± 0.2 pm, whereas Mn—P bond lengths in the range 226 to 240 pm are observed in manganese-phosphane complexes[6].

The phosphinidene complex *(2)* is thus the first compound in which phosphorus(I) has a trigonal planar coordination and is stabilized by metal-dπ-phosphorus-pπ bonds.

Received: June 13, 1975 [Z 282 IE]
German version: Angew. Chem. 87, 714 (1975)

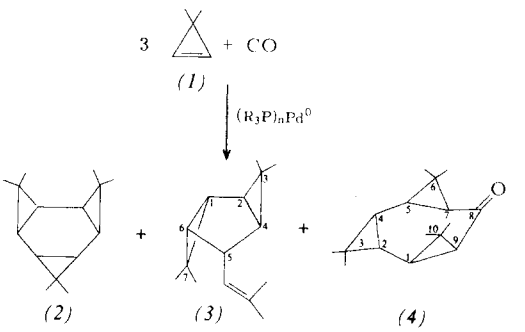
CAS Registry numbers:
(2), 55758-70-8; *(3)*, 55758-71-9; *(4)*, 56348-60-8

[1] *G. Huttner* and *H.-G. Schmid*, Angew. Chem. *87*, 454 (1975); Angew. Chem. internat. Edit. *14*, 433 (1975).
[2] *A. Ecker* and *U. Schmidt*, Chem. Ber. *106*, 1453 (1973); and literature cited therein.
[3] *G. Huttner, H.-D. Müller, A. Frank*, and *H. Lorenz*, Angew. Chem. *87*, 597 (1975); Angew. Chem. internat. Edit. *14*, 572 (1975).
[4] *G. Huttner, J. von Seyerl, M. Marsili*, and *H.-G. Schmid*, Angew. Chem. *87*, 455 (1975); Angew. Chem. internat. Edit. *14*, 434 (1975).
[5] $R = 0.05$; measurements: Syntex-$P2_1$; solution: Syntex-XTL.
[6] *W. K. Dean, G. L. Simon, P. M. Treichel*, and *L. F. Dahl*, J. Organometal. Chem. *50*, 193 (1973); and literature cited therein.

Hexamethyl-tris-σ-homotropone from 3,3-Dimethylcyclopropene and Carbon Monoxide

By *Paul Binger* and *Ulf Schuchardt*[*]

3,3-Dimethylcyclopropene *(1)* can be converted quantitatively on phosphane-modified palladium(0) catalysts into hexamethyl-tris-*trans*-σ-homobenzene *(2)*[1, 2]. On the same catalysts hexamethyl-tris-σ-homotropone *(4)*[3] can be prepared from *(1)* and carbon monoxide in yields of up to 90%. The homooligomers of *(1)*, compounds *(2)* and *(3)*[4], are the only other products formed.



The yield of *(4)* depends on the CO concentration as well as on the temperature and reaction time (cf. Table 1). High CO concentration and low temperatures favor formation of *(4)*.

Table 1. Dependence of the yield of *(4)* on CO concentration and reaction conditions. In each experiment 8 g (0.12 mol) of *(1)* was allowed to react.

Catalyst	CO-pressure [atm]	T [°C]	t [h]	Yield [%] *(2)*	*(3)*	*(4)*
A [a]	1	30	3	75	5	20
B [b]	70	30	20	7	4	89
B [b]	70	60	3	63	20	17

[a] 1 mmol $Pd(acac)_2$/1 mmol $P[CH(CH_3)_2]_3$/2 mmol $(C_2H_5)_2AlOC_2H_5$ in 40 ml diethyl ether.
[b] 0.15 mmol $[(C_6H_5)_3P]_4Pd$ in 20 ml benzene.

The mixed oligomerization leading to *(4)* is, to the best of our knowledge, the first smooth synthesis of a cyclic ketone from alkene and CO using a transition metal compound as a catalyst.

Formation of the tricycloheptane derivative *(3)* from *(1)* can most probably be attributed to the influence of a Pd catalyst modified by CO ligands on which *(1)* is transformed into the 2,2-dimethylvinylcarbene (cf. Ref. [5]).

(3) and *(4)* were identified with the aid of spectroscopic data (IR, MS, ^{1}H-NMR). The ^{1}H-NMR spectrum of *(4)* confirms its *syn,anti,syn*-structure [$\tau = 8.68$ (d, 7-H, 9-H; $J = 9.5$ Hz), 9.59 (d, 1-H, 5-H; $J = 10$ Hz), 9.66 ppm (s, 2-H, 4-H; $J_{4,5}$ and $J_{1,2} \approx 0$)].

[*] Dr. P. Binger and Dr. U. Schuchardt
Max-Planck-Institut für Kohlenforschung
433 Mülheim-Ruhr, Kaiser-Wilhelm-Platz 1 (Germany)

Experimental:

Tetrakis(triphenylphosphane)palladium(0) (0.2 g, 0.17 mmol) and *(1)* (8 g, 0.12 mol) are dissolved in benzene (20 ml) in a 60 ml V4A steel autoclave and CO is added to a pressure of 71 atm at −78 °C. The autoclave is shaken for 20 h at 30 °C. After release of 3.5 Nl of excess CO the autoclave contains 23.4 g of a yellow solution. After removal of benzene fractional distillation yields 0.6 g of a mixture (b.p. 55—60 °C/0.1 torr) having the composition (GC): 10.1 % benzene; 25.5% *(3)*, 56.8% *(2)*; 2.6% *(4)*, and remainder 5.1% (2 peaks). Sublimation of the residue at 100 °C (bath temperature)/0.1 torr affords 4.3 g of 97.6 %-pure (GC) colorless *(4)* [rest (GC) 0.2 % *(3)* and 2 % *(2)*] and at 120 °C 2.5 g of 100 %-pure (GC) *(4)*, m.p. 98 °C. Total yield of *(4)*: 6.7 g (89 %).

Received: July 4, 1975 [Z 283 IE]
German version: Angew. Chem. 87, 715 (1975)

CAS Registry numbers:
(1), 3907-06-0; *(2)*, 56390-01-3; *(3)*, 56348-21-1; *(4)*, 56348-22-2; $[(C_6H_5)_3P]_4Pd$, 14221-01-3

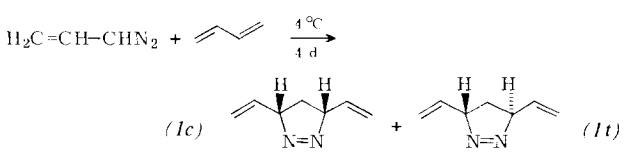
[1] *P. Binger, G. Schroth*, and *J. McMeeking*, Angew. Chem. *86*, 518 (1974); Angew. Chem. internat. Edit. *13*, 465 (1974).
[2] *P. Binger* and *U. Schuchardt*, unpublished.
[3] Systematic name: 3,3,6,6,10,10-Hexamethyl-*syn,anti,syn*-tetracyclo[7.1.0.0^{2,4}.0^{5,7}]decan-8-one.
[4] 3,3,7,7-Tetramethyl-5-(2-methyl-1-propenyl)-*trans*-tricyclo[4.1.0.0^{2,4}]heptane.
[5] *P. Binger* and *J. McMeeking*, Angew. Chem. *86*, 518 (1974); Angew. Chem. internat. Edit. *13*, 466 (1974).

Low Temperature Thermal and Photochemical Formation of Diallylic 1,3-Diradicals. Cope Rearrangement of *cis*-1,2-Divinylcyclopropane[**]

By *Manfred Schneider*[*]

The thermal and photochemical decomposition of 3-vinyl-substituted 1-pyrazolines leads to products which can be interpreted in terms of allylic 1,3-diradicals[1]. The decrease in decomposition temperature (by *ca.* 100 °C) and activation enthalpy (by 9 kcal/mol) on introduction of a vinyl group suggests substantial stabilization of an allylic 1,3-diradical.

1,3-Dipolar cycloaddition of 3-diazo-1-propene to 1,3-butadiene produces a 45 : 55 mixture of *cis*- and *trans*-3,5-divinyl-1-pyrazolines *(1c)* and *(1t)*, which decompose thermally around 0 °C[2, 3]. The sensitivity of *(1c)* has so far precluded



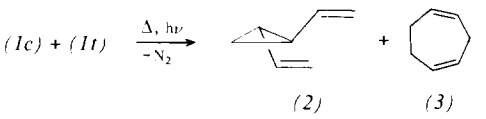
(1c) *(1t)*

separation of *(1c)* and *(1t)*, but pure *(1t)* can be obtained by partial decomposition of the mixture, since at 0 °C *(1c)* decomposes faster than *(1t)*[3]. The substantially lower decomposition temperature relative to monovinyl-substituted 1-pyrazolines indicates participation of both vinyl groups and suggests simultaneous cleavage of the two C—N bonds.

[*] Dr. M. Schneider
Institut für Chemie der Universität Hohenheim
7000 Stuttgart 70, Emil-Wolff-Strasse 14 (Germany)

[**] Presented in part at "Recent Developments in Physical Organic Chemistry" at Liège (Belgium) (March 1975) and the Chemiedozententagung 1975 at Düsseldorf (April 1975).
We thank Dr. *P. Fischer*, Universität Stuttgart, for assisting with NMR work, and the Deutsche Forschungsgemeinschaft for financial support.

The thermal and photochemical decomposition reactions of *(1c)* and *(1t)* yield *trans*-1,2-divinylcyclopropane *(2)* and 1,4-cycloheptadiene *(3)* (cf. Table 1).



(2) *(3)*

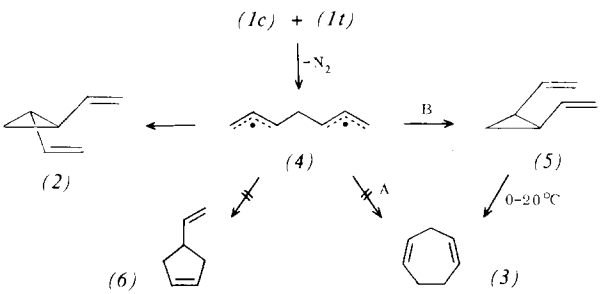
Table 1. Decomposition products of *(1c)* and *(1t)*.

	Yield [%] thermal (0—60 °C)		Yield [%] photochemical [a]		
	(2)	*(3)*	*(2)*	*(3)*	*(P)* [c]
(1c) [b]	38	62	42	56	0—2
(1t)	37	63	56	42	0—2

[a] *n*-Pentane, Pyrex filter, −5 °C.
[b] Calculated from the mixture and pure *(1t)*.
[c] Tentatively assigned as 1,3,5-heptatriene.

In contrast to 3,5-*dialkyl*-substituted 1-pyrazolines, both isomers *(1c)* and *(1t)* give similiar yields of *(2)* and *(3)*, suggesting, with support of recent kinetic evidence[3], the formation of a stabilized intermediate of extended lifetime *(4)*, which can undergo several rotations before ring closure occurs.

In order to test whether *(3)* is formed *via* path B from *cis*-1,2-divinylcyclopropane *(5)* or *via* path A from an isomer of *(4)* by direct ring closure, we have studied the low temperature photolysis of *(1c)* and *(1t)* ($CDCl_3$, Pyrex filter, −50 °C)[4]. The thermal reaction cannot serve this purpose.



(2) *(4)* *(5)* *(6)* *(3)*

Within the sensitivity of ^{1}H-NMR spectroscopy, low temperature photolysis is found to produce only *(2)* and *(5)*. Neither *(3)* nor 4-vinylcyclopentene *(6)* is observed; nor is *(6)* a product of the thermal reaction. This is reasonable since the direct formation of *(3)* and *(6)* from *(4)* would require rotations leading to the loss of resonance energy of up to 12—14 kcal/mol per allylic bond[5]. All *(3)* produced in the photochemical and probably also on the thermal decomposition of *(1c)* and *(1t)* is therefore formed *via* Cope rearrangement of initially produced *(5)*.

The low temperature photolysis of *(1c)* and *(1t)* has become a convenient source of *(5)*[6] and permits kinetic study of the Cope rearrangement *(5)* → *(3)* by integration of the NMR resonances of *(3)* at δ = 2.23 and 2.85 ppm (cf. Table 2).

Table 2. Kinetic data of the rearrangement *(5)* → *(3)*.

T [°C]	7.2	10.2	12.0	14.2	17.2	18.6
$10^4 k$ [s^{-1}]	4.3	6.1	6.8	9.0	13.5	14.5

$\Delta G^{+} = 20.7$ kcal/mol; $\Delta H^{+} = 17.8 \pm 2$ kcal/mol; $\Delta S^{+} = -8.5 \pm 4$ e.u.

The data are to be considered as tentative, since the conveniently observed temperature range is quite narrow, leading to uncertainties in ΔH^{+} and ΔS^{+}. The ΔG^{+} values thus

obtained can be compared with theoretical[7] (19 kcal/mol) and experimental[6] (20.6 kcal/mol) values. The stability of *(5)* is in agreement with other potential *cis*-1,2-divinylcyclopropanes[8].

Received: June 12, 1975 [Z 284 IE]
German version: Angew. Chem. *87*, 717 (1975)

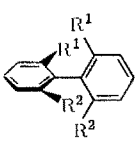
CAS Registry numbers:
(1c), 54050-87-2; *(1t)*, 54050-88-3; *(2)*, 22770-04-3; *(3)*, 7161-35-5; *(5)*, 2984-54-9

[1] *R. J. Crawford* and *D. M. Cameron*, Can. J. Chem. *45*, 691 (1967); *M. Schneider* and *I. Merz*, Tetrahedron Lett. *1974*, 1995; *M. Schneider*, *A. Erben*, and *I. Merz*, Chem. Ber. *108*, 1271 (1975).
[2] *M. Schneider* and *G. Mössinger*, Tetrahedron Lett. *1974*, 3081.
[3] *R. J. Crawford* and *M. Ohno*, Can. J. Chem. *52*, 3134 (1974).
[4] *M. Schneider* and *J. Rebell*, J. C. S. Chem. Commun. *1975*, 283.
[5] *W. v. E. Doering* and *G. H. Beasley*, Tetrahedron *29*, 2231 (1973); *W. R. Roth*, *G. Ruf*, and *P. W. Ford*, Chem. Ber. *107*, 48 (1974).
[6] Different preparation: *J. M. Brown*, *B. T. Golding*, and *J. J. Stofko*, J. C. S. Chem. Commun. *1973*, 319.
[7] *M. Simonetta*, *G. Farini*, and *P. Gramacciconi*, J. Am. Chem. Soc. *90*, 1280 (1968).
[8] Review: *H. M. Frey* and *R. Walsh*, Chem. Rev. *69*, 103 (1969); *T. J. Katz*, *J. J. Cheung*, and *N. Acton*, J. Am. Chem. Soc. *92*, 6641 (1970); *K. Hojo*, *R. T. Seidner*, and *S. Masamune*, *ibid.* *92*, 6643 (1970); *M. S. Baird* and *C. B. Reese*, Chem. Commun. *1970*, 1519; *W. Grimme* and *K. Seel*, Angew. Chem. *85*, 514 (1973); Angew. Chem. internat. Edit. *12*, 507 (1973).

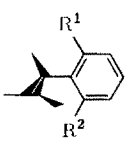
Enantiomerization of Optically Stable Substituted Butadienes[**]

By *Manfred Rösner* and *Gert Köbrich* (deceased)[*]

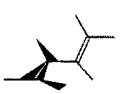
The chirality of non-planar butadienes was conceptually introduced in earlier papers[1]. Unlike the atropisomeric biphenyls *(1)* and styrene derivatives *(2)*, optically stable enantiomers of open-chain, chiral butadienes *(3)* were not hitherto observed.



(1)

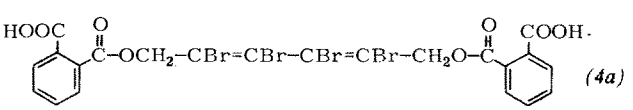


(2)



(3)

We have already reported the partial enantiomerization of tetrabromobutadienes *(4a)* and *(4b)* which at 25 °C have half-lives of 3 and 7.7 hours, respectively, and rotation barriers $\Delta G^{\ddagger}_{25} = 23.1 \pm 0.3$ and 23.7 ± 0.3 kcal mol^{-1}, respectively[2].



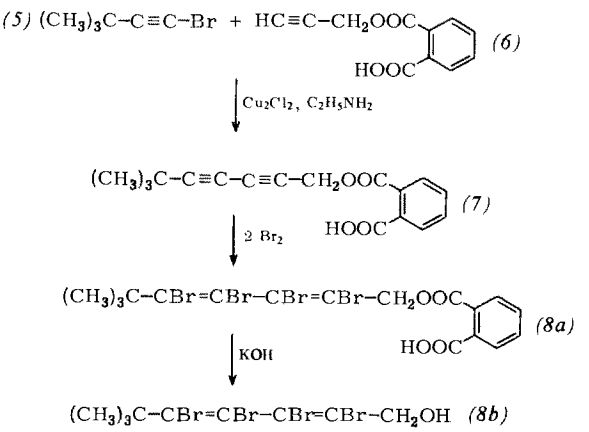
(4a)

$HOCH_2-CBr=CBr-CBr=CBr-CH_2OH$ *(4b)*

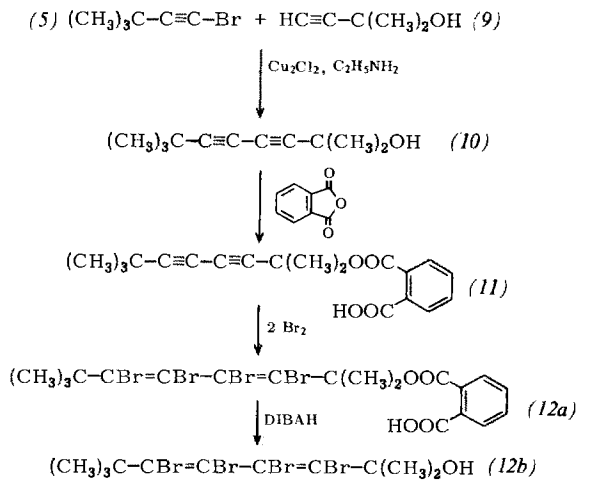
It is possible, by means of more bulky substituents, to raise the energy barrier to rotation about the central C—C single bond (*i.e.* for racemization). The extremely powerful buttressing effect, amounting to 8.3 kcal mol^{-1}, for the $C(CH_3)_2OH$ group in tetrachlorobutadienes was determined by NMR spectroscopy[3] and recently confirmed by partial resolution and by kinetic measurements[4].

We have now synthesized the *tert*-butyl- and $C(CH_3)_2OH$-substituted tetrabromobutadienes *(8a)*, *(8b)*, *(12a)*, and *(12b)*[5]. These are the first non-planar butadienes that could be resolved to optically stable atropisomers.

A Cadiot coupling reaction of 1-bromo-3,3-dimethyl-1-butyne *(5)*[6] with 2-propynyl hydrogen phthalate *(6)*[7] affords a 65% yield of 6,6-dimethyl-2,4-heptadiynyl hydrogen phthalate *(7)* (m.p. 110—112 °C, from CCl_4/light petroleum), which with bromine in CCl_4 at 50 °C gives 2,3,4,5-tetrabromo-6,6-dimethyl-2,4-heptadienyl hydrogen phthalate *(8a)* (yield 36%; m.p. 182—184 °C, from acetone/light petroleum)[8]. After hydrolysis of *(8a)* by KOH/ethanol, 2,3,4,5-tetrabromo-6,6-dimethyl-2,4-heptadien-1-ol *(8b)* is obtained in 30% yield by crystallization from light petroleum (m.p. 114—115 °C).



Cadiot coupling of *(5)* with 2-methyl-3-butyn-2-ol *(9)* leads to 2,7,7-trimethyl-3,5-octadiyn-2-ol *(10)* (yield 87%; m.p. 99—100 °C, from light petroleum) which on esterification by phthalic anhydride and triethylamine[9] gives a 60% yield of 1,1,6,6-tetramethyl-2,4-heptadiynyl hydrogen phthalate *(11)* (m.p. 125 °C, from ether/light petroleum). By reaction thereof with bromine in CCl_4 at 70—80 °C one obtains 2,3,4,5-tetrabromo-1,1,6,6-tetramethyl-2,4-heptadienyl hydrogen phthalate *(12a)* (yield 21%; m.p. 200—202 °C, from $CHCl_3$), whence reductive hydrolysis by diisobutylaluminum hydride (DIBAH) in ether at −20 °C gives 3,4,5,6-tetrabromo-2,7,7-trimethyl-3,5-octadien-2-ol *(12b)* in 30% yield (m.p. 59—60 °C, from light petroleum at −70 °C).



[*] Dr. M. Rösner and Prof. Dr. G. Köbrich (deceased)
Institut für Organische Chemie der Technischen Universität
3 Hannover, Schneiderberg 1 B (Germany)

[**] Part of the Dissertation by *M. Rösner*, Technische Universität, Hannover 1975.—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Chiral Butadienes, Part 7.—Part 6: [3].

For partial resolution the half-esters *(8a)* and *(12a)* are dissolved in boiling ether and then treated with a one-half-equivalent of (+)-α-methylbenzylamine. The dextrorotatory ammonium salts that crystallize are filtered off[10]; their optical rotations in methanol amount to $[\alpha]_D^{20} = +22.3°$ and +48.3°, respectively.

The optically active half-esters (+)-*(8a)* ($[\alpha]_D^{20} = +22.2°$) and (+)-*(12a)* ($[\alpha]_D^{20} = +53.9°$ (in acetone)) were liberated from these salts by 2 N H_2SO_4. Hydrolysis of these half-esters in the manner described above afforded the optically active tetrabromo alcohols (+)-*(8b)* ($[\alpha]_D^{20} = +14.4°$) and (+)-*(12b)* ($[\alpha]_D^{20} = 93.0°$ (in acetone)).

As previously found for the compounds *(4a)* and *(4b)*[2], the height of the energy barrier to rotation cannot be determined by NMR spectroscopy for *(8a)*, *(8b)*, *(12a)*, or *(12b)*; the peaks for the diastereotopic protons and methyl groups show no coalescence up to 140 °C, so that at most a minimum value of 22–23 kcal mol^{-1} can be given for the energy threshold. The barriers can also not be determined by polarimetry.

Solutions of the butadienes (+)-*(8a)*, (+)-*(8b)*, (+)-*(12a)*, and (+)-*(12b)* in DMSO proved stable: no reduction in the initial optical activity could be established after several days at room temperature or after 8 hours at 80 °C.

Received: July 10, 1975 [Z 286 IE]
German version: Angew. Chem. *87*, 715 (1975)

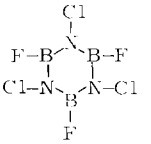
CAS Registry numbers:
(4a), 54445-67-9; *(4b)*, 54445-66-8; *(5)*, 13601-86-0; *(6)*, 6139-61-3; *(7)*, 56391-19-6; (±)-*(8a)*, 56404-32-1; (+)-*(8a)*, 56391-20-9; (+)-*(8a)* salt, 56420-99-6; (±)-*(8b)*, 56391-21-0; (+)-*(8b)*, 56391-22-1; *(9)*, 115-19-5; *(10)*, 56391-23-2; *(11)*, 56391-24-3; (±)-*(12a)*, 56391-25-4; (+)-*(12a)*, 56391-26-5; (+)-*(12a)* salt, 56421-00-2; (±)-*(12b)*, 56391-27-6; (+)-*(12b)*, 56391-28-7

[1] *G. Köbrich, A. Mannschreck, R. A. Misra, G. Rissmann, M. Rösner,* and *W. Zündorf,* Chem. Ber. *105*, 3794 (1972); *G. Köbrich, B. Kolb, A. Mannschreck,* and *R. A. Misra, ibid. 106*, 1601 (1973).
[2] *M. Rösner* and *G. Köbrich,* Angew. Chem. *86*, 775 (1974); Angew. Chem. internat. Edit. *13*, 741 (1974).
[3] *H.-O. Bödecker, V. Jonas, B. Kolb, A. Mannschreck,* and *G. Köbrich,* Chem. Ber. *108*, in press.
[4] *H.-O. Bödecker,* Dissertation, Technische Universität, Hannover 1975.
[5] The structures of all the new compounds were established by UV, IR, NMR, and mass spectra and by correct elemental analyses. The constitutional identity of the racemic and optically active substances was confirmed by spectral comparison.
[6] *L. Brandsma:* Preparative Acetylenic Chemistry. Elsevier, Amsterdam 1971, p. 98.
[7] *M. D. Cameron* and *G. E. Bennett,* J. Org. Chem. *22*, 557 (1957).
[8] We assume for this and the following compounds an ionic bromination mechanism and formation of (*E,E*)-tetrabromobutadienes.
[9] By analogy with directions of *A. G. Davies, J. Kenyon,* and *L. W. F. Salamé,* J. Chem. Soc. *1957*, 3148.
[10] The enantiomeric levorotatory salts can be obtained from the filtrate by working up and addition of (−)-α-methylbenzylamine.

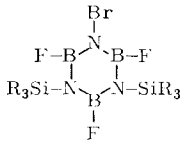
N-Haloborazines[**]

By *Gernot Elter, Heinz-Jürgen Külps,* and *Oskar Glemser*[*]

Boron trichloride reacts with *N*-chlorobis(trimethylsilyl)-amine *via* elimination of trimethylchlorosilane to form hexachloroborazine[1], the only *N*-halo derivative of borazine hitherto known[2]. While corresponding reactions of BCl_3 or BBr_3 with *N*-bromobis(trimethylsilyl)amine did not lead to the borazine system[1, 3], we have now been able to isolate two new *N*-haloborazines as products of the reaction of boron trifluoride with *N*-halosilylamines:



(1)



(2), R = CH_3

Simultaneous dropwise addition of equimolar quantities of $ClN(SiR_3)_2$ and $BF_3 \cdot O(C_2H_5)_2$ at −10 °C, removal of the volatile reaction products, and sublimation of the residue at 70 °C/50 torr affords 1,3,5-trichloro-2,4,6-trifluoroborazine *(1)* in 50% yield, m. p. 97 °C (after recrystallization from pentane).

$$3\ BF_3 \cdot O(C_2H_5)_2 + 3\ ClN(SiR_3)_2 \longrightarrow (1) + 6\ R_3SiF + 3\ (C_2H_5)_2O$$

During this reaction the nitrogen-halogen bond of the silylamine also undergoes some degree of cleavage since partially *N*-silylated borazines $B_3F_3N_3Cl_2SiR_3$ and $B_3F_3N_3Cl(SiR_3)_2$ could be detected as side products by mass spectrometry.

If gaseous BF_3 is passed at room temperature into a 25% solution of $BrN(SiR_3)_2$ in CCl_4 then analogous work-up of the reaction mixture (repeated sublimation at 50 °C/10^{-3} torr) affords 1-bromo-3,5-bis(trimethylsilyl)-2,4,6-trifluoroborazine *(2)* in 16% yield, m. p. 50 °C. No formation of an *N*-tribromo- or *N*-dibromo derivative was observed; only $B_3F_3N_3(SiR_3)_3$[4] could be isolated as side product.

(1) and *(2)* form colorless crystals which react vigorously with water; in the case of *(1)* hydrolysis proceeds with explosive violence. In the absence of moisture, however, the compounds can be stored indefinitely. Their compositions and structures are verified by elemental analysis, and mass, IR, Raman, and NMR (^{11}B, ^{19}F, ^1H) spectra. The IR gas phase spectrum of *(1)* shows the principal νBN band (1466 cm^{-1}) in the usual range for *B*-trifluoroborazines[5].

Received: July 4, 1975 [Z 287 IE]
German version: Angew. Chem. *87*, 741 (1975)

[1] *N. Wiberg, F. Raschig,* and *K. H. Schmid,* J. Organometal. Chem. *10*, 29 (1967).
[2] *P. I. Paetzold,* Z. Anorg. Allg. Chem. *326*, 47 (1963); *J. G. Haasnoot* and *W. L. Groeneveld,* Inorg. Nucl. Chem. Lett. *3*, 597 (1967).
[3] *R. E. Bailey* and *R. West,* J. Organometal. Chem. *4*, 430 (1965).
[4] *G. Elter, O. Glemser,* and *W. Herzog,* Chem. Ber. *105*, 115 (1972).
[5] *A. Meller,* Organometal. Chem. Rev. *2*, 1 (1967).

[*] Prof. Dr. O. Glemser, Dr. G. Elter, and Dipl.-Chem. H.-J. Külps
Anorganisch-chemisches Institut der Universität
34 Göttingen, Tammannstrasse 4 (Germany)

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

[2+2]-Cycloaddition of Allenes to Alkenes[**]

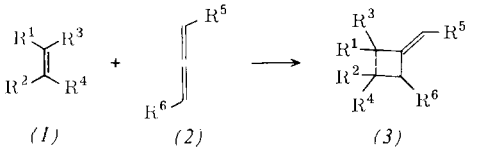
By *Joachim H. Lukas, Arjan P. Kouwenhoven,* and *Frank Baardman*[*]

The small number of [2+2]-cycloadditions which probably proceed *via* vinyl cations[1] include the cyclodimerization of 2-butyne with addition of Cl_2 to form 3,4-dichlorotetramethylcyclobutene[2], the cyclodimerization of 1-alkynes with addition of 2 mol of HCl to give 1,3-dichloro-1,3-dialkylcyclobutane[3], the cyclodimerization of allene with addition of 2 mol of HBr to yield 1,3-dibromo-1,3-dimethylcyclobutane[4], and the cyclodimerization of 2-butyne with $AlCl_3$ to give the tetramethylcyclobutadiene-aluminum chloride complex[5].

[*] Dr. J. H. Lukas, A. P. Kouwenhoven, and F. Baardman
Koninklijke/Shell-Laboratorium, Amsterdam (Shell Research B.V.)
Badhuisweg 3, Amsterdam (Netherlands)

[**] [2+2]-Cycloadditions, Part 1.

We have now found that [2+2]-cycloadditions of allenes *(2)* to alkenes *(1)*, giving methylenecyclobutanes *(3)*, are feasible in the presence of Lewis acids as catalysts. Examples are shown in Table 1.



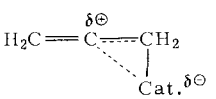
(1) *(2)* *(3)*

Table 1. Examples of the [2+2]-cycloaddition of allenes *(2)* to alkenes or cycloalkenes *(1)* to form methylenecyclobutanes *(3)*. All products were identified by elemental analysis, mass spectrometry, and ^{1}H- and ^{13}C-NMR spectra. Ethylene, propylene, cyclohexene, and 4,4-dimethyl-2-pentene did not react.

Cpd.	R^1	R^2	R^3	R^4	R^5	R^6	*t* [min]	Yield [%]
cis-(3a) [a]	CH_3	CH_3	H	H	H	H	15	40
trans-(3a) [b]	CH_3	CH_3	H	H	H	H	15	15
(3b)	C_2H_5	CH_3	H	H	H	H	15	45 / 45
(3c)	CH_3	C_2H_5	H	H	H	H		55
(3d)	CH_3	CH_3	CH_3	CH_3	H	H	10	>90
(3e)	$CH(CH_3)_2$	CH_3	CH_3	CH_3	H	H	<10	>90
(3f)	CH_3	$CH(CH_3)_2$	CH_3	CH_3	H	H		
(3g)	$-(CH_2)_3-$		H	H	H	H	15	50
(3h)	$-CH_2-CH=CH-CH_2-$		H	H	H	H	10	45
(3i)	CH_3	CH_3	H	H	H	CH_3	20	90
(3j)	CH_3	CH_3	H	H	CH_3	CH_3	15	5

[a] Prepared from *cis*-2-butene.
[b] Prepared from *trans*-2-butene.

The catalytic activity of the Lewis acids is probably due to complex formation with the allene which leads to polarization of one of its double bonds in the direction of a vinyl cation:



As may be seen from Table 1, this reaction provides a facile entry to methylenecyclobutanes. The factors limiting the choice of the alkene include:

1) A sufficient electron density at the double bond; 1-alkenes fail to react, the reaction rate increasing in the order 1,2-dialkyl- < 1,1,2-trialkyl- < 1,1,2,2-tetraalkylethylene (cyclohexene does not react!).

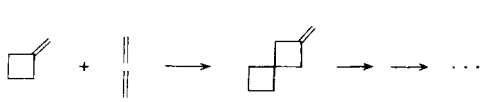
2) Steric hindrance; 4,4-dimethyl-2-pentene does not react.

3) The tendency of the alkene to undergo cationic polymerization.

Butadienes afforded only polymeric products. The most important competing reaction is polymerization of the olefin which finally leads to deactivation of the catalyst. While methylallene reacts in a manner comparable with allene, further alkyl substitution lowers the yields.

The following Lewis acids are suitable as catalysts: $C_2H_5AlCl_2$ (40); $GaCl_3$ (20), $AlBr_3$ (15), $AlCl_3$ (unknown), $FeCl_3$ (unknown). (The figures in parentheses are the numbers of conversions to methylenecyclobutane per catalyst molecule.)

Cycloadditions occurring as subsequent reactions lead to spiro compounds *(4)*.



(4)

1,1,2,2-Tetramethyl-3-methylenecyclobutane (3d)

The following compounds are consecutively dissolved in chlorobenzene under an inert gas at room temperature: 1) Allene to saturation (*ca.* 1 g/20 ml); 2) an equimolar amount of 2,3-dimethyl-2-butene; 3) ethylaluminum dichloride (usually 4 M in *n*-hexane) in a ratio of 1:50 relative to the alkene. During the slightly exothermic reaction the temperature is maintained below 40 °C. After 10 min the reaction solution is shaken with a little water to destroy the catalyst and decanted from the precipitate. The solution is dried over magnesium sulfate and *(3d)* isolated by fractional distillation; b. p. 118 °C, yield 90%.

Received: June 20, 1975 [Z 289 IE]
German version: Angew. Chem. 87, 740 (1975)

CAS Registry numbers:
cis-(1a), 590-18-1; *trans-(1a)*, 624-64-6; *(1b)*, 109-68-2; *(1d)*, 563-79-1; *(1e)*, 565-77-5; *(1g)*, 142-29-0; *(1h)*, 628-41-1; *(2)*, $R^5=R^6=H$, 463-49-0; *(2)*, $R^5=H$, $R^6=CH_3$, 590-19-2; *(2)*, $R^5=R^6=CH_3$, 59-96-8; *cis-(3a)*, 56391-07-2; *trans-(3a)*, 56391-08-3; *(3b)*, 54562-50-4; *(3c)*, 54562-51-5; *(3d)*, 54562-54-8; *(3e)*, 54562-57-1; *(3f)*, 54562-56-0; *(3g)*, 3642-22-6; *(3h)*, 36168-39-5; *(3i)*, 54562-53-7; *(3j)*, 56391-09-4

[1] *R. B. Woodward* and *R. Hoffmann*: The Conservation of Orbital Symmetry. Verlag Chemie, Weinheim 1970.
[2] *R. Criegee* and *A. Moschel*, Chem. Ber. 92, 2181 (1959).
[3] *K. Griesbaum* and *M. El-Abed*, Chem. Ber. 106, 2001 (1973).
[4] *K. Griesbaum*, J. Am. Chem. Soc. 86, 2301 (1964).
[5] *J. B. Koster*, *G. J. Timmermans*, and *H. van Bekkum*, Synthesis 1972, 139.

4-Hydroxyarsabenzene—An "Arsaphenol"

By *Gottfried Märkl*, *Horst Baier*, and *Siegfried Heinrich*[*]

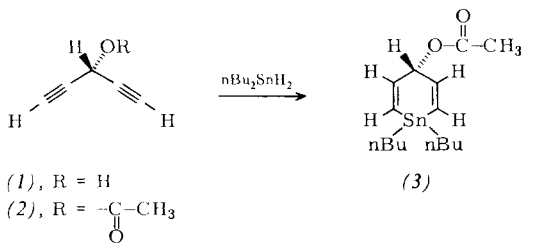
Unlike the situation in classical aromatic chemistry, introduction of functional groups into the phosphabenzene and arsabenzene ring systems has so far been unsuccessful, whether attempted by electrophilic or by nucleophilic substitution. The synthesis of arsabenzenes having functional groups (OR,

[*] Prof. Dr. G. Märkl, Dr. H. Baier, and S. Heinrich
Fachbereich Chemie und Pharmazie der Universität
84 Regensburg, Universitätsstrasse 31 (Germany)

[**] Elution with benzene affords di-*n*-butyltin dichloride, and elution with chloroform gives a mixture of *(4)* and *(5)*, and finally pure *(4)* [*(4b)*?].

$CH(OR)_2$, CHO, COOR) in position 4 can however be accomplished by Sn/As exchange reactions of suitably substituted 1,4-dihydrostannabenzenes[1].

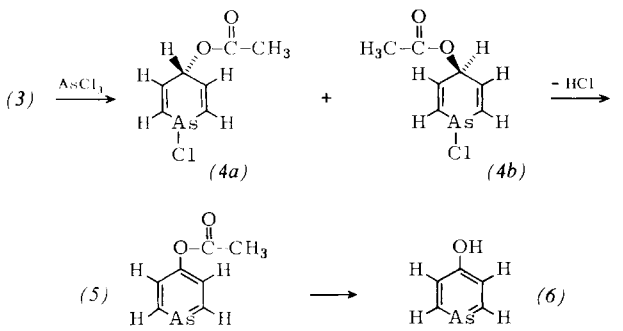
We now report the first preparation of 4-hydroxyarsabenzene *(6)* from 4-acetoxy-1,1-di-*n*-butyl-1,4-dihydrostannabenzene *(3)*. 1,4-Pentadiyn-3-ol *(1)*[2], accessible from ethynylmagnesium bromide and ethyl formate, is cleanly acetylated to 1-ethynyl-2-propynyl acetate (3-acetoxy-1,4-pentadiyne) *(2)* by acetic anhydride in ether over powdered potassium hydroxide[3].



(1), R = H
(2), R = $-C(=O)-CH_3$

(3)

(2), b.p. 57 °C/14 torr, yield 82%, undergoes a vigorous cycloaddition reaction with di-*n*-butyltin dihydride in boiling anhydrous methylcyclohexane in the presence of azoisobutyronitrile to give the 1,4-dihydrostannabenzene derivative *(3)*. Compound *(3)* is a pale yellow oil of b.p. 140 °C/0.01 torr (in bulb tube); yield 40—50%.



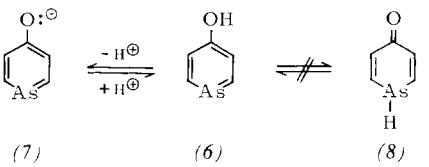
(4a) *(4b)*

(5) *(6)*

The Sn/As exchange reaction of *(3)* with $AsCl_3$ can be carried out in boiling tetrahydrofuran (3 h). Examination of the reaction mixture by ^{1}H-NMR spectroscopy shows that the 1-chloro-1,4-dihydroarsabenzene derivative *(4)* undergoes partial dehydrohalogenation to give 4-acetoxyarsabenzene *(5)* under the reaction conditions. Since the product distribution *(4)*/*(5)* does not change on work up of the reaction mixture either by column chromatography over silica gel[**] or by distillative separation it may be assumed that one of the possible *cis*/*trans* isomers *(4)* [probably *(4a)*] spontaneously eliminates HCl; the other isomer is only converted into *(5)* by reaction with triethylamine in benzene. Compound *(5)* can be purified by bulb tube distillation at 80 °C/0.01 torr; the yield [based on *(3)*] is 20—25%. ^{1}H-NMR ($CDCl_3$); $COCH_3$: 2.16 ppm (s); ring H: A_2X_2 spectrum H_X: 7.50 ppm (d) $J(H_A/H_X)$ 12 Hz; H_A: 9.62 ppm (d).

Saponification of *(5)* in methanolic sodium hydroxide (room temperature, 36 h) leads to 4-hydroxyarsabenzene *(6)*. Compound *(6)* is obtained as the Na salt after evaporation to dryness and is purified by digestion with benzene. After acidification with dilute hydrochloric acid the free arsaphenol *(6)* is taken up in benzene and, after removal of solvent, sublimed at 60 °C/0.1 torr. *(6)*, m.p. 102—105 °C (dec.), forms strongly refractive compact prisms (after sublimation) displaying an intense phenolic odor; no distinct $FeCl_3$ reaction is observed. On exposure to air, *(6)* proves to be more stable than the hitherto known arsabenzenes monosubstituted in position 4; however, it decomposes after some time to give brown compounds of unknown composition.

^{1}H-NMR *(6)* ($CDCl_3$); OH: 7.23 ppm (s); ring H: A_2X_2 spectrum, H_X 7.56 ppm (d having fine structure) $J(H_A/H_X)$ 11 Hz; H_A 9.61 ppm (d having fine structure) [^{1}H-NMR phenol (for comparison); OH: 6.11 ppm (s); ring H: 6.65—7.32 ppm (m)]; mass spectrum: M^+, *m/e* 156 (rel. int. 100%); $[M-As]^+$, 81 (18%); the degradation pattern displays the fragments [M−CO] and [M−CHO] characteristic of phenols. The IR spectrum [(KBr); ν(OH) 3180 cm^{-1}; ν(=CH) 3020, 3070 cm^{-1}; ν(C=C) 1500, 1560 cm^{-1}; ν(C=O) 1220 cm^{-1}; δ'(OH) 1320, 1380 (?) cm^{-1}] is also largely comparable with that of phenol. The UV spectrum [(ethanol), λ_{max} = 229 (ε = 17000); 290 nm (30300)] resembles that of 4-ethoxyarsabenzene[1a] very closely; relative to phenol [λ_{max} = 211 (ε = 6200); 273 nm (2400)], *(6)* exhibits the bathochromic effect observed for all arsa- and phosphabenzenes. In ethanol/1 N NaOH an additional pronounced longwave shift of 43 nm, λ_{max} = 233 (13600); 332 nm (34200), is observed for *(6)* owing to phenoxide formation; this shift is considerably more pronounced than for sodium phenoxide [λ_{max} = 238 (ε = 11300); 291 (3200)].



(7) *(6)* *(8)*

Thus the spectroscopic findings clearly show that 4-hydroxyarsabenzene *(6)* is indeed an arsaphenol. The phenoxide ion *(7)* is formed already on treatment with dilute aqueous alkali; in contrast to 4-pyridinol, which exists almost exclusively as γ-pyridone in neutral solution[4], no tautomeric equilibrium with 1-arsa-2,5-cyclohexadien-4-one *(8)* is to be observed.

Received: July 14, 1975 [Z 290 IE]
German version: Angew. Chem. 87, 743 (1975)

CAS Registry numbers:
(1), 56598-53-9; *(2)*, 56598-54-0; *(3)*, 56598-55-1; *(4a)*, 56629-72-2; *(4b)*, 56598-59-5; *(5)*, 56598-56-2; *(6)*, 56598-57-3; *(7)*, 56598-58-4; di-*n*-butyltin dihydride, 1002-53-5

[1] a) *G. Märkl* and *F. Kneidl*, Angew. Chem. *86*, 745, 746 (1974); Angew. Chem. internat. Edit. *13*, 667, 668 (1974); b) *G. Märkl*, *H. Kellerer*, and *F. Kneidl*, Tetrahedron Lett. *1975*, 2411.

[2] *E. R. H. Jones*, *L. Skatteböl*, and *M. C. Whiting*, J. Chem. Soc. *1956*, 4765; *E. R. H. Jones*, *H. H. Lee*, and *M. C. Whiting*, *ibid. 1960*, 3483.

[3] *R. D. Dillard* and *D. E. Pavey*, J. Org. Chem. *36*, 749 (1971); see also *K. G. Migliorese*, *Y. Tanaka*, and *S. I. Miller*, *ibid. 39*, 739 (1974).

[4] *S. F. Mason*, J. Chem. Soc. *1958*, 1253 (UV spectrum); *A. R. Katritzky* and *R. A. Jones*, *ibid. 1960*, 2947 (IR spectra); *R. A. Y. Jones*, *A. R. Katritzky*, and *J. M. Lagowski*, Chem. Ind. (London) *1960*, 870.

Formation and Trapping of 4,5-Didehydrotropone

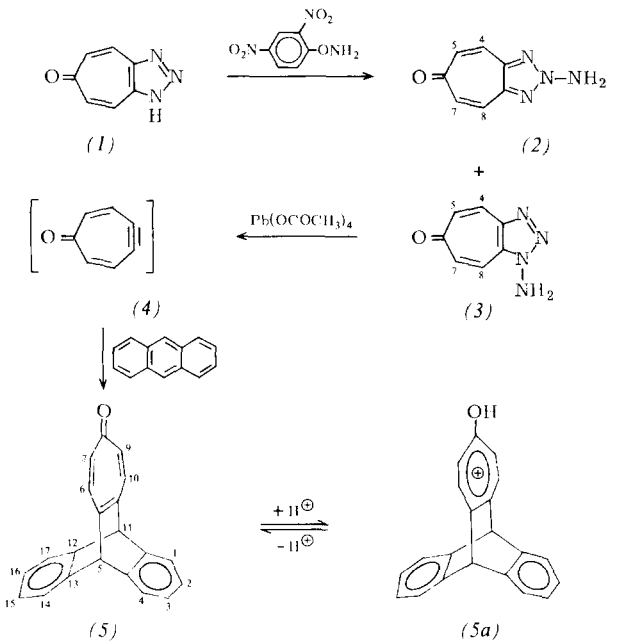
By *Tomoo Nakazawa* and *Ichiro Murata*[*]

Arynes such as dehydrobenzene possess considerable interest as important synthetic intermediates[1]. Among the didehydrotropone derivatives, didehydrotropolone[2] and didehydrodibenzotropone[3] have been described. We now report the intermediate formation and trapping of 4,5-didehydrotropone *(4)*.

Reaction of 1*H*-cycloheptatriazol-6-one *(1)*[4], accessible in several steps from tropolone, with *O*-(2,4-dinitrophenyl)hy-

[*] Doz. Dr. T. Nakazawa and Prof. Dr. I. Murata
Department of Chemistry, Faculty of Science
Osaka University, Toyonaka, Osaka 560 (Japan)

droxylamine[5] affords 1-amino-1*H*-cycloheptatriazol-6-one *(3)*[6], pale yellow needles of m. p. 220 °C, and the 2-amino-2*H* isomer *(2)*[6], pale yellow needles of m. p. 198—200 °C (dec.), in the ratio of 1.7:1 in 75% yield.



(1) *(2)* *(3)* *(4)* *(5)* *(5a)*

In analogy to the formation of dehydrobenzene from benzotriazole[7] compound *(3)* was oxidized with lead tetraacetate. Since the poor solubility of *(2)* and *(3)* precludes their quantitative separation the mixture was treated with lead tetraacetate in anhydrous dichloromethane at room temperature in the presence of excess anthracene as trapping reagent; evolution of nitrogen was observed during the reaction. The mixture of products remaining on crystallization of the anthracene is chromatographed over basic alumina, previously deactivated with 7.5% of water, with dichloromethane as eluant. The trapping product 5,11-dihydro-5,11-*o*-benzenocyclohepta[*b*]naphthalen-8-one *(5)*[6] can be isolated in *ca.* 12% yield as pale yellow needles (from benzene) of m. p. 260 °C (dec.).

The structure is proved by the 100 MHz ^{1}H-NMR spectrum: $\delta = 5.34$ (s, H-5, H-11); AX system at $\delta = 6.90$ (d, H-7, H-9; $J_{6,7} = J_{9,10} = 11.6$ Hz) and 7.39 (d, H-6, H-10); AA'XX' systems at $\delta = 7.39$ (m, H-1, -4, -14, -17) and 7.03 (m, H-2, -3, -15, -16). The IR spectrum (KBr) contains the characteristic $\nu_{C=C}$ and $\nu_{C=O}$ bands of the tropone series at 1614 and 1563 cm^{-1}. Typical absorptions of tropone derivatives are likewise observed in the UV spectrum; λ_{max} (cyclohexane) = 230 nm (sh, $\log\varepsilon = 4.32$), 243 (4.26), 280 (3.61), 314 (3.96), and 327 (3.93). The adduct *(5)* is present as the hydroxytropylium form *(5a)* in trifluoroacetic acid[8]; the protonation is reversible. Under the reaction conditions employed the conceivable product arising from *(2)* cannot be obtained[7, 9].

Received: July 14, 1975 [Z 292 IE]
German version: Angew. Chem. 87, 742 (1975)

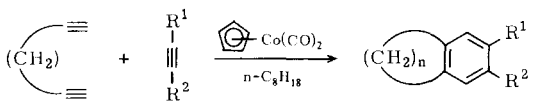
CAS Registry numbers:
(1), 56598-78-8; *(2)*, 56598-79-9; *(3)*, 56598-81-3; *(5)*, 56598-82-4; *(5a)*, 56598-80-2; *O*-(2,4-dinitrophenyl)hydroxylamine, 17508-17-7

[1] *R. W. Hoffmann:* Dehydrobenzene and Cycloalkynes. Academic Press, New York/Verlag Chemie, Weinheim 1967.
[2] *T. Yamatani, M. Yasumami,* and *K. Takase,* Tetrahedron Lett. *1970*, 1725, and references cited therein.
[3] *W. Tochtermann, K. Oppenländer,* and *U. Walter,* Chem. Ber. *97*, 1318 (1964).
[4] *T. Nozoe, S. Ito,* and *K. Matsui,* Proc. Jap. Acad. *30*, 313 (1954).
[5] *Y. Tamura, J. Minamikawa, K. Sumoto, S. Fujii,* and *M. Ikeda,* J. Org. Chem. *38*, 1239 (1973). We are grateful to Prof. Dr. *Y. Tamura*, Dr. *M. Ikeda*, and Dr. *J. Minamikawa* for information concerning the amination of *(1)*.
[6] All substances described gave correct analytical data.
[7] *C. D. Campbell* and *C. W. Rees,* Proc. Chem. Soc. *1964*, 296; J. Chem. Soc. *C 1969*, 742, 748.
[8] *(5a)*, 100 MHz ^{1}H-NMR (CF_3COOH): $\delta = 8.17$ (d, H-7, H-9; $J_{6,7} = J_{9,10} = 11.3$ Hz); 8.76 (d, H-6, H-10); 7.57 (m, H-1, -4, -14, -17); 7.17 (m, H-2, -3, -15, -16); 5.92 (s, H-5, H-11); UV, λ_{max} (CF_3COOH) = 303 nm ($\log\varepsilon = 3.95$), 343 (3.95).
[9] *C. D. Campbell* and *C. W. Rees,* Chem. Commun. *1965*, 192.

Transition Metal Catalyzed Acetylene Cyclizations. A General Synthesis of Indans and Tetralins[**]

By *R. L. Hillard III* and *K. P. C. Vollhardt*[*]

The preparation of polycycles containing functionalized benzene rings with control of substitution is a formidable task. We now present a general synthesis of indans *(3)* and tetralins *(4)* that offers a solution to this problem and could in principle be extended to the synthesis of larger and more complex polycycles. Our synthetic scheme involves the cooligomerization of 1,6-heptadiyne *(1)*, $n = 3$, or 1,7-octadiyne *(1)*, $n = 4$, with substituted monoacetylenes *(2)* catalyzed by dicarbonylcyclopentadienylcobalt[1] (see Table 1). The cyclotrimerization of terminal diynes by this catalyst is a known reaction[1a].



(1), n = 3,4 *(2)* *(3)*, n = 3 *(4)*, n = 4

Table 1. Indans *(3)* and tetralins *(4)* prepared [2].

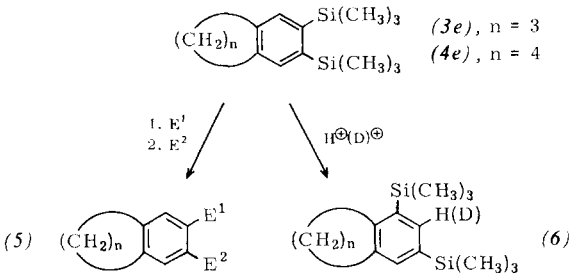
Compound	R^1	R^2	M.p. [°C] b.p. [°C/torr] [a]	Yield [%]	Ref.
(3a)	CO_2CH_3	CO_2CH_3	67—68	20	[3]
(3b)	C_6H_5	H	74—75	26	[4]
(3c)	C_6H_5	C_6H_5	119—120	24	
(3d)	n-C_6H_{13}	H	43/0.2	14	[5]
(3e)	$(CH_3)_3Si$	$(CH_3)_3Si$	68—69	50	
(4a)	CO_2CH_3	CO_2CH_3	115/0.05	26	[3]
(4b)	C_6H_5	H	97/0.5	18	
(4c)	C_6H_5	C_6H_5	110.5—112	21	
(4d)	n-C_6H_{13}	H	83/0.02	14	[6]
(4e)	$(CH_3)_3Si$	$(CH_3)_3Si$	45—46	49	
(4f)	$(CH_3)_3Si$	CH_3	90/0.15	34	

[a] Oil bath temperature.
[b] We thank *C. P. Baskin* for the preparation of this compound.

The major side products accompanying *(3)* and *(4)* arise by cyclotrimerization and complex cooligomerization[7]. The desired compounds *(3)* and *(4)* are, however, easily separated by column chromatography. The method described here extends the pioneering studies on the "diyne reaction" by *E. Müller et al.*[8].

[*] R. L. Hillard III and Prof. Dr. K. P. C. Vollhardt
Department of Chemistry, University of California
Berkeley, California 94720 (USA)
We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, the Research Corporation, and the National Institute of Health (Biomedical Sciences Supports Grant RR-7006) for generous financial support.
[**] First reported at the American Chemical Society 30th Annual Northwest Regional Meeting, Honolulu, Hawaii, June 12—13, 1975.

Of particular interest are the syntheses of the *o*-bis(trimethylsilyl) derivatives *(3e)* and *(4e)*. Although quite strained, these compounds form in relatively high yield because bistrimethylsilylacetylene does not trimerize under the reaction conditions[11d, 9]. Thus, slow addition of the diyne *(1)* to the alkyne *(2)* in this case leads to more efficient cocyclization, although side reactions are not entirely suppressed.



Compounds *(3e)* and *(4e)* are key intermediates in the synthesis of other functionalized indans and tetralins, and can be converted to derivatives of type *(5)* by high yield stepwise detrimethylsilylation with electrophiles[10], or *(6)* by treatment with dilute acid[11].

5,6-Bis(trimethylsilylindan) (3e)

To 5 g of refluxing *(2)*, $R^1 = R^2 = Si(CH_3)_3$ (5 g, large excess) in dried and degassed *n*-octane (70 ml) under nitrogen was added a solution of 1,6-heptadiyne *(1)*, $n = 3$ (0.46 g, 5 mmol) and $CpCo(CO)_2$ (20 µl) in dried and degassed *n*-octane (10 ml). The addition was controlled by means of a syringe pump over 36 h. Vacuum transfer of solvent, excess (reusable) *(2)*, and catalyst gave a dark oily residue that was chromatographed on silica (150 g). Eluting with petroleum ether (40—60 °C, 200 ml fractions) gave fraction 2—4 containing a colorless oil. Crystallization from ether gave 650 mg *(3e)* as colorless crystals.

Received: July 14, 1975 [Z 291 IE]
German version: Angew. Chem. 87, 744 (1975)

CAS Registry numbers:
(1), $n = 3$, 2396-63-6; *(1)*, $n = 4$, 871-84-1; *(2a)*, 762-42-5; *(2b)*, 536-74-3; *(2c)*, 501-65-5; *(2d)*, 629-05-0; *(2e)*, 14630-40-1; *(2f)*, 6224-91-5; *(3a)*, 56598-67-5; *(3b)*, 56598-68-6; *(3c)*, 56598-69-7; *(3d)*, 54889-55-3; *(3e)*, 56598-70-0; *(4a)*, 51510-78-2; *(4b)*, 41284-88-2; *(4c)*, 56598-71-1; *(4d)*, 56598-72-2; *(4e)*, 56598-73-3; *(4f)*, 56598-74-4; *(6)*, $n = 3$, 56598-75-5; *(6)*, $n = 4$, 56598-76-6; dicarbonylcyclopentadienylcobalt, 12078-28-8

[1] a) *K. P. C. Vollhardt* and *R. G. Bergman*, J. Am. Chem. Soc. 96, 4996 (1974); b) *K. P. C. Vollhardt, J. E. Bercaw*, and *R. G. Bergman*, J. Am. Chem. Soc. 96, 4998 (1974); c) The use of carbonyl (phosphane)nickel catalysts for the *copolymerization* of terminal unconjugated diynes with alkylacetylenes has been reported. In these reactions 5-alkylindans seem to be formed in low yield and in difficultly separable mixtures with other oligomers; *E. C. Colthup* and *L. S. Meriwether*, J. Org. Chem. 26, 5169 (1961); d) *W. G. L. Aalbersberg, A. J. Barkovich, R. L. Funk, R. L. Hillard III*, and *K. P. C. Vollhardt*, J. Am. Chem. Soc., in press.

[2] All isolated new compounds reported gave satisfactory analytical and spectral data.

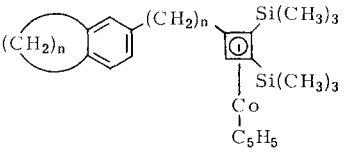
[3] *K. Alder, R. Muders, W. Krane*, and *P. Wirtz*, Liebigs Ann. Chem. 627, 59 (1959).

[4] *N. Barbulescu* and *M. Govela*, Analele Univ. C. I. Parhon. Ser. Stiint. Nat. 10, 151 (1961); Chem. Abstr. 59, 1506b (1963).

[5] *J. P. Wibaut* and *B. Paulis*, Rec. Trav. Chim. Pays-Bas 77, 792 (1958).

[6] *Je. S. Pokrowskaja* and *R. Ja. Ssuschtschik*, Zh. Obshch. Chim. 11, 170 (1941).

[7] In reactions with *(2)*, $R^1 = R^2 = C_6H_5$, stilbene is also formed. In reactions involving *(2)*, $R^1 = R^2 = Si(CH_3)_3$ the following cobalt complex arises ($n = 3$ or 4) [2]:



[8] See, for instance, *E. Müller*, Synthesis 1974, 761; *E. Müller, A. Scheller, W. Winter, F. Wagner*, and *H. Meier*, Chem.-Ztg. 99, 155 (1975).

[9] *H. Sakurai* and *J. Hayashi*, J. Organometal. Chem. 70, 85 (1974).

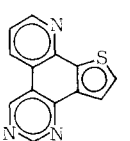
[10] a) The high efficiency of the stepwise displacement is due to steric acceleration of the first step [1d, 10b]. Kinetic measurements of deuteriodesilylation in $CF_3CO_2D/CD_3CO_2D/CCl_4$ (56:27:17) reveal displacement of the respective first silyl groups 37 *(3e)* and 36 *(4e)* times faster than the second; b) *C. Eaborn, D. R. M. Walton*, and *D. J. Young*, J. Chem. Soc. B 1969, 15; c) For instance treatment of *(3e)* or *(4e)* with bromine followed by ICl gives (>90%) *(5)*, $n = 2, 3$; $E^1 = Br$, $E^2 = I$.

[11] *D. Seyferth* and *D. L. White*, J. Am. Chem. Soc. 94, 3132 (1972).

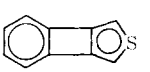
Synthesis of Heterocyclic Cyclopolyaromatics Containing Similar Kinds of Nuclei[1]

By *Thomas Kauffmann, Bernd Greving, Johann König, Alfred Mitschker*, and *Annegret Woltermann*[*]

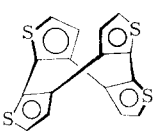
Owing to the large number of known carbo- and heterocyclic aromatic compounds thousands of cyclic combinations of aromatics (cyclopolyaromatics[2]) are conceivable. As far as those with heterocyclic ring members are concerned our knowledge is extremely scanty apart from the exceptional case of triplet combinations such as *(1)*[3] which are assigned to the condensed aromatic compounds: combinations of two aromatics, *e.g. (2)*[4], are known only in few cases, and of the corresponding compounds having four and more ring members apparently only cyclotetrathiophene *(3)*[5] has been described so far.



(1)



(2)



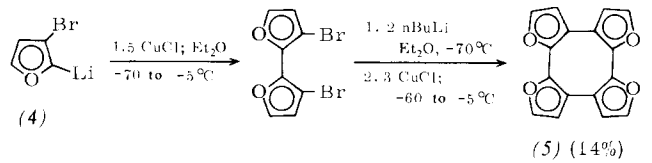
(3)

We have now accomplished an entry into the heterocyclic cyclopolyaromatics on a fairly broad front and wish to report a number of syntheses whose yields are, however, not yet entirely satisfactory.

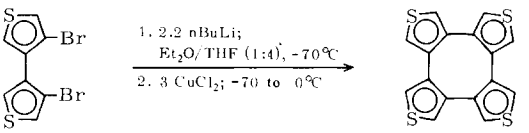
Nucleophilic heteroaromatics: Oxidative coupling of acetylenes *via* organocopper derivatives has proved to be a key reaction in the synthesis of annulenes. It can already be seen that the corresponding coupling of aromatic systems will play a similar role in the synthesis of carbo-[6] and heterocyclic cyclopolyaromatics. Starting from the compounds *(4)*[7], *(6)*[8], and *(8)*[9], use of this reaction afforded the cyclotetraaromatics *(5)* (m. p. 233 °C), *(7)* (m. p. 300—301 °C), and *(9)* (dec. 421—424 °C).

The synthesis of *(3)*[5] gave a small amount of a (not yet completely pure) cyclohexathiophene (dec. above 420 °C) as by-product. Since its ^{1}H-NMR spectrum is almost identical to that of *(3)*, it clearly has the centrosymmetric structure *(10)* and not a helical structure[6].

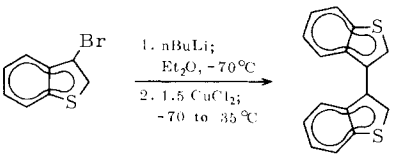
[*] Prof. Dr. Th. Kauffmann, Dipl.-Chem. B. Greving, Dipl.-Chem. J. König, Dr. A. Mitschker, and A. Woltermann
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)



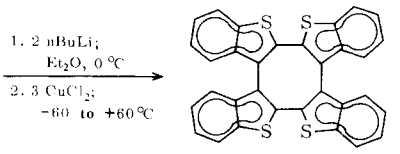
(4) (5) (14%)



(6) (7) (23%)

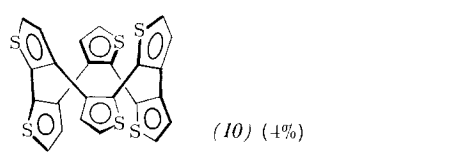


(8) (52%)

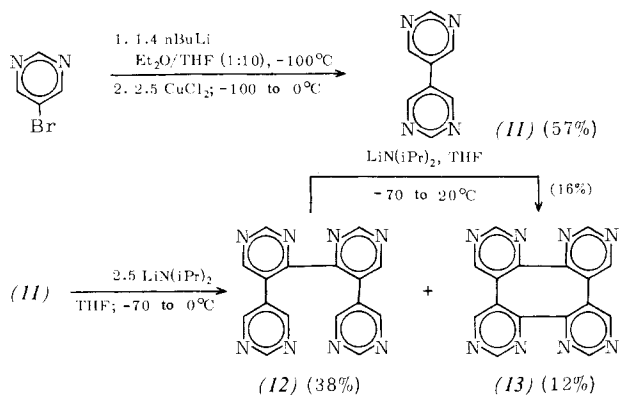


(9) (11%)

Electrophilic heteroaromatics: In order to become acquainted with cyclic combinations of such systems we first prepared the hitherto unreported 5,5'-bipyrimidinyl *(11)* (m. p. 196—197 °C)[11] and reacted it with lithium diisopropylamide[10]. The reaction afforded the cyclotetrapyrimidine *(13)* (dec. 362—365 °C) as by-product; the major product tetrapyrimidine *(12)* (m. p. 250—252 °C) was also cyclized to *(13)* [yield 38% based on reacted *(12)*] by renewed reaction with lithium diisopropylamide.



(10) (4%)



(11) (57%) (12) (38%) (13) (12%)

Analogous reaction with 3,3'-bipyridyl afforded the expected cyclotetrapyridine *(14)* (dec. 339—341 °C) in only 0.7% yield. Elucidation of the other products is still in progress.

The structures of the new compounds, which are all colorless and crystalline, follow from elemental analysis, mass, ^{1}H-NMR, and UV spectra. All yields given are based upon weights of starting materials.

Received: July 16, 1975 [Z 293a IE]
German version: Angew. Chem. 87, 745 (1975)

CAS Registry numbers:
(3), 57757-43-0; *(4)*, 56598-41-5; *(5)*, 56598-42-6; *(6)*, 5556-13-8; *(7)*, 56598-43-7; *(8)*, 40306-93-2; *(9)*, 56598-44-8; *(10)*, 56598-45-9; *(11)*, 56598-46-0; *(12)*, 56598-47-1; *(13)*, 56598-48-2; *(14)*, 56598-49-3; 3,3'-bipyridyl, 587-46-4

[1] Protophanes and polyaromatics, Part 20. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 19: *Th. Kauffmann*, Forschungsber. des Landes Nordrhein-Westfalen, No. 2450 (1975).

[2] We have proposed extension of the class name "arene" to include heteroaromatic compounds. Not wishing to anticipate a decision by the IUPAC Commission, we have still retained the term "aromatic" in the present work.—In naming unbranched chains made up of identical ring systems, IUPAC Rule A-54.1 prescribes use of the numerical prefixes bi, ter, quater, quinque, sexi, *etc.* Since most of the possible polyaromatics fail to meet these requirements and expressions like sexiaromatic or cyclosexifuran are not without comical undertones, we employ the usual prefixes di, tri, tetra, *etc.*

[3] *A. Mitschker, U. Brandl*, and *Th. Kauffmann*, Tetrahedron Lett. *1974*, 2343.

[4] *P. J. Garratt* and *K. P. C. Vollhardt*, Chem. Commun. *1970*, 109; J. Am. Chem. Soc. *94*, 7087 (1972).

[5] *B. Greving, A. Woltermann*, and *Th. Kauffmann*, Angew. Chem. *86*, 475 (1974); Angew. Chem. internat. Edit. *13*, 467 (1974).

[6] Cf. *G. Wittig* and *K.-D. Rümpler*, Liebigs Ann. Chem. *751*, 1 (1971); *L. Ernst, A. Mannschreck*, and *K.-D. Rümpler*, Org. Magn. Reson. *5*, 125 (1973).

[7] *G. M. Davies* and *P. S. Davies*, Tetrahedron Lett. *1972*, 3507.

[8] *S. Gronowitz*, Acta Chem. Scand. *15*, 1393 (1961).

[9] A less favorable synthesis of *(8)* (11% yield) is described by *L. J. Pandya, D. S. Rao*, and *B. D. Tilak*, J. Sci. Ind. Res. (India) *B 18*, 516 (1959); Chem. Abstr. *54*, 17391d (1960).

[10] *A. J. Clarke, S. McNamara*, and *O. Meth-Cohn*, Tetrahedron Lett. *1974*, 2373.

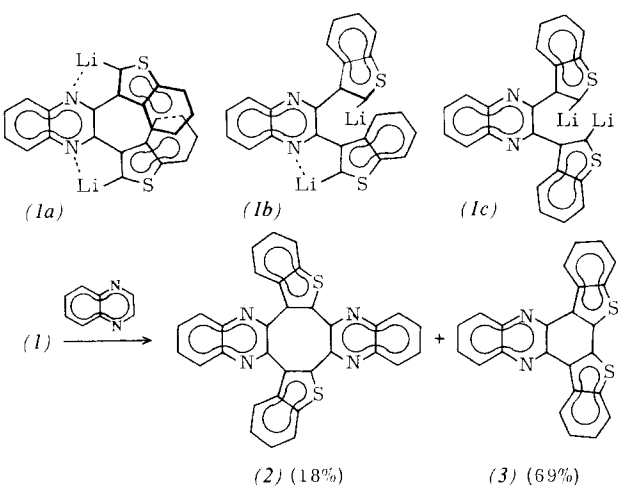
[11] Cf. *S. Gronowitz* and *J. Röe*, Acta Chem. Scand. *19*, 1741 (1965).

Synthesis of Heterocyclic Cyclopolyaromatics Containing Different Kinds of Nuclei[1]

By *Thomas Kauffmann, Bernd Muke, Rolf Otter*, and *Dieter Tigler*[*]

The classical aromatic systems possess predominantly nucleophilic (*e. g.* benzene, furan) or predominantly electrophilic character (*e. g.* pyridine, pyrimidine). Expectedly, "Ar_{Nu}—Ar_{El} linkage" proved particularly useful in syntheses *via* organometallic compounds[2]. However, attempts to cyclize the resulting di-, tri-, and tetraaromatic compounds themselves by Ar_{Nu}—Ar_{El} linkage have so far merely led to alternative reactions.

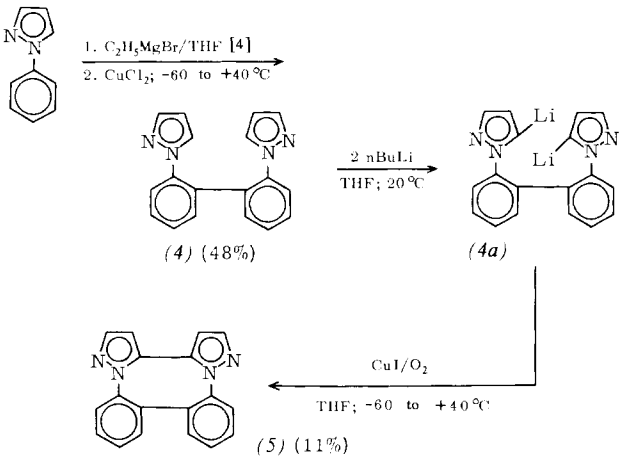
It is therefore to be regarded as a step forward that reaction of the dilithiated triaromatic *(1)*[3] with quinoxaline not only



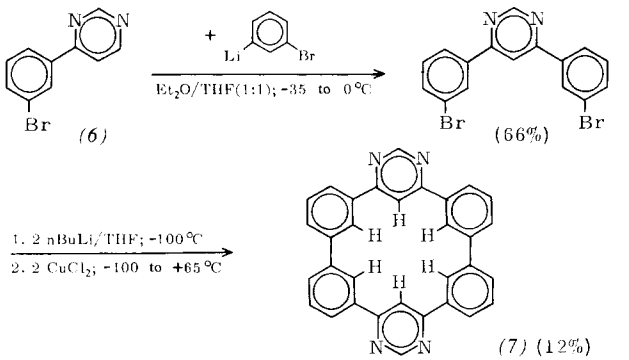
(1a) (1b) (1c) (1) (2) (18%) (3) (69%)

yielded *(3)* (m. p. 333 °C) but also afforded the cyclotetraaromatic compound *(2)* (m. p. 307 °C) by double Ar_{Nu}—Ar_{El} linkage. Since only cyclization reactions occurred in this case it may be presumed that, owing to crowding in the conforma-

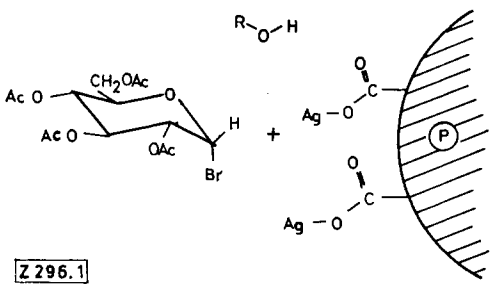
[*] Prof. Dr. Th. Kauffmann, Dipl.-Chem. B. Muke, Dipl.-Chem. R. Otter, and Dipl.-Chem. D. Tigler
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)



tions *(1a)* and *(1b)*, the conformation *(1c)*, which is more conducive to cyclizations, is favored. Moreover, conformation *(1c)* could be stabilized by intramolecular ate-complex formation.



Two other cyclic combinations of unlike aromatics became accessible by syntheses with oxidative coupling as the cyclization step: cyclization of *(4)* (m.p. 135—136 °C) *via (4a)* to give *(5)* (m.p. 214 °C) succeeded only on use of CuI/O_2 as



Z 296.1

coupling reagent. The proven reagent $CuCl_2$ led predominantly to replacement of lithium by chlorine.

In the synthesis of the cyclohexaaromatic *(7)* (m.p. 475—477 °C) the intermediate *(6)* (m.p. 91—93°; yield 44%) was prepared by reaction of 1-bromo-3-lithiobenzene[5] with 1 mol of pyrimidine (ether/THF (3:1); −35 to 20 °C)[6]. The ^{1}H-NMR signals of the inner phenylene protons of *(7)* are shifted downfield by 0.66 ppm relative to the corresponding signals of the analogous hexa-*m*-phenylene (both in [D$_6$]DMSO[7]). This indicates more pronounced mutual crowding of the inner protons of *(7)* owing to more extensive flattening of the molecule.

The structure of the new compounds, which are all colorless and crystalline, follow from elemental analysis, mass, ^{1}H-NMR, and UV spectra. All yields given are based upon the weights of starting materials.

Received: July 16, 1975 [Z 293b IE]
German version: Angew. Chem. 87, 746 (1975)

CAS Registry numbers:
(1), 56598-83-5; *(2)*, 56598-84-6; *(3)*, 56598-85-7; *(4a)*, 56598-86-8; *(5)*, 56598-87-9; *(6)*, 56598-88-0; *(7)*, 56598-89-1; 1-bromo-3-lithiobenzene, 2592-86-1; quinoxaline, 91-19-0; pyrimidine, 289-95-2

[1] Protophanes and polyaromatics, Part 21. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.— Part 20: *Th. Kauffmann, B. Greving, J. König, A. Mitschker*, and *A. Woltermann*, Angew. Chem. 87, 745 (1975); Angew. Chem. internat. Edit. 14, 713 (1975).
[2] Reviews: a) *Th. Kauffmann*, Chimia 26, 511 (1972); b) Forschungsber. Landes Nordrhein-Westfalen, No. 2450 (1975).
[3] Preparation of *(1)* (53%) was accomplished by reaction of 3-benzo[*b*]-thienyllithium with ½ mol of quinoxaline (−70 to 10 °C, 16 h).—Conditions of bislithiation: 2.5 mol of LiN(iPr)$_2$, THF, −50 °C, 1 h.—For the cyclization reaction, *(1)* and quinoxaline were simultaneously added dropwise to THF under N_2 at 20 °C.
[4] *A. Marxer* and *M. Siegrist*, Helv. Chim. Acta 57, 1988 (1974).
[5] *H. Gilman* and *T. S. Soddy*, J. Org. Chem. 23, 1584 (1958).
[6] In the syntheses leading to *(1)*, *(2)*, *(3)*, and *(6)*, the crude product had to be oxidized with $KMnO_4$ in acetone or acetone/chloroform to aromatize dihydro compounds formed.
[7] We are grateful to Prof. *H. A. Staab* for providing hexa-*m*-phenylene.

Preparations of Glycosides with Polymeric Acid-Binding Reagents

By *Volker Eschenfelder, Reinhard Brossmer*, and *Margot Wachter*[*]

In the presence of silver salts of dicarboxylic acids or hydroxycarboxylic acids, alcohols undergo extremely mild reaction with α-acetobromoglucose to form 2,3,4,6-tetra-*O*-acetyl-β-D-glucosides[1]. We have carried out this reaction on polymeric acid-binding reagents. The highest yield was obtained with a copolymer of maleic acid and 1,4-bis(vinyloxy)butane; the silver salt of this polymer was obtained by several hours' shaking of the Na^+ form in aqueous solution with the stoichiometric amount of $AgNO_3$. With this system we obtained, *e.g.*, yields of 55% and 43% respectively of cholesteryl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside [m.p. 160 °C; $[\alpha]_D^{20} = -25.3°$ ($c = 1.0$; $CHCl_3$)] (Fig. 1) on reacting α-acetobromoglucose with cholesterol in the molar ratio of 3:1 and 2:1 (12 h in ether at 25 °C). The yields are comparable with those

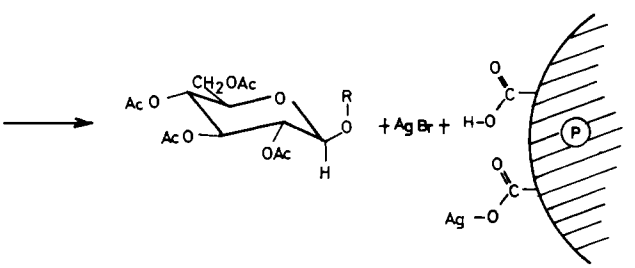


Fig. 1. Synthesis of glycosides with polymeric acid-binding reagents Ⓟ.

reported in the literature[2]. Other alcohols and aceto halo sugars react similarly.

The reaction on the polymer support is subject to the same solvent influence as has already been observed for the monomer; it apparently proceeds *via* the concerted trimolecular mechanism required for the silver 1,4-dicarboxylates[3]. This does not apply to other exchangers, *e.g.* a copolymer of methacrylic acid and divinyl benzene. In this case the carboxy groups do not display the favorable steric arrangement corresponding to the 1,4-system.

This further development of the Koenigs-Knorr synthesis has the following advantages: Removal of the γ-hydroxy- or 1,4-dicarboxylic acid in a separate step is no longer necessary. The polymers can be rapidly and quantitatively filtered off or centrifuged off and re-used after regeneration. By-products which, like 1-*O*-acylglucose, remain linked to the polymer

[*] Dr. V. Eschenfelder, Prof. Dr. Dr. R. Brossmer, and M. Wachter
Institut für Biochemie II (Med. Fakultät) der Universität
69 Heidelberg, Im Neuenheimer Feld 328 (Germany)

can be eliminated in the same mechanical work-up step. Synthesis of glycosides having different functional groups is thus facilitated. The desired glycoside can be concentrated or isolated directly by crystallization if the reaction is carried out in a suitable manner.

Received: July 28, 1975 [Z 296 IE]
German version: Angew. Chem. 87, 747 (1975)

CAS Registry numbers:
α-Acetobromoglucose, 572-09-8; cholesterol, 57-88-5; cholesteryl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, 6907-84-2

[1] *G. Wulff, G. Röhle*, and *W. Krüger*, Angew. Chem. *82*, 480 (1970); Angew. Chem. internat. Edit. *9*, 455 (1970); *B. Helferich* and *W. M. Müller*, Chem. Ber. *103*, 3350 (1970).
[2] *H. Lettré* and *A. Hagedorn*, Hoppe-Seylers Z. Physiol. Chem. *242*, 210 (1936); *N. K. Kochetkov, A. J. Khorlin*, and *A. F. Bochkov*, Tetrahedron *23*, 693 (1967); *G. Wulff, G. Röhle*, and *W. Krüger*, Chem. Ber. *105*, 1097 (1972).
[3] *G. Wulff* and *G. Röhle*, Chem. Ber. *105*, 1122 (1972).

A New Modification of the Ozone Cleavage Reaction

By *Karl Griesbaum* and *Helmut Keul*[*]

In studies on the oxidation of olefins incorporating vinyl chloride moieties, we have also examined the course of ozone cleavage reactions[1]. It was found that chloroolefins *(1)* are converted essentially quantitatively into the methyl esters *(3)* and *(7)* (Table 1).

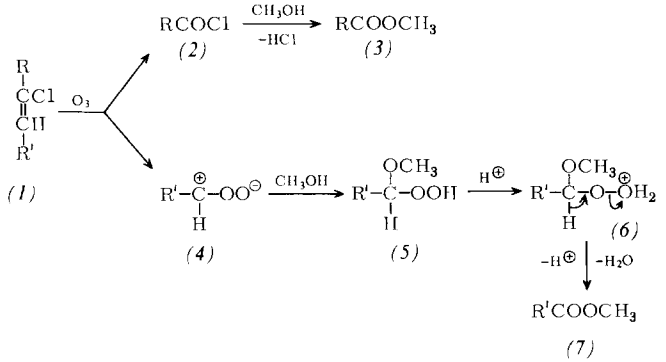


Table 1. Ozone cleavage of chloroolefins of structure *(1)* in methanol.

R (*1*)	R′	Ozonolysis product(s)	Yield [%]
CH_3	CH_3 [a]	2 $H_3CCOOCH_3$	95 [b]
$(CH_3)_3C$	H	$(CH_3)_3CCOOCH_3 + HCOOCH_3$	95 [b]
—$(CH_2)_4$—		$H_3COOC(CH_2)_4COOCH_3$	83 [c, d]
—$(CH_2)_3$—		$H_3COOC(CH_2)_3COOCH_3$	82 [c, d]

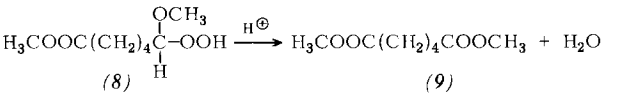
[a] *trans*-2-Chloro-2-butene.
[b] Determined by NMR spectroscopy, 1,1,1-trichloroethane as internal standard.
[c] Yield of isolated product.
[d] GLC and NMR analysis of the reaction mixture showed yields of >90%.

The substrate *(1)* is initially converted selectively into the fragments *(2)* and *(4)* by ozone in a Criegee-type cleavage. The acyl chloride *(2)* reacts spontaneously with methanol to form the ester *(3)* and hydrogen chloride, while the zwitterion *(4)* combines with methanol to form the methoxy hydroperoxide *(5)*, as it is generally known[2]. The latter is subsequently cleaved into *(7)* and water by way of a novel acid-catalyzed intramolecular redox reaction.

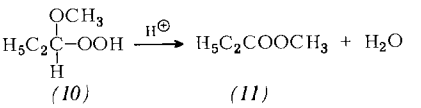
The reaction course postulated receives support from the following observations:

1) Ozonolysis of the chloroolefins listed in Table 1 at −78 °C in methanol afforded in each case strongly peroxidic reaction products, which upon warm-up to room temperature underwent exothermic reaction with concurrent loss of peroxide content.

2) Ozonolysis of 1-chloro-1-cyclohexene in methanol at −78 °C and subsequent addition of one equivalent of sodium methoxide to the cold reaction product afforded the methoxy-hydroperoxy ester *(8)*. [^{1}H-NMR in $CDCl_3$: δ = 4.72 (CH, t, J = 5 Hz); 3.50 (OCH_3, s); 3.68 ppm ($COOCH_3$, s)]. Treatment of isolated *(8)* with HCl/CH_3OH at ambient temperature quantitatively produced dimethyl adipate *(9)*.



3) Treatment of the methoxy hydroperoxide *(10)* (prepared by ozonolysis of 3-hexene in methanol) with HCl/CH_3OH at ambient temperature quantitatively afforded methyl propionate *(11)*.



Typical experiment:

A mixture of 1-chloro-1-cyclohexene (5 g, 0.043 mol) and dry methanol (50 ml) was ozonized to completion (blue coloration) at −78 °C. After displacement of excess ozone by a stream of oxygen, warm-up of the strongly peroxidic solution led to an exothermic reaction which raised the temperature of the mixture to approximately 55 °C. From the mixture, which was then free of peroxide, methanol was removed (rotary evaporator, approx. 15 torr) and the residue was dissolved in ether (250 ml) washed with water (100 ml), 10% NaOH solution (100 ml), and again water (100 ml), and then dried over Na_2SO_4. The ether was removed under reduced pressure (rotary evaporator) and the residue was vacuum distilled. The distillate (b. p. 110 °C/14 torr; yield 6.2 g ≈83%) was identified as dimethyl adipate by comparison with an authentic sample. The gas chromatogram (5 m Carbowax—20 M) showed no impurities.

Received: August 8, 1975 [Z 298 IE]
German version: Angew. Chem. 87, 748 (1975)

CAS Registry numbers:
(1), R = R′ = Me, 2211-69-0; *(1)*, R = *t*-Bu, R′ = H, 27843-27-2; *(1)*, R,R′ = —$(CH_2)_4$—, 930-66-5; *(1)*, R,R′ = —$(CH_2)_3$—, 930-29-0; *(8)*, 56598-77-7; *(9)*, 627-93-0; *(10)*, 25080-89-1; *(11)*, 554-12-1; 3-hexene, 592-47-2; CH_3COOCH_3, 79-20-9; $(CH_3)_3CCOOCH_3$, 598-98-1; $HCOOCH_3$, 107-31-3; $CH_3OOC(CH_2)_3COOCH_3$, 1119-40-0

[1] For previous work see: a) *K. Griesbaum* and *J. Brüggemann*, Chem. Ber. *105*, 3638 (1972); b) *K. Griesbaum* and *P. Hofmann*, Preprints of Symposia, Division of Petroleum Chemistry, American Chemical Society, Vol. 19, No. 4, 691 (1974).
[2] *R. Criegee*, Chimia *22*, 392 (1968).

Addendum

In a recent paper by *Downie et al.*[1] none of our papers[2] on the use of alkoxytris(dimethylamino)phosphonium salts were cited.

B. Castro
Laboratoire de Chimie Organique
Université de Nancy (France)

[1] *I. M. Downie et al.*, Angew. Chem. internat. Edit. *14*, 370 (1975).
[2] *R. Boigegrain, B. Castro*, and *C. Selve*, Tetrahedron Lett. *1975*, 2529, and literature cited therein.

[*] Prof. Dr. K. Griesbaum and Dr. H. Keul
Engler-Bunte-Institut der Universität
7500 Karlsruhe, Kaiserstrasse 12 (Germany)

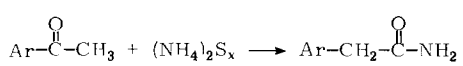
Reviews

Abstracts of selected progress reports and review articles

Impaired hormonal regulation of enzyme activity during aging is discussed in an article by *R. C. Adelman*. The main theme of this article centers around the influence of the hormones insulin and corticosterone on the regulation of enzymes of the rat liver. The areas currently of particular interest are the regulation of hormone concentration in the blood, the integrity of the receptor systems in the liver, and the effectiveness of endogenic hormone supplies. [Impaired Hormonal Regulation of Enzyme Activity during Aging. Fed. Proc. *34*, 179—182 (1975); 24 references]

[Rd 792 IE—R]

The Willgerodt reaction is discussed in a review by *E. V. Brown*. Although originally used for the conversion of aryl methyl ketones *via* a reduction oxidation process into an amide *(1)* by heating with yellow ammonium sulfide, it was soon found possible to use other starting materials (aliphatic ketones, aldehydes, unsaturated and saturated hydrocarbons, alcohols, amines, thiols). The modification by *Kindler* (using sulfur and dry amines, ammonia, primary or secondary amines) affords thioamides which can usually be hydrolyzed to the acids in almost quantitative yields. Further possible reactions of thiomides are hydrolysis to the amides and reduction to the amines. The Kindler-Willgerodt reaction has been extended

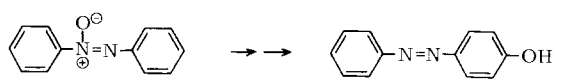


(1)

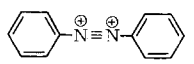
from the original alkyl ketones to aldehydes, hydrocarbons, amines, imines and numerous other compounds. The Willgerodt reaction has also been applied to heterocyclic ketones, aldehydes, hydrocarbons and alcohols. [The Willgerodt Reaction. Synthesis *1975*, 358—375; references]

[Rd 795 IE—M]

Catalysis in strongly acidic media and the Wallach rearrangement is the title of a paper authored by *E. Buncel*. The Wallach rearrangement of azoxyarenes such as *(1)* to *p*-hydroxyazobenzenes such as *(2)* requires the use of strong acids, *e.g.* 65—100% sulfuric acid; the rearrangement is characterized



(1) *(2)*

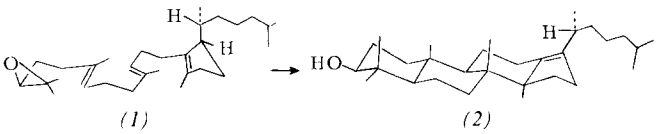


(3)

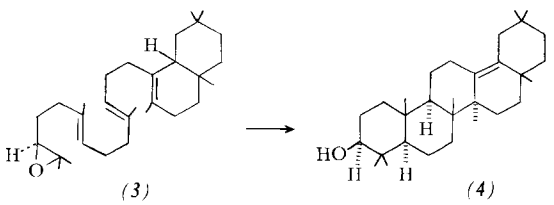
by two proton transfer stages. The delocalized dication *(3)* is proposed as intermediate. [Catalysis in Strongly Acidic Media and the Wallach Rearrangement. Accounts Chem. Res. *8*, 132—139 (1975); 49 references]

[Rd 798 IE—L]

Total syntheses of tetra- and pentacyclic triterpenoids *via* biogenetic-type pathways are discussed by *E. E. van Tamelen*. The goal of these investigations is to mimic the gentle approach of Nature in the organic laboratory (without enzymes!). One-step cyclizations of the epoxides *(1)* and *(3)* with Lewis



(1) *(2)*

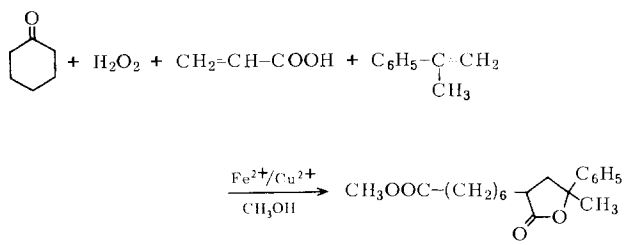


(3) *(4)*

acids to form isoeuphenol *(2)* and DL-δ-amyrin *(4)* may be cited as examples. [Bioorganic Chemistry: Total Synthesis of Tetra- and Pentacyclic Triterpenoids. Acc. Chem. Res. *8*, 152—158 (1975); 24 references]

[Rd 801 IE—L]

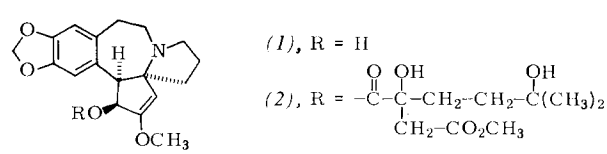
Addition of radicals to olefins in the presence of redox systems is the topic of a survey by *F. Minisci*. The redox systems formed *e.g.* in the presence of Fe or Cu salts may (i) influence the propagation of conventional chain reactions or (ii) permit novel additions. Formation of the monoadduct $Cl_3C-CH_2-CHCl-CN$ from CCl_4 and acrylonitrile on working in steel autoclaves ($FeCl_2$ formation!) represents an example of case (i), and case (ii) is illustrated by the following reaction:



[Free-Radical Additions of Olefins in the Presence of Redox Systems. Acc. Chem. Res. *8*, 165—171 (1975); 40 references]

[Rd 803 IE—L]

Synthesis of *Cephalotaxus* alkaloids is reported by *S. M. Weinreb* and *M. F. Semmelhack*. In Nature the alkaloid cephalotaxine *(1)* is accompanied by small amounts of the antileukemia-active ester harringtonine *(2)* and similar, likewise active esters. So far the synthesis of *(1)* has been accomplished



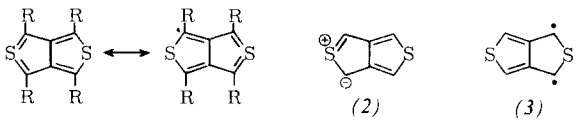
(1), R = H

(2), R = $-C(=O)-C(OH)(CH_2-CO_2CH_3)-CH_2-CH_2-C(OH)(CH_3)_2$

via two routes; linkage with the side chain to form *(2)* has yet to be achieved. [Synthesis of the *Cephalotaxus* Alkaloids. Acc. Chem. Res. *8*, 158—164 (1975); 38 references]

[Rd 802 IE—L]

Nonclassical condensed thiophenes, *i.e.* compounds such as *(1)* whose uncharged singlet structure can only be formulated as containing tetracovalent sulfur, are described in an article by *N. P. Cava* and *M. V. Lakshmikantham. (1)* would appear to be a good example for sulfur d-orbital participation; otherwise it would have to be present as ylide *(2)* or diradical



(1), R = H
(4), R = C_6H_5

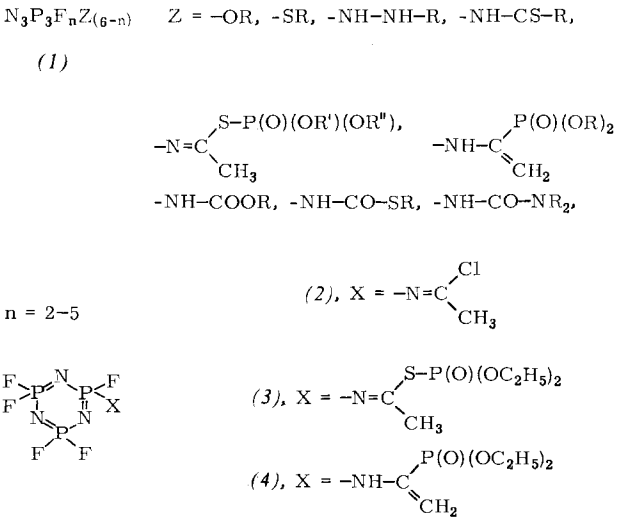
(3). Tetraphenylthieno[3,4-*c*]thiophene *(4)* was the first example of an isolable nonclassical condensed thiophene. It is nonpolar and has a singlet ground state. Both halves of the molecule are identical. The electronic structure of *(4)* is still a subject of controversy. [Nonclassical Condensed Thiophenes. Accounts Chem. Res. *8*, 139—144 (1975); 24 references]

[Rd 799 IE—L]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i.e.* provisionally published specifications as filed with the German Patent Office

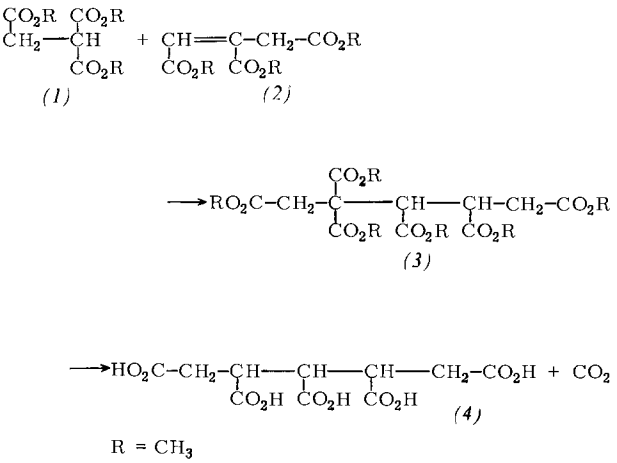
Substituted fluorocyclotriphosphazenes *(1)* are a new group of insecticidally active compounds, *e.g.* against flies, cockroaches, and caterpillars. The products *(1)* are obtained by treatment of fluorocyclotriphosphazenes with alcohols, hydra-



zines, and the like or by treatment of the derivatives *(2)* with thiocarboxamides, alkali metal thiophosphates, or trialkyl phosphites. The compounds *(3)* and *(4)* are specifically mentioned. [DOS 2334917; Badische Anilin- & Soda-Fabrik AG, Ludwigshafen]

[PR 288 IE—S]

1,2,3,4,5-Pentanepentacarboxylic acid *(4)* is formed by the condensation of trimethyl 1,1,2-ethanetricarboxylate *(1)* with trimethyl aconitate *(2)* to yield hexamethyl 1,2,2,3,4,5-pentanehexacarboxylate *(3)* and by hydrolysis and subsequent



R = CH_3

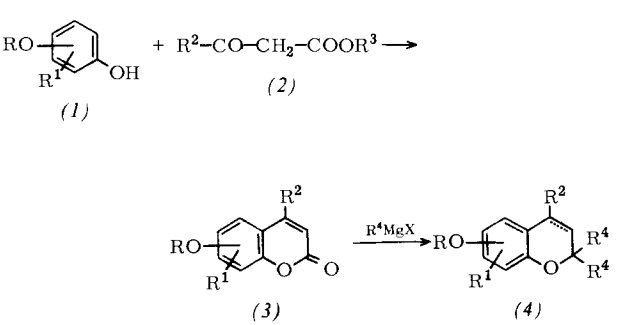
treatment thereof with an acidic ion-exchanger, carbon dioxide being split off. *(4)* and its alkali metal salts are well suited for biologically degradable complexing agents for use in washing and cleansing agents. [DOS 2342539; Henkel & Cie GmbH, Düsseldorf]

[PR 279 IE—D]

For the preparation of benzene derivatives containing an isocyanatomethyl side chain, (chloromethyl)benzene derivatives can reacted with sodium cyanate in dimethylformamide at 60—160 °C in presence of a catalytic amount of a compound of an acid metal chloride, *e.g.* calcium chloride, and dimethylformamide. [DOS 2449607; Kao Soap Co., Tokyo (Japan)]

[PR 291—D IE]

Chroman and chromene compounds *(4)* acting on the central nervous system are obtained by treating a derivative of dihydroxybenzene *(1)* with a keto ester *(2)* to yield the coumarin *(3)* and then allowing *(3)* to react with a Grignard compound;



R = H, alkyl, acyl; R^1 = alkyl, alkoxy; R^2 = cycloalkyl, cycloalkenyl; R^3 = alkyl; R^4 = alkyl

hydrogenation of the double bond or alkylation (acylation) of the hydroxyl group in *(4)*, R = H, affords further derivatives. [DOS 2434659; Smith Kline Corp., Philadelphia (USA)]

[PR 283 IE—K]

Formale Kinetik (Formal Kinetics). By *H. Mauser*. Bertelsmann Universitäts-Verlag, Düsseldorf 1974. 1st edit., 368 pages, bound, DM 78.—.

This book describes the concentration and time laws for simple and multistage reactions in homogeneous systems at constant temperatures and constant volume with detailed consideration of photoreactions and of the methods for evaluation of kinetic measurements. Basic knowledge of kinetics is a prerequisite for its understanding; theories of the molecular course of elementary reactions are not a subject of this textbook.

The first part describes, with numerous examples, first simple and equilibrium reactions, then parallel and successive reactions that can be traced back to two linearly independent steps. The method used for setting up the differential equations is always simple and clear, being assisted by a rectangular scheme of stoichiometric coefficients. The result of integration is set out without explanation, but in more difficult cases with brief references to the method or the literature. Diagrams showing the relation between the extents of reaction are used to explain multistage systems. Relaxation processes are not considered in the discussion of approximation methods for integrating differential equations.

In the second part of the book, after a brief introduction to photochemical primary processes, the quantum yields are derived schematically again with use of examples, for simple and complicated photoreactions, and there is a rather detailed explanation of the integration of differential equations that describe the relation between concentration, time, extinction coefficients, and intensity.

Evaluation of kinetic measurements provides the content of the third and last part. Here the author differentiates between analyses of concentration measurements and of physical numerical data, with extinction measurements providing most of the examples. There is an interesting and extensive compilation of the methods used for determining the number of linearly independent partial reactions and reaction orders, and for evaluating the differential equations and the integrated time laws. The possibility of using digital and analog computers is touched on only in passing.

In places the mathematical part the book is difficult to read. It can be recommended for scientists and students interested in kinetic measurements.

Gerhard Platz [NB 270 IE]

Comprehensive Biochemistry. Vol. 31. A History of Biochemistry. Part III: History of the Identification of the Sources of Free Energy in Organisms. Edited by *M. Florkin* and *E. H. Stotz*. Elsevier Scientific Publ. Comp., Amsterdam 1975. 1st Edit., XX, 475 pp., 170 tables, 42 figs., 3 tables, bound, Dfl. 130.—.

Following the establishment of elementary cell constituents and localization of the signs of life of the cell, development of ideas on the energy balance became one of the fundamental concepts in biochemistry that was just becoming an independent science. Following *Lavoisier*'s classical work, with its nevertheless misleading equation of organisms and heat engines, intuition and feedback of critical testing brought biochemistry by trial and error onto intersecting paths—with constant interaction of the state of theoretical knowledge and the methodical progress of related sciences.

This third part of the History of Biochemistry pictures the intertwining connections in a manner such that it is hard to decide which to admire more: the enthusiasm and detailed knowledge of the world-ranging author *M. Florkin* or his critical and just assessment of the great controversies—he had often known the protagonists personally, so that he describes the theses and arguments and often the final settlement of polemics and disputed problems with stimulation derived from his own experience. His knowledge of the world is also shown in his judgments on the formation of scientific "schools" and the role of independent Institutions in and for research. It is found again and again that naive and incorrect interpretations devised by scientists fettered to their times became fruitful in independent heads—provided they were kept on the shoulders'—but is is found also that, as in other fields of endeavor, apparently trouble-free genius is the crowning achievement of long development and thus actually a very conservative and hoarding, though also open-minded, spirit. He is able to give the all too narrow forms of thought an infusion from new disciplines and thus to uproot previously fixed concepts. In this area lies the recognition that energy-generating processes are centered in specific structures whose organization is suitably differentiated and that they need phosphoric acid, which is bound in "energy-rich" form in the processes of anaerobic, respiratory and photocontrolled phosphorylation and can thus serve as the driving force of the isothermal chemical power machine.

The present volume, packed with material and easy to read, is an outstanding enrichment of the total work[*], undoubtedly a pioneering performance, based on intense activity, pleasure in aphoristic penetration, and brilliant skill in presentation, with convincing and stimulating effects. These are not found elsewhere covering such a wide span. Finally, an extensive portrait section promotes interest in this book as a picture book and for studies of physiognomy.

Lothar Jaenicke [NB 282 IE]

[*] Cf. Angew. Chem. internat. Edit. *14*, 190 (1975).

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Solutions and Solubilities, Part I. Edited by *M. R. J. Dack*. Vol. VIII of the series "Techniques of Chemistry". Edited by *A. Weissberger*. John Wiley & Sons, New York 1975. XII, 475 pp., bound, £ 16.00.

Physical Chemistry. An Advanced Treatise. Edited by *H. Eyring, D. Henderson*, and *W. Jost*. Vol. VII: Reactions in Condensed Phases. Academic Press, New York 1975. XXII, 794 pp., bound, $ 58.00.

Physical Chemistry. An Advanced Treatise. Edited by *H. Eyring, D. Henderson*, and *W. Jost*. Vol. XIB: Mathematical Methods. Academic Press, New York 1975. XX, 565—1151 pp., bound, $ 47.00.

Pollution Control in the Asbestos, Cement, Glass and Allied Mineral Industries. By *M. Sittig.* Pollution Technology Review No. 19. Noyes Data Corporation, Park Ridge 1975. IX, 333 pp., bound, $ 36.00.

Detergency—Theory and Test Methods, Part II. Edited by *W. G. Cutler* and *R. C. Davis.* Vol. 5 of the series "Surfactant Science Series". Edited by *M. J. Schick* and *F. M. Fowkes.* Marcel Dekker, New York 1975. XI, 727 pp., bound, $ 21.75.

Oil from Shale and Tar Sands. By *E. M. Perrini.* Chemical Technology Review No. 51. Noyes Data Corporation, Park Ridge 1975. X, 392 pp., bound, $ 36.00.

Radiochemistry, Vol. 2. Senior Reporter: *G. W. A. Newton.* The Chemical Society, London 1975. VIII, 248 pp., bound, £ 13.00.—A volume of the series "Specialist Periodical Reports".

Natural Products Chemistry, Vol. 2. Edited by *K. Nakanishi, T. Goto, S. Itô, S. Natori,* and *S. Nozoe.* Kodansha, Tokio/ Academic Press, New York 1975. X, 586 pp., bound, $ 34.00.

Waste Oil Recovery and Disposal. By *V. S. Kimball.* Pollution Technology Review No. 20. Noyes Data Corporation, Park Ridge 1975. X, 270 pp., bound, $ 24.00.

Methodicum Chimicum. Edited by *F. Korte.* Band 6: C—N-Verbindungen. Edited by *F. Zymalkowski.* Georg Thieme Verlag, Stuttgart/Academic Press, New York 1974. VIII, 864 pp., bound, DM 390.00.

Festkörperthermodynamik. Chemie des festen Zustandes. By *H. Schmalzried* and *A. Nawrotsky.* Verlag Chemie GmbH, Weinheim 1975. X, 269 pp., bound, DM 78.00.

Index of Vibrational Spectra of Inorganic and Organometallic Compounds, Vol. 2. By *N. N. Greenwood* and *E. J. F. Ross.* Butterworths, London 1975. VII, 908 pp., bound, £ 40.00.

Allgemeine und Anorganische Chemie. By *V. Gutmann* and *E. Hengge.* Verlag Chemie GmbH, Weinheim 1975. 2nd new and revised edition, XI, 397 pp., stitched, DM 39.00.

Interfacial Electrochemistry. An Experimental Approach. By *E. Gileadi, E. Kirowa-Eisner,* and *J. Penciner.* Addison-Wesley Publishing Co., Reading, Mass. 1975. XVIII, 525 pp., bound, $ 19.50/stitched, $ 13.50.

Gmelins Handbuch der Anorganischen Chemie. Supplementary Volume 19: Borverbindungen. Part 3: Verbindungen des Bor mit den Nichtmetallen S, Se, Te, P, As, Sb, Si und mit Metallen. Springer-Verlag, Berlin 1975. 8th Edit., VI, X, 201 pp., bound, DM 343.00.

Atom-Absorptions-Spektroskopie. By *B. Welz.* Verlag Chemie GmbH, Weinheim 1975. 2nd completely new and revised edit., XII, 269 pp., bound, DM 68.00.

Molecular Association, Vol. 1. Edited by *R. Foster.* Academic Press, New York 1975. XIV, 365 pp., bound, $ 31.25.

Molecular Spectroscopy, Vol. 3. Senior Reporters: *D. A. Long, R. F. Barrow,* and *D. J. Millen.* The Chemical Society, London 1975. XV, 588 pp., bound, £ 24.00.—A volume of the series "Specialist Periodical Reports".

Das lachende Labor. By *H.-H. Vogt.* Aulis Verlag Deubner & Co. KG, Köln 1975. 106 pp., bound, DM 16.80.

Warning on copyright

Before photocopying, xerocopying or reproducing an article from this journal please check whether you may be violating the legal provisions of copyright and thus rendering yourself liable to prosecution.
Copyright law allows the photocopying of individual articles only, and then only as single copies for private or personal use. The production of copies for any other purpose is not permitted without payment of copyright fees.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. - Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 14036, Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson.*

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and 24/28 Oval Road, London NW1, England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*), D-6940 Weinheim, Pappelallee 3, P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 11
November 1975
Pages 721–774

Tetracyclines: Chemistry, Biochemistry, and Structure-Activity Relations[**]

By Walter Dürckheimer[*]

Tetracycline antibiotics continue to play an important role in human and veterinary medicine and in animal nutrition. The classical tetracyclines obtained by fermentation have been supplemented by products of partial synthesis which provide, in particular, the advantages of better pharmacokinetic properties and greater tolerance. Following a brief review of older work, the present article describes partial and total syntheses of tetracyclines, the influence of electronic, steric, and lipophilic factors and of complex formation on biological activity. The inhibition of biochemical systems invoked in interpretation of the mode of action of tetracyclines and problems involved in the development of resistance are discussed.

1. Introduction

The antibiotic era dawned about 30 years ago, the prototypes of most antibiotics significant in modern therapy being discovered between 1940 and 1960. Characteristically, a rapid succession of discoveries was closely followed by practical implementation.

Since 1960 relatively few antibiotics of thoroughly novel structure and action have come into use, although the number of new microbial metabolites being discovered has not slackened off[1]. One of the main reasons for this phenomenon is that the stipulations imposed on new antibiotics have steadily become more stringent. Toxicity, pharmacokinetics, stability, purity, and metabolism occupy central positions in their assessment. The time and costs incurred in developing a new antibiotic have increased enormously.

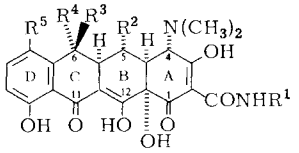
[*] Dr. W. Dürckheimer
Hoechst AG
623 Frankfurt a. M.-Höchst 80, Postfach (Germany)

[**] Based on a lecture presented to the Gesellschaft Deutscher Naturforscher und Ärzte at Berlin on September 17, 1974.

In 1945 *Waksman*[2] stated that much of the responsibility for further development of antibiotics would rest with chemists, who would recognize these natural products as working models and optimize their action by chemical modification or total synthesis. This hypothesis has proved fruitful in many cases: the advances during the last decade have been achieved mainly by chemical modifications of the classical antibiotics.

2. Discovery and Elucidation of Structure

The first tetracycline was aureomycin *(1)* (Table 1), isolated by *Duggar*[3] in 1948 from the culture filtrate of *Streptomyces aureofaciens*. Terramycin *(2)* was isolated by *Finlay et al.*[4] in 1950 from *S. rimosus*. It was the first member of this class of compounds whose structure was elucidated by *Woodward* and a research team at Chas. Pfizer and Co.[5]. The prototype compound tetracycline *(3)* was first prepared by catalytic hydrogenation of aureomycin *(1)*[6, 7], but shortly afterwards it became accessible by fermentation[8]. In 1957 *McCormick et al.*[9] discovered 6-demethylchlortetracycline *(4)*, a metabolite of a *S. aureofaciens* mutant.



(1)–(8)

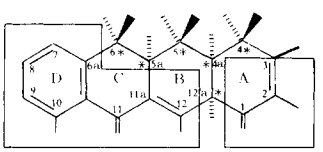
Table 1. Therapeutically important tetracyclines (1)—(8).

	R^1	R^2	R^3	R^4	R^5	Abbr. chemical name	Abbreviation	Trade name [a]	Year of discovery
(1)	H	H	OH	CH_3	Cl	Chlortetracycline	CTC	Aureomycin	1948
(2)	H	OH	OH	CH_3	H	Oxytetracycline	OTC	Terramycin, Terravenös, Vendarcin, Macocyn	1950
(3)	H	H	OH	CH_3	H	Tetracycline	TC	Achromycin, Hostacycline, Supramycin, Tetralution, Tetracitro, Tefilin	1953
(4)	H	H	OH	H	Cl	Demethylchlortetracycline	DMCT	Ledermycin	1957
(5)	CH_2-Pyrrolidino	H	OH	CH_3	H	Rolitetracycline, Pyrrolidinomethyltetracycline	PMT	Reverin	1956
(6)	H	OH	CH_2=		H	Methacycline	MOTC	Rondomycin	1961
(7)	H	OH	H	CH_3	H	Doxycycline	DOOTC	Vibramycin Vibravenös	1963
(8)	H	H	H	H	$N(CH_3)_2$	Minocycline	MITC	Klinomycin	1967

[a] Rote Liste 1974. Ed. Cantor, Aulendorf/Württ., 11187B-11213B.

3. Parent Structure

As the name indicates, tetracyclines are derived from a system (9) of four linearly annelated six-membered rings, namely 1,4,4a,5,5a,6,11,12a-octahydronaphthacene containing a characteristic arrangement of double bonds. Two distinct chromophoric regions A and BCD are separated by the sp^3 carbon atom 12a. The carbon atoms 4,4a,5,5a,6,12a become asymmetric on appropriate substitution. Terramycin (2) contains six asymmetric centers, while aureomycin (1), tetracycline (3), and demethylchlortetracycline (4) each contain five such centers, which make the molecule optically active. The absolute configuration was determined by X-ray structure analysis[10–14] and supplemented by NMR[15,16] and CD measurements[17].

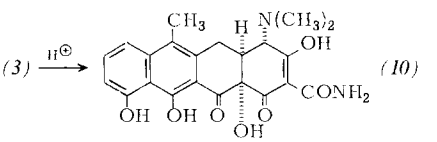


(9)

4. Characteristic Physical and Chemical Properties

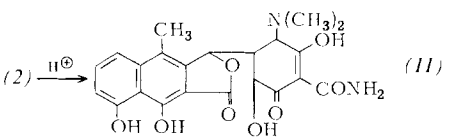
The tetracyclines are yellow, odorless, bitter, light-sensitive, crystalline compounds. The natural members are sparingly soluble (*ca.* 1 mg/ml) in the physiological pH region. They show amphoteric behavior because of the acidic substituents and the basic dimethylamino group. The measured pK_a values of, for example, tetracycline are 3.30, 7.68, and 9.69 and the isoelectric point is 4.8[18]. The UV spectra of tetracyclines are highly characteristic: the BCD chromophore absorbs at 225, 285, 320, and 360 nm and the ring A chromophore at 262 nm; a band at 275 nm is composed of several absorptions[19]. The fluorescence of tetracyclines, which is enhanced by complexing with cations, can be utilized for qualitative and quantitative determination of these substances in drugs and biological material (see Section 7.1). Chemical and physical methods of tetracycline assay have been summarized by *Hughes* and *Wilson*[20].

Tetracyclines undergo a series of degradations and rearrangements under mild conditions, with interesting differences between the individual members (for reviews see [21–28]).



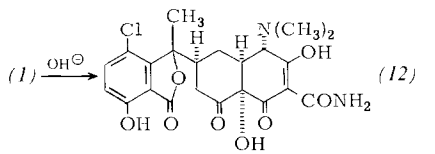
(3) $\xrightarrow{H^\oplus}$ (10)

At pH ≤ 2 tetracyclines containing a hydroxyl group at C-6 readily eliminate water with concomitant aromatization of ring C to form anhydrotetracyclines, *e.g.* (10) from tetracycline (3). From oxytetracycline (2) the epimeric α- and β-apooxytetracyclines (11) are formed in a series of rapid successive reactions and are isolated in place of the anhydro compound.



(2) $\xrightarrow{H^\oplus}$ (11)

In the presence of bases the tetracyclines isomerize to isotetracyclines; chlortetracycline (1) is particularly labile and forms isochlortetracycline (12) even when warmed at pH 7.5. Compounds without a methyl group at C-6 are more stable towards bases. Epimerization at C-4 occurs readily at pH values between 2 and 6; this is a reversible first-order reaction and is influenced by phosphate, citrate[29], multivalent cations[30], neutral compounds such as urea[31], and solubilizers[32].



(1) $\xrightarrow{OH^\ominus}$ (12)

Strong intramolecular interactions occurring between the acidic hydroxyl groups at positions 3, 10, and 12 and neighboring carbonyl groups lead to greatly diminished reactivity towards reagents typical for these groups. The 4-dimethylamino and the 12a-hydroxy groups can be removed by reduction.

5. Antimicrobial Spectrum and Application

The tetracyclines opened a new era of antibacterial chemotherapy. They are active orally and parenterally, are relatively well tolerated[33, 34], and their antimicrobial spectrum[34] was broader than that of any other antibiotic then known. Together with the penicillins they therefore became the most widely used antibiotics.

In accord with their mutual chemical similarity all tetracyclines have a very similar activity. It includes gram-positive and gram-negative bacteria and cocci, spirochetes, rickettsiae, large viruses, and mycoplasma, has marked gaps in the activity on species of Pseudomonads, Proteus, and Salmonella, but is only exceeded by the spectrum of chloramphenicol. Mycobacteria, protozoa, fungi, and yeasts are resistant. The individual tetracyclines differ less in their potency than in pharmacokinetic properties such as resorption, tissue diffusion, and elimination, and this is also true for the partially synthetic members of the group. The main indications for their use are infections due to *E. coli* and *Haemophilus influenzae*, infections of the bile duct, bacterial respiratory disorders including bronchitis prophylaxis, mixed infections arising from the mouth, pharynx, or intestinal tract, brucellosis, tularemia, plague and other pasteurelloses, leptospirosis, lymphogranuloma inguinale, cholera, and rickettsiosis. Nowadays tetracyclines are no longer the drugs of first choice for treatment of staphylococcal, streptococcal, or pneumococcal infections[35].

6. Methods of Enhancing Activity

In spite of their broad spectrum of activity, tetracyclines are by no means ideal chemotherapeutic agents for the cure of all bacterial infections. As the years passed by various weaknesses and side effects were observed on their frequent use. Since clinicians make ever-greater demands on activity and safety, attempts have been made worldwide to develop new tetracyclines with improved properties. In the course of this work the structures of these molecules have been modified by chemical or enzymatic methods to correlate the individual structural elements with biological activity. Such studies have also made an important contribution to the elucidation of their mode of action. What were the aims of the individual studies in this field?

1) To enhance the inhibitory action (MIC value) in order to attack less sensitive microorganisms.

2) To overcome secondary resistance, which has increased enormously owing to the frequent administration of tetracyclines.

3) To exclude or at least diminish side effects.

4) To improve resorption and to optimize pharmacokinetics.

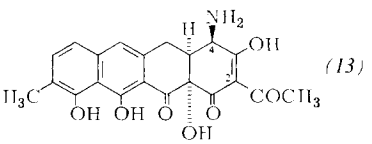
5) To enhance stability and solubility in order to improve application and "bioavailability".

6.1. Microbiological Methods

Some twenty new tetracyclines have been obtained by isolation of new strains, mutation of known *Streptomyces* strains, variation of fermentation media, and addition of precursors and inhibitors; some of these are of medicinal interest, others only for the study of biogenesis or as synthetic precursors[35–39].

6-Demethyltetracycline *(4)*, $R^5 = H$, and 6-demethylchlortetracycline *(4)* have been isolated from an *S. aureofaciens* mutant[9]. The latter drug *(4)* has excellent antibacterial properties and has found wide application as an oral, broad-spectrum antibiotic; it is more stable to acids and bases and gives a longer-lasting blood level than tetracycline, but leads more often to photodermatosis[33, 40].

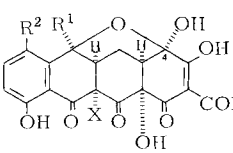
Chelocardin *(13)*[41, 42], a broad-spectrum antibiotic from a *Norcardia sulphurea* strain, was isolated as early as 1956—its structure was determined in 1970[43]. Its antimicrobial spectrum resembles that of chloramphenicol. Chelocardin has good *in-vivo* activity, but it produces liver damage in animals and was therefore not developed further. The primary 4-amino group with the β-configuration (natural tetracyclines have dimethylamino groups in the α-configuration) and the aromatic ring C are worth noting.



(13)

6.2. Partial Syntheses

The route used most often for the development of new tetracyclines has been chemical modification of compounds readily accessible by fermentation, namely tetracycline *(3)*, oxytetracycline *(2)*, 6-demethyltetracycline *(4)*, $R^5 = H$, and 6-demethylchlortetracycline *(4)*. Hydrogenolysis of the benzylic hydroxyl groups on C-6 in the two last-mentioned tetracyclines provided an entry into a series of acid-stable 6-deoxytetracyclines[44–46] which undergo electrophilic substitutions at positions 7 and 9[23, 25]. Addition can be effected to the exocyclic double bond of methacycline *(6)*[47]. Tetracycloxides of type *(14)* were favorable starting materials for modifications at position 4 of ring A[48, 49]; numerous derivatives that are readily soluble in water at physiological pH have been prepared from tetracyclines by the Mannich reaction[50, 51].



(14), $R^1 = CH_3$, H; $R^2 = Cl$, H; X = H, Cl, Br

In the following sections only those products of partial synthesis are discussed which have found worldwide application owing to their excellent antibiotic properties.

Pyrrolidinomethyltetracycline *(5)* (Reverin) was the first partially synthetic tetracycline. It is produced by a Mannich reaction of tetracycline *(3)*, formaldehyde, and pyrrolidine[50–52]. Its antimicrobial spectrum is almost the same as that of tetracycline[53], but its great advantage over the latter is its extremely high solubility in water at physiological pH. Reverin is an ideal form for parenteral administration of tetracycline, especially in acute potentially lethal infections demanding rapid onset of action[54–57]. Although it is completely stable as a solid, Reverin slowly decomposes in aqueous solutions to afford an equilibrium mixture[58] with regeneration of tetracycline[59–61].

Methacycline *(6)* and doxycyclin *(7)* are further developments from terramycin *(2)*. Methacycline *(6)* is obtained from 11a-chloro-5-hydroxytetracycline by dehydration with hydrogen fluoride and subsequent dehalogenation by mild reducing agents[62]. Doxycycline *(7)* is formed by radical addition of thiols to the 6-methylene double bond of methacycline *(6)* and subsequent desulfuration with Raney nickel[47].

Methacycline *(6)* is similar to demethylchlortetracycline *(4)* in its bacteriostatic and pharmacokinetic properties[63, 64]. Doxycycline *(7)* has a tetracycline-specific spectrum of activity; it is more efficient than older tetracyclines against some staphylococcal and streptococcal strains that are only slightly sensitive to tetracycline, and in isolated cases against *Enterobacteriaceae*[64, 65]; it is lipophilic and shows a high resorption level, resorption rate, and tissue affinity; its rate of elimination is diminished by strong binding to the serum; the half-life in blood is of the order of 15—20 hours[63, 66-68]; a single dose of 200 mg on the first day and 100 mg on subsequent days usually suffices for adults.

Minocycline *(8)* is the newest member of the tetracycline group. It is obtained by reductive methylation of the nitro compound *(8)*, $R^5 = NO_2$[69]. The antimicrobial spectrum of *(8)* is characterized by enhanced activity towards a series of gram-positive staphylococcal strains that are already resistant to other tetracyclines[70, 71]. As for doxycycline, its most important advantages are pharmacokinetic in nature[71, 72]: the half-life in blood (20 hours) is distinctly longer than those of other tetracyclines; the daily dose for adults is 200 mg.

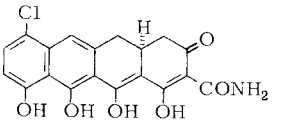
6.3. Total Syntheses

Soon after the structures of the first tetracyclines had been determined the possibility of their total synthesis was considered. Because of the complicated stereochemistry and substitution *Woodward*[73] once described these compounds as a "diabolical concatenation of reactive groupings". The many substituents in the tetracyclines, which render these drugs very sensitive to acidic, alkaline, and reducing reagents, made it hard to find a stereospecific synthesis for this molecular type, for which no synthetic prototype was known.

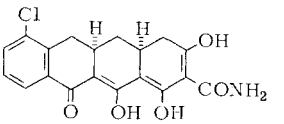
6.3.1. Tetracycline Precursors

The primary aim of total synthesis was construction of simply substituted tetracyclines, some of which are obtained by degradation of naturally occurring tetracyclines.

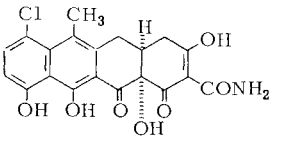
Fields, Kende, Bothe et al.[74-77] succeeded in synthesizing *(15)* and *(16)* in 1959—1961.



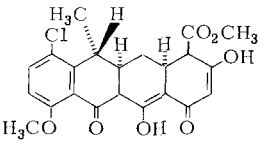
(15)



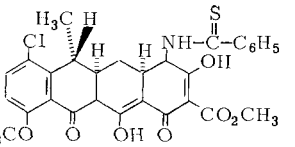
(16)



(17)



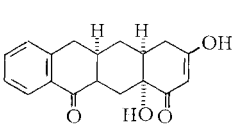
(18)



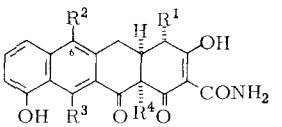
(19)

At about the same time *Muxfeldt*'s group synthesized the precursors *(17)*—*(19)*[22, 78-80].

Shemyakin and a large team of chemists studied the total synthesis of tetracyclines for about a decade. Compounds *(20)*—*(24)* should be mentioned from that work[81-85].



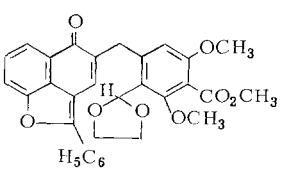
(20)



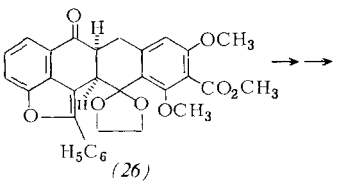
(21), $R^1 = R^2 = R^3 = R^4 = H$
(22), $R^1 = R^3 = R^4 = H$, $R^2 = CH_3$
(23), $R^1 = N(CH_3)_2$, $R^2 = CH_3$, $R^3 = OH$, $R^4 = H$
(24), $R^1 = H$, $R^2 = CH_3$, $R^3 = R^4 = OH$

Compounds *(20)*, *(21)*, and *(22)* contain an incomplete keto-enol system, and moreover, the 4-dimethylamino group that is important for antibiotic activity is still missing. *(23)* can be hydroxylated at position 12a. Since anhydrotetracyclines can be transformed into tetracyclines by photooxidation at C-6 and subsequent reduction of the hydroperoxide[86, 87], *Shemyakin* saw a formal total synthesis of DL-tetracycline in the synthesis of *(23)*; however, the photooxidation has been effected only with chlortetracyclines and, according to *Muxfeldt*[88], succeeds only in this case.

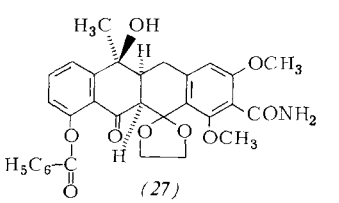
In 1957 *Barton* and his school began work on the total synthesis[89]. Their strategy was to build up a four-ring system in which rings A and D are aromatic and to try partial



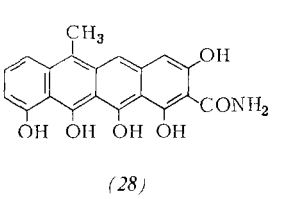
(25)



(26)



(27)



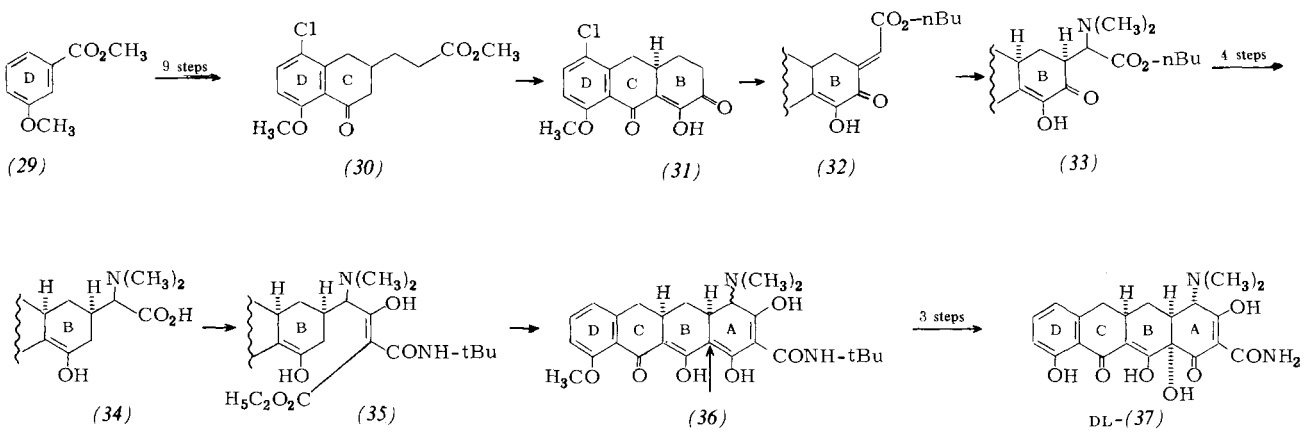
(28)

hydrogenation of ring A later. After many unsuccessful attempts a precursor was found in the easily accessible acetal *(25)* which furnished the tetracycle *(26)* on proton-catalyzed photocyclization. The stereospecific course of the reaction was demonstrated by X-ray structure analysis of the products.

In a sequence of reactions [ester cleavage and amidation (82%), methylation at C-6 by CH_3Li (54%), ozonization and reduction of the ozonide (30%)] the compound *(27)* was obtained, which contains the structural elements of tetracycline except for ring A; the total yield based on 1,5-naphthalenediol amounted to *ca.* 0.4%. On removal of the protecting groups *(27)* was transformed into the fully aromatic 6-methylpretetramide *(28)*, which is the first isolable intermediate in the biosynthesis of tetracycline.

6.3.2. Total Synthesis of DL-6-Demethyl-6-deoxytetracycline by the Woodward/Pfizer Method

In 1962, after a decade of intensive experimentation, *Woodward* and a research team at Chas. Pfizer and Co. succeeded in a total synthesis of the simplest, biologically active DL-6-demethyl-6-deoxytetracycline *(37)*[90, 91]. Details of the synthesis were published in 1968[92]. In 1965 *Muxfeldt* and *Rogalski*[93] were able to obtain this compound in a simpler manner.



The Woodward/Pfizer synthesis begins with the aromatic ring D, onto which rings C, B, and A are built on stepwise by condensation reactions. Methyl *m*-methoxybenzoate *(29)* is converted in nine steps (mostly Claisen condensations) into the tetralone *(30)* which is condensed to the tricycle *(31)* by oxalic ester and sodium hydride. Stepwise construction of the last ring (A) was the most difficult problem, since all the ring elements are substituted and C-4, C-4a, and C-12a are asymmetric. *n*-Butyl glyoxylate is condensed with *(31)* to afford *(32)*, and dimethylamine then adds stereospecifically to the exocyclic double bond, giving *(33)*; the bulky side chain takes up the equatorial and the hydrogen the axial position in this reaction. The acid *(34)* is obtained from *(33)* by reduction of the keto group in ring B and hydrolysis of the ester, and is converted after reductive dehalogenation into a mixed anhydride which yields *(35)* on reaction with ethyl *N*-(*tert*-butyl)malonamate. Cyclization of *(35)* by use of sodium hydride as a condensation agent gives the tetracycline *(36)*.

Stereospecific introduction of the hydroxyl group at C-12a (see arrow) by autoxidation, inversion of the 4-dimethylamino group from the β- to the natural α-configuration by way of Ca complexes, and removal of the protecting groups were difficult steps necessitating chromatographic separations and a countercurrent distribution.

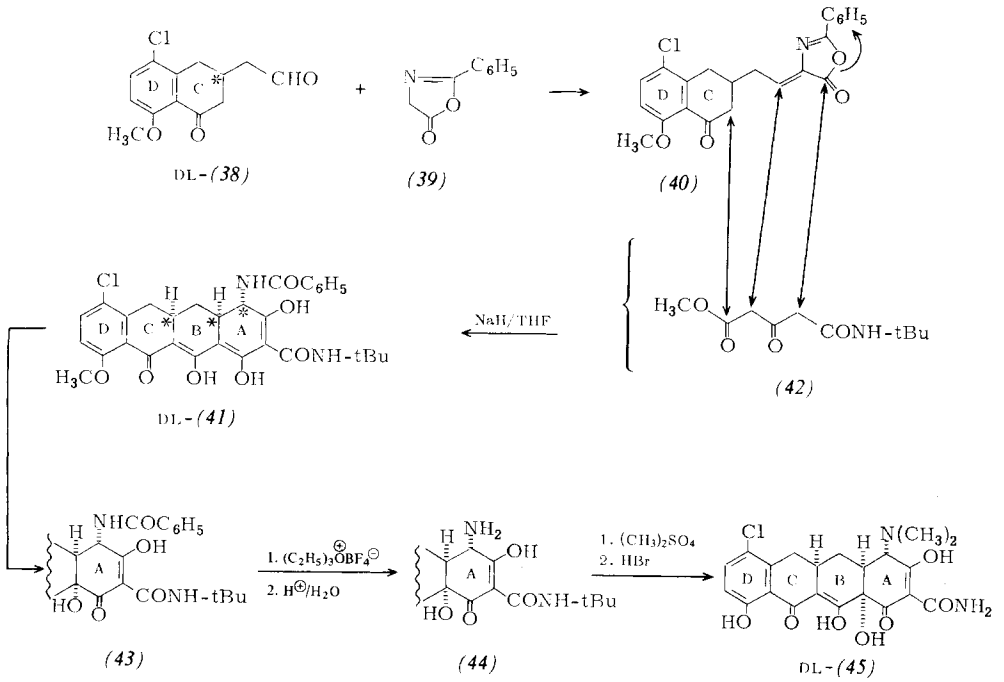
DL-6-Demethyl-6-deoxytetracycline *(37)* could be obtained only in mg quantities; the overall yield from the 22-step synthesis amounted to *ca.* 10^{-3}%, *i.e.* a kilogram of starting material *(29)* affords only *ca.* 10 mg of the end product *(37)*. When tested biologically, this product *(37)* had 50% of the activity of the optically active 6-demethyl-6-deoxytetracycline obtained from natural material; clearly, only the enantiomer with the natural configurations at the asymmetric centers is biologically active

6.3.3. Total Synthesis of DL-6-Demethyl-6-deoxychlortetracycline by *Muxfeldt*'s Method

After many years of intensive preliminary experiments *Muxfeldt* and his school developed an extremely useful method by which not only natural tetracyclines, *e.g.* the complicated terramycin with its six asymmetric centers, but also new types of tetracyclines can be prepared.

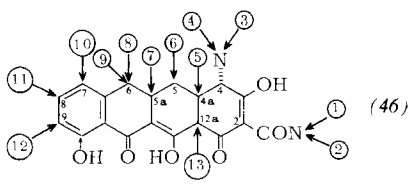
The principle of this synthesis will be illustrated here for the case of DL-1,6-demethyl-6-deoxychlortetracycline *(45)*[93, 94], which is built up from the fragments *(38)*, *(39)*, and *(42)* that are each relatively easily prepared. *(38)* and *(39)* condense to give the intermediate *(40)*, reaction of which with the glutaramate *(42)* affords the tetracycle *(41)* by double ring closure. This elegant condensation in which three new C—C bonds are produced in a single step (as indicated by the arrows) is the heart of the synthesis. The additions occur stereounspecifically, *i.e.* the eight possible stereoisomers are formed in different amounts, but their number is reduced to four (=two pairs of enantiomers) by epimerization of the 4-benzoylamino group in pyridine[95]. After this rearrangement the hydrogen atoms on C-4 and C-4a are *trans* to one another in all four isomers. The desired pair of enantiomers *(41)* is isolated by fractional crystallization or by chromatography. Introduction of the 12a-hydroxyl group, giving *(43)*, is effected smoothly by autoxidation in DMF in the presence of sodium hydride. After debenzoylation, methylation of the amino group, and removal of the protecting groups by hydrogen bromide, the product *(45)* is obtained as its hydrobromide.

This synthesis can be set up to yield very many different products by using differently substituted starting units. In principle, many positions in the molecule can be varied, as



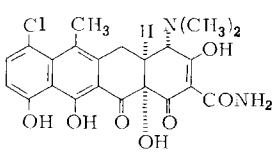
DL-(38) (39) (40) (42) DL-(41) (43) (44) DL-(45)

indicated by arrows in the general formula *(46)*, so that it becomes possible to build up "tailor-made" tetracyclines. Examples are terramycin *(2)*, the most highly substituted and chemically the most reactive member of the tetracycline

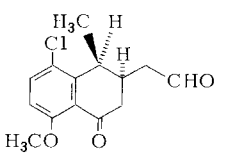


(46)

family, which *Muxfeldt et al.*[96] synthesized in racemic form in 1968, and also DL-anhydroaureomycin *(48)*[97]. Since this anhydro compound regenerates aureomycin by photooxida-



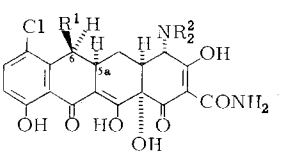
DL-(48)



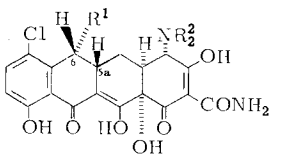
DL-(47)

tion and subsequent reduction[86, 87], the synthesis of *(48)* can also be regarded as a total synthesis of DL-aureomycin.

For further elucidation of structure-activity relations, a group at Hoechst AG[98] synthesized new tetracyclines of the normal, 5a-*epi*-, and 6-*epi*-series. Starting from the aldehydes *(38)* and *(47)* afforded the di-*N*-demethyltetracyclines *(49)*, *(50)*, *(52)*, and *(53)*, and, by their alkylation, the derivatives *(45)*, *(51)*, and *(54)*. Whereas tetracyclines epimerize readily, these four nortetracyclines with the natural α-configuration of the 4-amino group are stable.

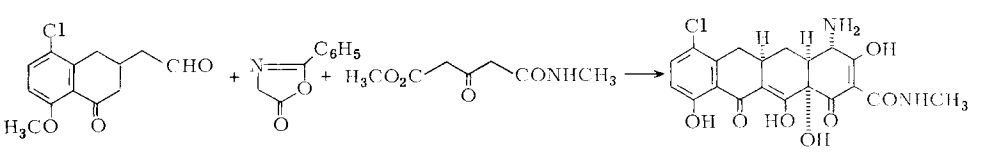


DL-(49), $R^1 = R^2 = H$
DL-(50), $R^1 = CH_3$, $R^2 = H$
DL-(45), $R^1 = H$, $R^2 = CH_3$
DL-(51), $R^1 = R^2 = CH_3$

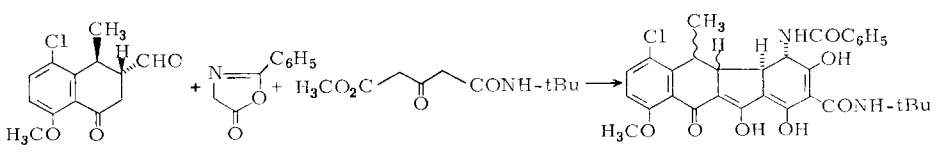


DL-(52), $R^1 = CH_3$, $R^2 = H$
DL-(53), $R^1 = R^2 = H$
DL-(54), $R^1 = H$, $R^2 = C_2H_5$

Treatment of the *N*-methylated component *(55)* with the aldehyde *(38)* and the azlactone *(39)* provided a successful synthesis of a tetracycline *(56)* that is monomethylated on the 2-carboxamide group[99]. Tetracyclines with a contracted ring B, *e. g. (59)*, are obtained by using the aldehyde *(57)* which lacks one carbon atom of the side chain[100].



(38) (39) (55) DL-(56)



(57) (39) (58) DL-(59)

The synthetic tetracyclines *(45)*, *(49)* to *(54)*, and *(56)* are appreciably more lipophilic than the natural members. In the serial dilution test, except for *(54)*, they show the same activity spectrum as tetracycline, and, in addition, a high activity against some highly resistant bacterial strains. The *in vitro* activity was reduced on the addition of serum and was disappointing in animal tests[101]; the cause of this seems to lie in a strong, unspecific binding of these materials to serum and tissue constituents, so that the concentration of free chemotherapeutically active tetracycline does not suffice for bacteriostasis in the organism.

Muxfeldt et al. do not always give the overall yields of their total syntheses. In the series studied at Hoechst[98-100] these are of the order of 0.05—0.10% and thus about two orders of magnitude better than those in the Woodward/Pfizer synthesis: one obtains about 1 g of the end product from one kilogram of the starting material. Tetracycline derivatives can be prepared in the laboratory in 10 to 100 g quantities. Special advantages of the *Muxfeldt* synthesis are easy purification of the intermediates and rapid separation of isomers by fractional crystallization.

7. Complex Formation

Tetracyclines have a great tendency to form reversible complexes with cations and anions as well as with substances of low or high molecular weight[17, 19, 23, 102-113]. This property is important for understanding their antibiotic activity, pharmacokinetics, and side effects. A selection of complex-forming agents is shown in Table 2.

Table 2. Complexing agents for tetracyclines.

Metal cations:	Fe^{3+}, Fe^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, Mn^{2+}, Mg^{2+}, Ca^{2+}, Be^{2+}, Al^{3+}, Zr^{4+}, $^{99}Tc^{4+}$
Anions:	Phosphate, citrate, salicylate, *p*-hydroxybenzoate, saccharin anion
Neutral compounds:	Caffeine, urea, thiourea, polyvinylpyrrolidone
Biopolymers:	Serum albumin, lipoproteins, globulins, RNA

7.1. Metal Cations

The complex formation depends on the nature and charge of the cation and on the pH of the solution. Tetracyclines do not form complexes below pH 3. In the pH region between 3 and 7.5 the phenol-diketone system of rings BCD binds one cation. If the 4-dimethylamino group is deprotonated by an increase in pH a further cation can be bound by the combined action of this group and the 12a-hydroxyl group in the *cis*-position thereto. 4-*epi*-Tetracyclines, whose 4- and 12a-substituents are *trans*-related, form only 1:1 complexes, as do the biologically inactive isotetracyclines such as *(12)*. Oxytetracyclines possess at position 5 an additional ligand for complex formation. Above pH 7, Mg^{2+} ions form a chelate between the 5- and the 12a-hydroxyl group. According to *Noseworthy*[112], the reverse epimerization of 4-*epi*-tetracyclines in alkaline solution proceeds *via* Ca complexes.

Most of the metal complexes fluoresce more strongly than the tetracyclines themselves, and this effect is utilized in the analytical determination of these antibiotics in drugs and biological material[20, 113]. As little as 10^{-9} g of tetracycline can be detected by means of the Be complexes in an ammonium buffer (pH 7)[114]. *Caswell et al.*[115, 116] showed that the fluorescence of Ca^{2+} and Mg^{2+} chlortetracycline is a function of the polarity of the surrounding milieu and can be used for the detection of these ions in cell membranes. A complexometric method involving nickel ions for the determination of tetracyclines has been described by *Stahlavska et al.*[117].

Simultaneous administration of tetracyclines and foodstuffs or drugs that contain metal compounds can lead to disturbances[33]. For example, the serum level is reduced by 50—90% on simultaneous administration of tetracyclines and iron(II) sulfate[118, 119]; and milk, which is rich in Ca and Mg ions, reduces the serum level of tetracycline, methacycline, and oxytetracycline[120]. A decrease in the bactericidal action of the serum itself by tetracyclines, and in particular by doxycycline, is ascribed to complex formation with the magnesium and calcium ions in the blood[121].

It has long been known that tetracyclines are incorporated as calcium phosphate complexes into tissues rich in Ca^{2+} ions *e.g.* the growing bones and embryo teeth of the newborn child as well as in the period of rapid bone growth and the first dentition; the bones and teeth can be damaged in this way[33]; administration of these antibiotics is no longer recommended for children up to eight years of age or for pregnant women.

7.2. Anions and Neutral Substances

Anions such as phosphate, citrate, salicylate, *p*-hydroxybenzoate, and the saccharin anion, as well as natural products such as caffeine, *N*-methylpyrrolidone, urea, and thiourea, form weak complexes with tetracyclines and increase the latters' solubility[122]. Polyvinylpyrrolidone[123], which serves as a plasma expander, is used to improve the solubility in preparations of oxytetracycline (Vendarcin)[124] and doxycycline (Vibravenös)[125]. It also increases the stability of the solutions and is said to improve the tissue tolerance of these preparations on parenteral application.

7.3. Biopolymers

The reversible binding of tetracyclines to macromolecular structures in blood and tissues is important for the pharmacokinetics and activity of these substances within the organism. Equilibria of this type are difficult to analyze quantitatively, except for bonding to plasma protein for which several methods of determination have been worked out (dialysis, ultrafiltration, ultracentrifugation, Sephadex gel filtration, electrophoresis)[126].

Tetracyclines can be bound not only to albumin, the chief serum protein, but also to globulins and lipoproteins[127-131]. The bonding to proteins is reversible, dependent on pH and temperature, and a function of the serum concentration[128, 129, 132, 133]. The serum proteins of man and animals differ in their affinity for specific tetracyclines[127].

The binding to serum is hydrophobic in nature, *i.e.* it is increased by apolar lipophilic groups such as alkyl groups and halogen atoms and decreased by polar groups such as hydroxyls and amino groups[128, 129, 134]. It increases with increasing concentrations of Ca^{2+} and Mg^{2+} ions but depends on the nature of the tetracycline derivative. The largest percentage increase in complex formation is found with doxycycline, the smallest with oxytetracycline; the effects with methacycline and minocycline are intermediate between these[132].

The regularities found for serum albumin apply also to the reversible binding of tetracyclines to ribonucleic acid[129].

The influence of serum bonding on the chemotherapeutic activity of antibiotics is still unclear[135-140]. Approximate data about the blood level and serum bonding provide little information about the curative action of a preparation. The current interpretation is that only the unbound antibiotic in the immediate neighborhood of the bacterium in the infected region exerts an antibacterial action; the higher the concentration of the free drug at that point, the better is also the bacteriostasis.

8. Structure-Activity Relations

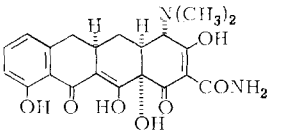
After the synthesis of a tetracycline its biological activity is investigated. The first test of a new preparation is for its antibacterial activity *in vitro*, by means of the serial dilution test, plate diffusion test, streak test, or turbidimetric test[141]. The *M*inimal *I*nhibitory *C*oncentration (MIC in μg/ml) obtained by such a test provides, by itself, no basis for a critical evaluation[142]; its value lies mainly in that it permits a rapid decision whether structural modification of the molecule has led to a partial or complete loss of activity.

When compounds with favorable MIC values comparable with, or better than, those of a standard substance (*e. g.* tetracycline), are found, their activity must be tested on a representative collection of clinically relevant pathogens under standard conditions (*e. g.* standardized inoculation with pathogens, standard nutrient medium). Quantitative activity data from different laboratories have only limited value for intercomparison, because of their strong dependence on the experimental parameters. In the following discussions of structure-activity relationships, therefore, the comparative values are recorded only in qualitative terms (for detailed collections of MIC values see refs.[26, 27, 143-148]).

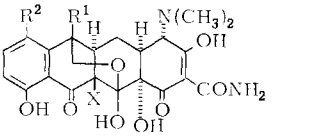
In-vitro results do not suffice for an assessment of tetracyclines. In therapeutic concentrations they act only bacteriostatically and a curative effect follows only by cooperation of the bacteriostasis with the cellular and humoral defense mechanisms of the body. A total assessment comprises data for bacteriological resistance together with pharmacological data on resorption, blood and tissue levels, diffusability, serum binding, elimination, metabolism, side effects, and toxicity. Acquisition of such information requires very demanding animal experiments and measurements on isolated organs, which are naturally carried out only for a few highly active representatives. The final assessment of the value of an antibiotic can be provided only by the doctor after long, careful, and unprejudiced testing in clinical practice.

8.1. Basic Structural Requirements for Activity

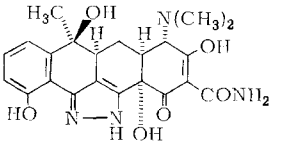
The structurally simplest tetracycline displaying full biological activity is the partially synthetic 6-demethyl-6-deoxytetracycline *(37)*[149]. The linear arrangement of the four rings and the two chromophoric keto-enol systems in ring A and in rings BCD together constitute an important prerequisite for antibiotic activity. All partially or totally synthetic derivatives containing fewer than four rings are inactive. 12a-Deoxytetracycline[150] and 11a-halotetracyclines *(60)*[151] containing a more extended or shorter chromophore have a reduced activity; pyrazolotetracycline *(61)*[152] is inactive.



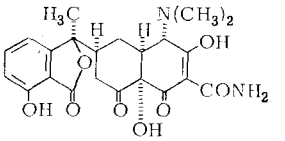
(37)



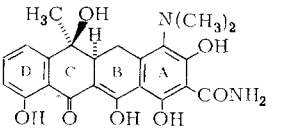
(60), $R^1 = CH_3$, H; R^2 = Cl, H; X = Halogen



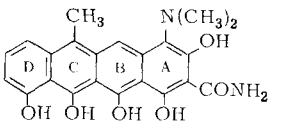
(61)



(62)



(63)

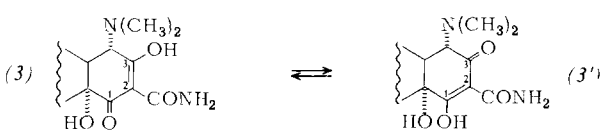


(64)

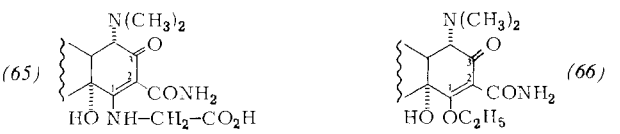
Opening of one ring, to give isotetracycline *(62)*[144], or aromatization of additional rings, to give, *e. g.* 5a,6-anhydrotetracycline *(10)*[153], 4a,12a-anhydrotetracycline *(63)*[154], or 4-dimethylamino-6-methyl-1,3,10,11,12-pentahydroxy-2-naphthacenecarboxamide *(64)*[155], leads to a strong decrease of *in-vitro* activity and to a complete loss of *in-vivo* activity.

8.2. Modifications at Positions 1 and 3

The keto-enol system between carbons 1 and 3 [formulas *(3)* and *(3')*] is strongly delocalized, leading to an extremely low reactivity. Alkylation, giving *(66)*, can be effected by triethyloxonium tetrafluoroborate with base catalysis[156], but the activity is destroyed by this etherification.



(3) ⇌ *(3')*



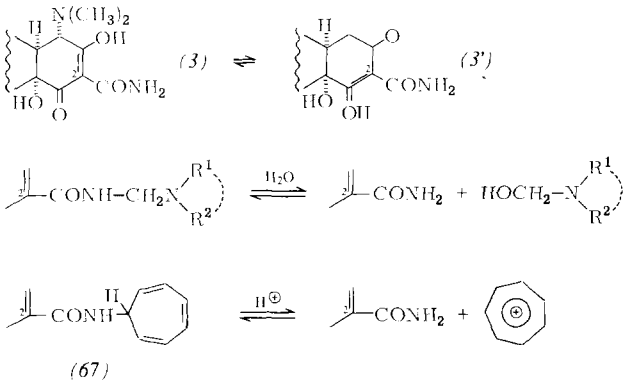
(65) *(66)*

Replacement of the 1-ethoxy group by a glycine residue leads to compound *(65)*, which shows moderate bacteriostasis but is as active as chlortetracycline *(1)* against rickettsia of the type of *Aegyptianella pullorum*[157].

8.3. Modifications at Position 2

Replacement of the 2-carboxamide group by an aldehyde[158], aldimine[159], or an acetyl group[160] leads to gaps in the antimicrobial spectrum. Tetracyclinenitriles[161] are inactive. Replacement of one amide-hydrogen atom by a methyl group has no effect on the activity *in vitro*[99], but larger groups such as *tert*-butyl[47] and cycloheptyl[162] give unfavorable results.

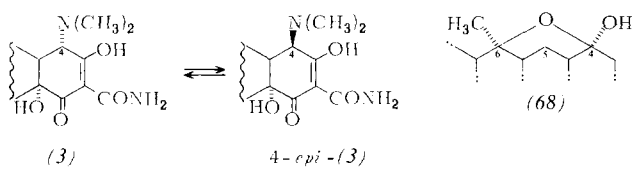
Aminoalkylation of the amide group by a Mannich reaction[50, 51] leads to preparations such as *(5)* which are readily



soluble in water at physiological pH, are hydrolyzed slowly, and have almost the same spectrum of activity as the unsubstituted tetracyclines. *N*-Cycloheptatrienyltetracyclines *(67)*[163] behave similarly to the tetracycline Mannich bases.

8.4. Modifications at Position 4

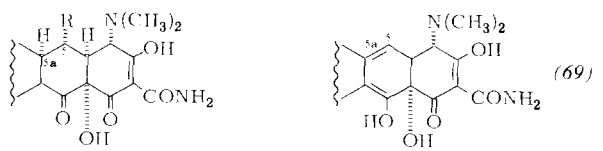
The α-configuration of the 4-dimethylamino group is important for high antibiotic activity: 4-*epi*-tetracyclines have weak inhibitory action *in vitro* and none at all *in vivo*[144]. Replacement of the α-dimethylamino group by a primary amino group has no effect on the *in-vitro* activity[98, 99], but a methylamino[100] or diethylamino group[98] leads to depressed activity. Removal of the amino group[164] or destruction of its basic character by quaternization[164], acylation[100], conversion into an oxime, hydrazone[49] or tetracycloxide *(68)*[48] diminishes or abolishes the activity.



(3) 4-*epi*-*(3)* *(68)*

8.5. Modifications at Positions 5 and 5a

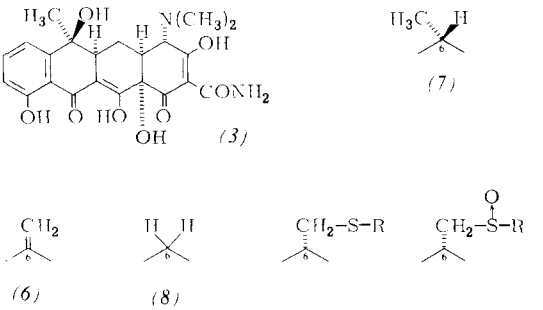
Positions 5 and 5a appear to be not very critical for tetracycline activity. A 5-hydroxyl group, as in terramycin, does not affect the bacteriostatic action[26] but only the stability, absorption, and pharmacokinetics. Acylation of the 5-hydroxyl group provides no advantage. Active as well as inactive derivatives have been described among the 5,5a-didehydrotetracyclines *(69)*; according to *Martell et al.*[165], 5,5a-didehydrotetracycline is inactive, but 5,5a-didehydro-6-*epi*-aureomycin is highly active *in vitro* and *in vivo*. All wholly synthetic 5a-*epi*-tetracyclines[98] show a high activity *in vitro* but prove disappointing in animal experiments[101].



(69)

8.6. Modifications at Position 6

The greatest success in the development of new highly active tetracyclines was provided by modifications at position 6[144]. Neither the 6-methyl nor the hydroxyl group is essential for antibacterial activity. Elimination of the 6-hydroxy group leads to more lipophilic, acid-stable tetracyclines such as doxycycline *(7)* and methacycline *(6)*, which are both prepared from terramycin. 6-*epi*-Doxycycline, with a β-methyl group at C-6,

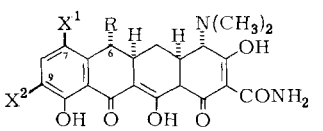


(3) *(7)* *(6)* *(8)*

is less active[166]. Among the 6-demethyltetracyclines, 6-demethylchlortetracycline *(4)* is the most active antibiotic; its hydrogenation leads to the less active 6-deoxy-6-demethyltetracycline *(37)*[44], the starting material for minocycline *(8)*. Larger lipophilic groups (phenyl or benzyl) in position 6 obtained by radical addition of thiols to a 6-methylene group[62] depress the bacteriostatic activity, which is regained on oxidation of the thioether to the sulfoxide[144].

8.7. Modifications at Positions 7 and 9

Many monosubstituted and disubstituted derivatives can be obtained by electrophilic substitution of the acid-stable 6-deoxytetracyclines in position 7 and/or 9[125, 144]. It is remarkable that the activity of tetracyclines is enhanced both by substituents that are strong electron-donors and by those with strong acceptor action. Substitution is more advantageous at position 7 than at position 9. A nitro or dimethylamino group in position 7 provides the greatest enhancement in activity. Thus, minocycline has a dimethylamino group in position 7 and is two to eight times as active as tetracycline against tetracycline-sensitive strains[125, 144].



R = H, CH_3; X^1, X^2 = F, Cl, Br, I, NO_2, $NHCOCH_3$, OH, NH_2, $N(CH_3)_2$, H

Cammarata and *Yau*[167] correlated the inhibitory action of some 7- and 9-substituted tetracyclines with physicochemical parameters. For 7-substituted 6-deoxytetracyclines they derived the following equation:

$$\log K = 0.64\,\sigma^2 + 1.87$$

K is the inhibition constant for *E. coli* strains, determined by using bacterial growth kinetics in the presence of 20 μg/ml for each tetracycline derivative. σ denotes the Hammett constant of the substituent in position 7. In this relationship the unusual feature is that the σ is squared, so that substituents with negative and those with positive σ values increase the activity. A similar equation applies to 9-substituted 6-deoxytetracyclines.

Further regression procedures for correlating structure and activity in the tetracycline series are given in refs.[148, 168-170].

8.8. Modification at Positions 11a and 12

It was indicated above that modifying the 11,12-β-diketone system (the BCD chromophore) diminishes the activity. This applies also to the activity of 11a-halogenated tetracyclines *in vitro*, but some compounds of this type, being readily reduced to the parent tetracyclines both chemically or biologically, show a certain degree of activity *in vitro* and *in vivo* owing to this "reactivation"[144].

The 12a-hydroxyl group can be esterified by acid anhydrides. Only the formyl ester[154], which is rapidly hydrolyzed in water, has an activity comparable with that of tetracycline; all the higher esters[171] are less active.

8.9. Results of Structure-Activity Investigations

As a result of the structure-activity investigations we can draw the following conclusions:

The basic skeleton of the tetracycline molecule, including the chromophoric keto-enol systems in rings A and BCD and also the basic group in ring A, is an important prerequisite for antibiotic activity. Retention of the configuration of the asymmetric centers C-4, C-4a, and C-12a is essential whereas the configurations at C-5 and C-5a and C-6 may be altered. The amide hydrogen may be substituted by a methyl group, but larger groups have a deleterious effect except for those that are eliminated spontaneously in water. The dimethylamino group may be replaced by a primary amino group without loss of *in-vitro* activity but all other changes so far lead to a decreased bacteriostatic action. The hydrophobic part of the molecule from C-5 to C-9 may be altered in various ways; modifications of C-6 and C-7 in particular afford products having greater chemical stability, increased antibiotic activity, and more favorable pharmacokinetics.

9. Resistance of Bacteria to Tetracyclines

Frequent use of tetracyclines has been accompanied by an increase in resistant bacterial strains[172-176]. The extent and the distribution of the resistance vary from region to region and, moreover, are not the same for the various causative organisms; yet, all the investigations show that the increase in resistance runs parallel to frequent use of tetracyclines. The situation is particularly unfavorable in view of the extensive cross-resistance between the individual tetracyclines.

9.1. Types of Resistance

The concept of resistance is closely related to the therapeutic and pharmacological properties of an antibiotic. The medical interpretation of this concept is dependent on the tolerance and therapeutically attainable tetracycline level in the serum and tissues. Microorganisms that are not inhibited at a concentration of 3 μg/ml are considered to be tetracycline resistant.

Three types of resistance are distinguished[177-179]:

1) Primary or natural resistance, equivalent to a natural insensitivity of the given strain to the drug and thus constituting a gap in the latter's spectrum of action.

2) Acquired chromosomal resistance, which in a bacterial population is caused by spontaneous gene mutation in bacterial chromosomes. This resistance is directed only against the selective antibiotic.

3) Transferable resistance, which is transferred from one microorganism to another by chromosomal or extrachromosomal DNA elements (R factors, plasmids, episomes). Such a DNA element generally contains several resistance genes, so that the carrier bacteria become resistant simultaneously against chemically differentiable, non-cross-resistant antibiotics. The greatest multiple resistance observed affects six antibiotics, namely tetracycline, streptomycin, chloramphenicol, kanamycin, neomycin, and ampicillin, as well as sulfonamides[179].

It has become clear during the last decade that transferable resistance of bacterial organisms predominates in humans and animals and is dangerous. It has contributed markedly to the development of tetracycline-resistant strains, in particular among staphylococci, streptococci, and members of the Enterobacteria family[173, 180-183]. All attempts to develop a tetracycline that can overcome the increasing resistance on a wide front have been unsuccessful. Even minocycline is no true alternative, though it has more favorable inhibitory properties against a series of organisms and partially defeats the resistance of staphylococci[69, 184, 185].

9.2. Tetracyclines in Animal Nutrition

Tetracyclines, especially chlortetracycline and oxytetracycline, have been applied not only in therapy but also to increase growth and have been fed to healthy animals in so-called nutritive doses. In this way, a large number of bacteria in the intestinal tract of the animal come into permanent contact with these antibiotics and the internal flora is shifted toward resistant strains[186, 187]. It is not yet known exactly to what extent this causes the formation and spread of resistant strains in humans. This use of tetracyclines, which was permitted on a large scale up to 1971, has now been greatly limited by governmental restrictions[188].

9.3. Causes of Tetracycline Resistance

A number of laboratories have been able to show that the resistance to tetracyclines is due to diminished permeability of the bacterial cell wall (for reviews see[189-192]).

Unlike mammalian cells, bacterial cells have the ability to accumulate tetracyclines against a concentration gradient. The difference between the intracellular and the medium concentrations for *E. coli* organisms can increase to a factor of 20—30 at bacteriostatic levels and a factor of up to 50 at bactericidal concentrations. This uptake process which is of importance for the selective chemotherapeutic activity of the tetracyclines, is energy-dependent and is inhibited by decouplers of oxidative phosphorylation[190, 193]. Divalent ions, particularly magnesium ions, appear to play a role in this process, since the ability of the membranes to bind tetracyclines is destroyed by pretreatment with the complexing agent EDTA. The molecular components that effect the selective transport are firmly bound to the cell membrane; an osmotic shock does not affect the uptake by *E. coli* organisms.

Reynard et al.[194] tested a large number of clinical strains of *E. coli* and found that resistant strains take up less tetracy-

cline than sensitive ones. *Sompolinsky*[195] found the same effect with staphylococci. *Kuck* and *Forbes*[184] confirmed these findings for tetracycline, but observed no difference for the more lipophilic minocycline. In a cell-free system ribosomes from sensitive and resistant *E. coli* organisms show the same degree of tetracycline sensitivity[191]. *Craven*[196] isolated a highly resistant *E. coli* strain whose protein-synthesizing system was resistant to tetracycline. Enzymatic inactivation of tetracyclines has not been observed in resistant bacterial cells.

10. Mode of Action of Tetracyclines

Tetracyclines inhibit many enzyme reactions important for the vital processes of bacterial and mammalian cells, *e.g.* oxidative phosphorylation and electron transport[191, 197]. The inhibitory concentrations are often higher than is necessary for bacteriostasis. Such reactions cannot explain the antibiotic activity of tetracyclines, but they can be important for the interpretation of toxic side effects caused by accumulation in specific organs or by overdosage.

10.1. Inhibition of Protein Biosynthesis

The most sensitive biochemical reaction that is inhibited by tetracyclines is the biosynthesis of proteins[198, 199]. The exact molecular course of the inhibitory reaction is not known, but the phases of protein biosynthesis that are affected have been established.

Protein biosynthesis is effected at the ribosomes in the cell cytoplasm and resembles a conveyor belt process[199, 200]. The base sequence of an m-RNA is translated in a series of many successive steps into the amino-acid sequence of a protein. This process, known as translation, is divided into initiation, elongation, and termination.

In the chain elongation, a single amino acid that is bound to a specific RNA is transferred to the growing polypeptide chain and incorporated by means of an amide bond. As the first step in this second phase the amino acid to be incorporated must be bound to the ribosome as an aminoacyl-t-RNA. It is at this point that the tetracyclines interfere, by inhibiting the binding of this aminoacyl-t-RNA to the specific acceptor site of the ribosome[191, 199]. Furthermore, other steps are also affected by tetracyclines[192].

10.2. Inhibition of Cell-Free Protein Biosynthesis

If the biological activity of tetracyclines is due to inhibition of protein biosynthesis, this inhibition should also be observable in a system where *Nirenberg* and *Matthaei* demonstrated cell-free protein biosynthesis[201].

Such a system requires intact purified ribosomes and a supernatant liquid, obtained by high-speed centrifugation, from a cell extract containing all the types of t-RNA and related enzymes. Synthetic polynucleotides are used as templates, and the inhibition of incorporation of labeled amino acids is measured. If such a system contains polyuridylic acid as the template, then the formation of polyphenylalanine coded for by this polynucleotide is inhibited by tetracyclines. This inhibition can be correlated satisfactorily with the activity of the tetracyclines[191, 199b, 202].

Summ[203, 204] used the serial dilution test to compare the inhibition exerted by several tetracycline derivatives on cell-free protein biosynthesis in the *E. coli* system with inhibition in intact cells. According to his results, the strongly active tetracyclines (examples 1 to 7 in Table 3) are strong inhibitors of protein biosynthesis. The fundamental bacteriostatic character of the tetracyclines cannot be altered by changing the lipophilicity.

Biologically inactive tetracyclines, *e.g.* tetracyclinenitrile, are weak inhibitors of protein biosynthesis, although there are exceptions: tetracycline methiodide, which is practically inactive in the serial dilution test, has an inhibitory activity only four times weaker than that of tetracycline *(3)*; one can assume that the salt-like character of the methiodide hinders permeation and transport to the site of activity. Anhydrotetracycline *(10)* and 12a-deoxytetracycline inhibit in the cell-free system to a lesser degree than would be expected from the serial dilution test, which indicates that these molecules attack other sites in the bacteria or. are activated by metabolic processes occurring in the cell.

Experiments on inhibition in cell-free systems are very valuable for investigating the structure-activity relationships because they provide a parameter for the activity at the biologically active center while disturbing influences due to permeation and/or metabolism are excluded.

Tetracyclines also inhibit protein biosynthesis in mammalian cells, but only at higher concentrations.

Table 3. Comparison of inhibition by various tetracyclines (TC) of the cell-free synthesis of poly-U-dependent polyphenylalanine in enzyme systems from *E. coli* and from rat liver [203, 204]. DI_{50} is the concentration of the antibiotic that leads to a 50% inhibition of polyphenylalanine synthesis.

Drug (see Table 1)	Cell-free enzyme system from *E. coli* DI_{50} [μmol/l]	Liver DI_{50} [μmol/l]	$\frac{DI_{50}\text{ (liver)}}{DI_{50}\text{ (coli)}}$
1 Minocycline *(8)*	6.22	620	100
2 Pyrrolidinomethyl-TC *(5)*	6.84	233	34.0
3 Chlor-TC *(5)*	7.55	103	13.6
4 Demethylchlor-TC *(4)*	9.68	39.9	41.1
5 Doxycycline *(7)*	9.76	287	29.4
6 Tetracycline *(3)*	9.77	168	17.2
7 Oxy-TC *(2)*	12.1	437	36.1
8 TC methiodide	39.2	345	8.8
9 4-Dedimethylamino-TC	410	968	2.4
10 Anhydro-TC *(10)*	493	590	1.2
11 12a-Deoxy-TC	126	470	3.7
12 TC-nitrile	887	1785	2.0

Table 3 shows the inhibition of protein biosynthesis by tetracyclines in cell-free systems from *E. coli* and rat liver. It is clear that the effective and well tolerated tetracyclines are considerably better inhibitors of protein biosynthesis in the *E. coli* than in the liver system. Anhydrotetracycline *(10)*, a degradation product of tetracycline, inhibits almost equally in the two systems and is therefore more toxic. The ratio DI_{50} (liver)/DI_{50} *(coli)* of the inhibitory values in the two systems is a measure of the selectivity of the tetracyclines; it is essential that protein biosynthesis in the host cell will be affected little or not at all at the bacteriostatic concentration of the antibiotic. This ratio is not, in fact, a quantitative measure of the toxicity or the chemotherapeutic index of the drug since these are influenced by the pharmacokinetics and the metabolism.

11. Summary and Conclusions

The chemical, physical, and biological properties of few drugs have been so thoroughly investigated as those of the tetracyclines. These efforts have not been in vain. Tetracyclines with greater solubility and stability have been developed, ones with faster and more complete resorption, enhanced activity, and more favorable pharmacokinetics. Work with this class of compounds has stimulated many practical and theoretical studies of general importance to the natural sciences and medicine.

Not all the desired goals have been attained. It has not proved possible to alter the fundamental bacteriostatic character of the tetracyclines by chemical modifications. The activity spectrum could not be decisively broadened. The growing number of tetracycline-resistant strains due to the frequent and uncritical use of these antibiotics now causes concern and leads to restricted application. In spite of considerable advances in the chemotherapy of infectious diseases the task still remains of seeking ever new drugs and of selecting and evaluating them by strict criteria prior to their general application.

Received: February 26, 1975 [A 78 IE]
German version: Angew. Chem. *87*, 751 (1975)
Translated by Express Translation Service, London

[1] *L. H. Conover*, Advan. Chem. Ser. *108*, 33 (1971).
[2] *S. A. Waksman:* Microbial Antagonisms and Antibiotic Substances. The Commonwealth Fund, New York 1945.
[3] *B. M. Duggar*, Ann. N. Y. Acad. Sci. *51*, 177 (1948).
[4] *A. C. Finlay, G. L. Hobby, S. Y. P'an, P. P. Regna, J. B. Routien, D. B. Seeley, G. M. Shull, B. A. Sobin, I. A. Solomons, J. W. Vinson*, and *J. H. Kane*, Science *111*, 85 (1950).
[5] *F. A. Hochstein, C. R. Stephens, L. H. Conover, P. P. Regna, R. Pasternack, P. N. Gordon, F. J. Pilgrim, K. J. Brunings*, and *R. B. Woodward*, J. Amer. Chem. Soc. *75*, 5455 (1953); *74*, 3706 (1952).
[6] *J. H. Boothe, J. Morton, J. P. Petisi, R. G. Wilkinson*, and *J. H. Williams*, J. Amer. Chem. Soc. *75*, 4621 (1953).
[7] *L. H. Conover, W. T. Mordand, A. R. English, C. R. Stephens*, and *F. J. Pilgrim*, J. Amer. Chem. Soc. *75*, 4623 (1953).
[8] *P. P. Minieri, M. C. Firman, A. G. Mistretta, A. Abbey, C. E. Bricker, N. E. Rigler*, and *H. Sokol*, Antibiotics Annual 1953–1954, 81. Med. Encyclop. Inc., New York.
[9] *J. R. D. McCormick, N. O. Sjolander, U. Hirsch, E. R. Jensen*, and *A. P. Doerschuk*, J. Amer. Chem. Soc. *79*, 4561 (1957).
[10] *S. Hirokawa, Y. Okaya, F. M. Lovell*, and *R. Pepinsky*, Acta Crystallogr. *72*, 811 (1959); Z. Kristallogr., Kristallgeometrie, Kristallphys. Kristallchem. *112*, 439 (1959).
[11] *Y. Takeuchi* and *M. J. Buerger*, Proc. Nat. Acad. Sci. USA *46*, 1366 (1960).
[12] *J. Donohue, J. D. Dunitz, K. N. Trueblood*, and *M. S. Webster*, J. Amer. Chem. Soc. *85*, 851 (1963).
[13] *H. Cid-Dresdner*, Z. Kristallogr., Kristallgeometrie, Kristallphys. Kristallchem. *121*, 170 (1965).
[14] *R. E. Hughes, H. Muxfeldt*, and *R. B. von Dreele*, J. Amer. Chem. Soc. *93*, 1037 (1971).
[15] *M. Schach von Wittenau, R. K. Blackwood, L. H. Conover, R. H. Glauert*, and *R. B. Woodward*, J. Amer. Chem. Soc. *87*, 134 (1965).
[16] *M. Schach von Wittenau* and *R. K. Blackwood*, J. Org. Chem. *31*, 613 (1966).
[17] *L. A. Mitscher, B. Slater-Eng*, and *T. D. Sokoloski*, Antimicrob. Ag. Chemother. *1972*, 66, and references cited therein.
[18] *C. R. Stephens, K. Murai, K. J. Brunings*, and *R. B. Woodward*, J. Amer. Chem. Soc. *78*, 4155 (1956).
[19] *L. A. Mitscher, A. C. Bonacci*, and *T. D. Sokoloski*, Tetrahedron Lett. *1968*, 5361.
[20] *D. W. Hughes* and *W. L. Wilson*, Can. J. Pharm. Sci. *8*, 67 (1973); and references cited therein.
[21] *H. Muxfeldt* and *R. Bangert*, Fortschr. Chem. Org. Naturst. *21*, 80 (1963).
[22] *H. Muxfeldt*, Angew. Chem. *74*, 443, 825 (1962); Angew. Chem. internat. Edit. *1*, 372 (1962).
[23] *D. L. J. Clive*, Quart. Rev. Chem. Soc. *22*, 435 (1968).
[24] *T. Money* and *A. I. Scott*, Progr. Org. Chem. *7*, 1 (1968).
[25] *R. K. Blackwood* in: Kirk-Othmer Encyclopedia of Chemical Technology. 2nd Edit., Vol. 18, Wiley, New York 1969.
[26] *G. C. Barrett*, J. Pharm. Sci. *52*, 309 (1963).
[27] *J. J. Hlavka* and *J. H. Boothe*, Fortschr. Arzneimittelforsch. *17*, 211 (1973).
[28] *G. Ehrhart* and *H. Ruschig*: Arzneimittel. 2nd Edit. Verlag Chemie, Weinheim 1972, Vol. 4, p. 368.
[29] *E. G. Remmers, G. M. Sieger*, and *A. P. Doerschuk*, J. Pharm. Sci. *52*, 752 (1963).
[30] *D. A. Hussar, P. J. Niebergall, E. T. Sugita*, and *J. T. Doluisio*, J. Pharm. Pharmacol. *20*, 539 (1968).
[31] *C. T. Agostini* and *Ch. R. Kowarski*, Pharm. Acta Helv. *47*, 560 (1972).
[32] *V. Naggar, N. A. Daabis*, and *M. M. Motawi*, Pharmazie *29*, 129 (1974).
[33] *E. Reuter*, Med. Klin. (München) *67*, 1256 (1972).
[34] *A. M. Walter* and *L. Heilmeyer:* Antibiotika-Fibel. 3rd Edit. Thieme, Stuttgart 1969, p. 16.
[35] Med. Lett. Drugs Therap. *14*, No. 2, Issue 340, 7, 11 (1972).
[36] *J. R. D. McCormick* in *Z. Vanek* and *Z. Hostalek*: Biogenesis of Antibiotic Substances. Academic Press, New York 1965, p. 73.
[37] *L. A. Mitscher*, J. Pharm. Sci. *57*, 1633 (1968).
[38] *C. H. Hassall* and *G. J. Thomas*, Chem. Commun. *1970*, 1053.
[39] *E. Brandl* in *R. Brunner* and *G. Machek:* Die Antibiotica. Vol. 1, Part 2. Verlag H. Carl, Nürnberg 1962, p. 375.
[40] *H. Ippen*, Arch. Klin. Exp. Dermatol. *212*, 519 (1961).
[41] *T. J. Oliver, J. F. Prokop, R. R. Bower*, and *R. H. Otto*, Antimicrob. Ag. Chemother. *1962*, 583.
[42] *A. C. Sinclair, J. R. Schenk, G. G. Post, E. V. Cordinal, S. Borukas*, and *H. H. Fricke*, Antimicrob. Ag. Chemother. *1962*, 592.
[43] *L. A. Mitscher, W. M. Rosenbrook, Jr., W. W. Andres, R. S. Egan, J. Schenk*, and *J. V. Invarkar*, Antimicrob. Ag. Chemother. *1970*, 38.
[44] *J. R. D. McCormick, E. R. Jensen, P. A. Miller*, and *A. P. Doerschuk*, J. Amer. Chem. Soc. *82*, 3381 (1960).
[45] *C. R. Stephens, K. Murai, H. H. Rennhard, L. H. Conover*, and *K. J. Brunings*, J. Amer. Chem. Soc. *80*, 5324 (1958).
[46] *M. Schach von Wittenau, J. J. Beereboom, R. K. Blackwood*, and *C. R. Stephens*, J. Amer. Chem. Soc. *84*, 2645 (1962).
[47] *C. R. Stephens, J. J. Beereboom, H. H. Rennhard, P. N. Gordon, K. Murai, R. K. Blackwood*, and *M. Schach von Wittenau*, J. Amer. Chem. Soc. *85*, 2643 (1963).
[48] *R. C. Esse, J. A. Lowery, C. R. Tamorria*, and *G. M. Sieger*, J. Amer. Chem. Soc. *86*, 3874 (1964).
[49] *R. K. Blackwood* and *C. R. Stephens*, Can. J. Chem. *43*, 1382 (1965).
[50] *F. Lindner, W. Siedel*, and *A. Söder*, DBP 1044806 (1959) and 1063598 (1960); see also München. Med. Wochenschr. *100*, 661 (1958).
[51] *W. J. Gottstein, W. F. Minor*, and *L. C. Cheney*, J. Amer. Chem. Soc. *81*, 1198 (1959).
[52] *H. Hartung, F. Cavagna, W. Martin*, and *W. Dürckheimer*, Arch. Pharm. *307*, 651 (1974).
[53] *R. Fussgänger*, München. Med. Wochenschr. *100*, 663 (1958).
[54] *L. Ther, J. Hergott*, and *G. Vogel*, Arzneim.-Forsch. *9*, 63 (1959).
[55] *R. Bucher* and *T. Wegmann*, Schweiz. Med. Wochenschr. *95*, 1621 (1965).
[56] *G. Stoetter*, München. Med. Wochenschr. *114*, 836 (1972).
[57] *B. Schölkens, K. Gerhards*, and *E. Lindner*, Arzneim.-Forsch. *24*, 312 (1974).
[58] *H. Hartung* and *W. Dürckheimer*, unpublished experiments.
[59] *A. Brunzell*, Acta Chem. Scand. *16*, 245 (1962).
[60] *W. Diemair* and *W. Rödder*, Z. Lebensm.-Unters. Forsch. *111*, 365 (1960).
[61] *D. W. Hughes, W. L. Wilson, A. G. Butterfield*, and *N. J. Pound*, J. Pharm. Pharmacol. *26*, 79 (1974).
[62] *R. K. Blackwood, J. J. Beereboom, H. H. Rennhard, M. Schach von Wittenau*, and *C. R. Stephens*, J. Amer. Chem. Soc. *85*, 3943 (1963).
[63] See ref. [34], pp. 260ff.
[64] *H. Knothe*, Deut. Med. Wochenschr. *95*, 2500 (1970).
[65] *J. Meyer-Rohn*, Med. Welt *1968*, 837.
[66] *J. Fabre, J. S. Pitton, C. Virieux, F. L. Laurencet, J. P. Bernhardt*, and *J. C. Godel*, Schweiz. Med. Wochenschr. *97*, 915 (1967).
[67] *M. Schach von Wittenau*, Chemotherapy, Suppl. to Vol. *13*, 41 (1968).
[68] *M. Schach von Wittenau* and *I. M. Twomey*, Chemotherapy *16*, 217 (1971).
[69] *M. J. Martell* and *J. H. Boothe*, J. Med. Chem. *10*, 44 (1967); see also *R. F. R. Church, R. E. Schaub*, and *M. J. Weiss*, J. Org. Chem. *36*, 723 (1971).
[70] *E. Lauschner*, München. Med. Wochenschr. *115*, 2156 (1973).
[71] *E. Lauschner* and *G. Stüttgen:* Minocyclin-Symposium, Bad Reichenhall 1971. G. Thieme, Stuttgart 1972.
[72] *H. Macdonald, R. G. Kelly, E. S. Allen, J. F. Noble*, and *L. A. Kanegis*, Clin. Pharmacol. Ther. *14*, 852 (1973).
[73] *R. B. Woodward* in *A. Todd*: Perspectives in Organic Chemistry. Interscience, New York 1956, p. 160.
[74] *J. H. Boothe, A. S. Kende, T. L. Fields*, and *R. G. Wilkinson*, J. Amer. Chem. Soc. *81*, 1006 (1959).
[75] *T. L. Fields, A. S. Kende*, and *J. H. Boothe*, J. Amer. Chem. Soc. *82*, 1250 (1960).

[76] *T. L. Fields, A. S. Kende*, and *J. H. Boothe*, J. Amer. Chem. Soc. *83*, 4612 (1961).
[77] *A. S. Kende, T. L. Fields, J. H. Boothe*, and *S. Kushner*, J. Amer. Chem. Soc. *83*, 439 (1961).
[78] *H. Muxfeldt* and *A. Kreutzer*, Chem. Ber. *94*, 881 (1961).
[79] *H. Muxfeldt, W. Rogalski*, and *K. Striegler*, Angew. Chem. *72*, 170 (1960).
[80] *H. Muxfeldt*, Angew. Chem. *74*, 825 (1962).
[81] *I. G. Bolesov, M. N. Kolosov*, and *M. M. Shemyakin*, Izv. Akad. Nauk SSSR, Ser. Khim. *1965*, 1039.
[82] *M. N. Kolosov, V. V. Onoprienkop*, and M. M. Shemyakin, Zh. Obshch. Khim. *35*, 659 (1965).
[83] *A. I. Gurevich, M. G. Karapetjan, M. N. Kolosov, V. G. Korobko*, and *M. M. Shemyakin*, Zh. Obshch. Khim. *35*, 668 (1965).
[84] *A. I. Gurevich, M. G. Karapetyan, M. N. Kolosov, V. G. Korobko, V. V. Onoprienko, S. A. Popravko*, and *M. M. Shemyakin*, Tetrahedron Lett. *1967*, 131.
[85] *A. I. Gurevich, M. N. Kolosov, V. G. Korobko*, and *S. A. Popravko*, Zh. Obshch. Khim. *38*, 57 (1968).
[86] *A. I. Scott* and *C. Y. Bedford*, J. Amer. Chem. Soc. *84*, 2271 (1962).
[87] *M. Schach von Wittenau*, J. Org. Chem. *29*, 2746 (1964).
[88] *H. Muxfeldt*, personal communication.
[89] *D. H. R. Barton*, Chem. Brit. *1970*, 301; Proc. Roy. Soc. *A 319*, 145 (1970); *D. H. R. Barton et al.*, J. Chem. Soc. *C 1971*, 2164, 2166, 2175, 2184, 2193, 2204, 2215, 2225, 2231, 2241.
[90] *L. H. Conover, K. Butler, J. D. Johnston, J. J. Korst*, and *R. B. Woodward*, J. Amer. Chem. Soc. *84*, 3222 (1962).
[91] *R. B. Woodward*, Pure Appl. Chem. *6*, 561 (1963).
[92] *J. J. Korst, J. D. Johnston, K. Butler, E. J. Bianco, L. H. Conover*, and *R. B. Woodward*, J. Amer. Chem. Soc. *90*, 439 (1968).
[93] *H. Muxfeldt* and *W. Rogalski*, J. Amer. Chem. Soc. *87*, 934 (1965).
[94] *H. Muxfeldt*, Antimicrob. Ag. Chemother. *1965*, 977.
[95] *J. Michael*, Dissertation, University of Wisconsin, Madison, Wisc. 1968.
[96] *H. Muxfeldt, G. Hardtmann, F. Kathawala, E. Vedejs*, and *J. B. Mooberry*, J. Amer. Chem. Soc. *90*, 6534 (1968).
[97] *H. Muxfeldt, H. Döpp, J. E. Kaufman, J. Schneider, P. E. Hansen, A. Sasaki*, and *T. Geiser*, Angew. Chem. *85*, 508 (1973); Angew. Chem. internat. Edit. *12*, 497 (1973).
[98] *W. Martin, H. Hartung, H. Urbach*, and *W. Dürckheimer*, Tetrahedron Lett. *1973*, 3513.
[99] *H. Urbach, H. Hartung, W. Martin*, and *W. Dürckheimer*, Tetrahedron Lett. *1973*, 4907.
[100] *W. Dürckheimer*, unpublished experiments.
[101] *E. Schrinner*, unpublished experiments.
[102] *C. I. Jarowski*, Lecture at 6th Pan-Am. Congr. Pharm. Biochem., Mexico City 1963.
[103] *D. A. Hussar*, J. Pharm. Pharmacol. *20*, 539 (1968).
[104] *E. G. Remmers, N. C. Barringer, G. M. Sieger, N. Anagnostakos, J. Corbett*, and *P. A. Doerschuk*, J. Pharm. Sci. *54*, 49 (1965); and references cited therein.
[105] *W. A. Baker* and *P. M. Brown*, J. Amer. Chem. Soc. *88*, 1314 (1966).
[106] *J. T. Doluisio* and *A. N. Martin*, J. Med. Chem. *6*, 16 (1963).
[107] *K. Taguchi*, Chem. Pharm. Bull. *8*, 205, 212, 217 (1960).
[108] *A. Albert*, Nature *172*, 201 (1953).
[109] *A. Albert* and *C. W. Rees*, Nature *177*, 434 (1956).
[110] *L. A. Mitscher, A. C. Bonacci*, and *T. D. Sokoloski*, Antimicrob. Ag. Chemother. *1968*, 78.
[111] *L. A. Mitscher, A. C. Bonacci, B. Slater-Eng, A. K. Hacker*, and *T. D. Sokoloski*, Antimicrob. Ag. Chemother. *1969*, 111.
[112] *M. M. Noseworthy*, US-Pat. 3009956 (1961), Chas. Pfizer and Co.
[113] *J.-C. Mani* and *G. Foltran*, Bull. Soc. Chim. Fr. *1971*, 4141.
[114] *T. V. Alykowa*, Antibiotiki *17*, 353 (1972).
[115] *A. H. Caswell*, J. Membr. Biol. *7*, 345 (1972).
[116] *A. H. Caswell* and *J. D. Hutchison*, Biochem. Biophys. Res. Commun. *43*, 625 (1971).
[117] *A. Stahlavska, M. S. Tawakkol, V. Slansky*, and *M. Frslinkowa*, Pharmazie *27*, 456 (1972).
[118] *P. J. Neuvonen, G. Gothoni, R. Hackmann*, and *K. Bjorksten*, Brit. Med. J. *1970* (Vol. 4), 532.
[119] Brit. Med. J. *1970* (Vol. 4), 509.
[120] *M. J. Mattila, P. J. Neuvonen, G. Gothoni*, and *C. R. Hackman*, Proc. Eur. Soc. Study Drug Toxicity *13*, 128 (1972).
[121] *A. Forsgren* and *H. Gnarpe*, Nature New Biol. *244*, 82 (1973).
[122] *E. H. Gans* and *T. Higuchi*, J. Amer. Pharm. Assoc. *46*, 458 (1957).
[123] *W. Wessel, M. Schoog*, and *E. Winkler*, Arzneimittelforsch. *21*, 1468 (1971).
[124] *J. Wieriks* and *H. E. Schornagel*, Chemotherapy *16*, 85 (1971).
[125] DOS 1767891 (1968), Pfizer GmbH.
[126] *J. Krieglstein*, Arzneimittelforsch. *23*, 1527 (1973).
[127] *M. Schach von Wittenau* and *R. Yeary*, J. Pharmacol. Exp. Ther. *140*, 258 (1963).
[128] *W. Scholtan*, Arzneimittelforsch. *13*, 347 (1963).
[129] *W. Scholtan*, Arzneimittelforsch. *18*, 505 (1968).
[130] *G. Powis*, J. Pharm. Pharmacol. *26*, 113 (1974).
[131] *R. L. Searcy, J. A. Forman, H. D. Myers*, and *L. M. Berquist*, Antimicrob. Ag. Chemother. *1963*, 471.
[132] *E. Genazzani, L. J. Bononi, G. Pagnini*, and *F. DiCarlo:* Progress in Antimicrobial and Anticancer Chemotherapy. Proc. 6th Int. Congr. Chemother., Tokyo 1970, Vol. I, p. 245, and references cited therein.
[133] *T. Perenyi, S. Szoke*, and *E. K. Nowak*, Acta Pharm. Hung. *42*, 220 (1972).
[134] *J. K. H. Ma, H. W. Jun*, and *L. A. Luzzi*, J. Pharm. Sci. *62*, 1261 (1973).
[135] *G. N. Rolinson*, Int. J. Clin. Pharmacol. Ther. Toxicol. *1972*, Suppl. 5, p. 2.
[136] *J. P. F. Whelan* and *J. McFadzean* in *T. B. Binns:* Absorption and Distribution of Drugs. Livingstone, Edinburgh 1964.
[137] *W. Scholtan* and *J. Schmid*, Arzneimittelforsch. *12*, 748 (1962).
[138] *A. Albert:* Selected Toxicity. 5th Edit. Chapman and Hall, London 1973, p. 20.
[139] *E. Krüger-Thiemer* in *E. Freerksen:* Jahresbericht Borstel. Springer, Berlin 1961, Vol. 5, p. 316.
[140] *J. Crofton*, Brit. Med. J. *1969*, Vol. 2, p. 211.
[141] *R. Reiner:* Antibiotica. Thieme, Stuttgart 1974, p. 11.
[142] See ref. [34], pp. 2–28.
[143] *L. A. Mitscher, J. H. Martin, P. A. Miller, P. Shu*, and *N. Bohonos*, J. Amer. Chem. Soc. *88*, 3647 (1966).
[144] *R. K. Blackwood* and *A. R. English*, Advan. Appl. Microbiol. *13*, 237 (1970).
[145] *J. H. Boothe*, Antimicrob. Ag. Chemother. *1962*, 213.
[146] *V. K. Plakunow*, Dokl. Akad. Nauk SSSR *151*, 1207 (1963).
[147] *M. M. Shemyakin* and *M. N. Kolosov*, Pure Appl. Chem. *6*, 305 (1963).
[148] *G. H. Miller, S. A. Kahlil*, and *A. N. Martin*, J. Pharm. Sci. *60*, 33 (1971).
[149] *J. R. D. McCormick* and *E. R. Jensen*, Belgian Pat. 565024 (1958), American Cyanamid Co.
[150] *A. Green*, Belgian Pat. 572382 (1958), American Cyanamid Co.
[151] *R. E. Blackwood, H. H. Rennhard, J. J. Beereboom*, and *C. R. Stephens*, Belgian Pat. 603760 (1961), Chas. Pfizer and Co.
[152] *U. Valcavi, G. Campanella*, and *N. Pacini*, Gazz. Chim. Ital. *93*, 916 (1963).
[153] *C. W. Waller, B. L. Hutchings, R. W. Broschard, A. A. Goldman, W. J. Stein, C. F. Wolf*, and *J. H. Williams*, J. Amer. Chem. Soc. *74*, 4981 (1952).
[154] *R. K. Blackwood, H. H. Rennhard*, and *C. R. Stephens*, J. Amer. Chem. Soc. *82*, 5194 (1960).
[155] *J. R. D. McCormick*, US-Pat. 3345409 (1967), American Cyanamid Co.
[156] *W. Dürckheimer* and *W. Martin*, unpublished experiments.
[157] *W. Raether* and *E. Schrinner*, unpublished experiments.
[158] *J. J. Korst*, DOS 2065149 (1972), Pfizer Inc.
[159] *J. J. Korst*, DOS 2049941 (1972), Pfizer Inc.
[160] *M. W. Miller* and *F. A. Hochstein*, J. Org. Chem. *27*, 2525 (1962).
[161] *C. R. Stephens*, US-Pat. 3028409, Chas. Pfizer and Co.
[162] *H. Reinshagen* and *E. Schütze*, unpublished experiments.
[163] *H. Reinshagen* and *E. Schütze*, French Pat. 1559914 (1969), DOS 1618406 (1971), both Hoechst AG.
[164] *J. H. Boothe, G. E. Bonvicino, C. W. Waller, J. P. Petisi, R. W. Wilkinson*, and *R. B. Broschard*, J. Amer. Chem. Soc. *80*, 1654 (1958).
[165] *M. J. Martell, A. S. Ross*, and *J. H. Boothe*, J. Amer. Chem. Soc. *89*, 6780 (1967).
[166] *J. Petisi, J. L. Spencer, J. J. Hlavka*, and *J. H. Boothe*, J. Med. Pharm. Chem. *5*, 538 (1962).
[167] *A. Cammarata* and *S. J. Yau*, J. Med. Chem. *13*, 93 (1970).
[168] *S. M. Free, Jr.* and *J. W. Wilson*, J. Med. Chem. *7*, 395 (1964).
[169] *A. Cammarata, S. J. Yau, J. H. Collett*, and *A. N. Martin*, Mol. Pharmacol. *6*, 61 (1970).
[170] *F. Peradejordi, A. N. Martin*, and *A. Cammarata*, J. Pharm. Sci. *60*, 576 (1971).
[171] *R. K. Blackwood* and *C. R. Stephens*, US-Pat. 3047617 (1962), Chas. Pfizer and Co.
[172] *P. Bischoff*, München. Med. Wochenschr. *113*, 353 (1971).
[173] *D. Fritsche* and *A. Schulz-Stübner*, Deut. Med. Wochenschr. *97*, 1963 (1972).
[174] *G. B. Roemer* and *K. Metz*, Deut. Med. Wochenschr. *97*, 1878 (1972).
[175] *W. Ritzerfeld*, München. Med. Wochenschr. *115*, 1641 (1973).
[176] *H. Bloch*, Schweiz. Med. Wochenschr. *98*, 611 (1968).
[177] See ref. [34], pp. 52 and 260.
[178] *G. Lebek*, Deut. Med. J. *23*, 460 (1972).
[179] *E. Reinhard*, Pharm. Unserer Zeit *1*, 9, 67 (1972).
[180] *D. C. Hirsh, G. C. Burton*, and *D. C. Blenden*, Antimicrob. Ag. Chemother. *4*, 69 (1973).
[181] *G. M. Shub, B. A. Shenderow, V. V. Vorobiew*, and *V. I. Pylaev*, Antibiotiki *17*, 1025 (1972).
[182] *G. Pulverer*, Deut. Med. Wochenschr. *97*, 252 (1972).
[183] *K. V. Gopalakrishna* and *P. I. Lerner*, Amer. Rev. Resp. Dis. *108*, 1007 (1973).

[184] *N. A. Kuck* and *M. Forbes*, Antimicrob. Ag. Chemother. *3*, 662 (1973).
[185] *E. C. R. Reeve* and *J. M. Robertson*, J. Gen. Microbiol. *16*, 73 (1972).
[186] *R. Stephan*, Zentralbl. Bakteriol., Parasitenk., Infektionskr. Hyg., Abt. *B. 156*, 199 (1972).
[187] *E. Bulling* and *R. Stephan*, Zentralbl. Veterinärmed. *B. 19*, 268 (1972), and previous communications.
[188] Richtlinie des Rates der Europäischen Gemeinschaften vom 17. 12. 1973 über Festlegung von Höchstgehalten an unerwünschten Stoffen und Erzeugnissen in Futtermitteln, Anhang 2.
[189] *R. Benveniste* and *J. Davies*, Annu. Rev. Biochem. *42*, 471 (1973).
[190] *T. J. Franklin*, CRC Crit. Rev. Microbiol. *1973*, 263.
[191] *A. I. Laskin* and *J. A. Last*, Antibiot. Chemother. (Basel) *17*, 1 (1971).
[192] *H. Kersten* and *G. Tey* in *V. Krcmery, L. Resival*, and *T. Watanabe:* Bacterial Plasmids and Antibiotic Resistance. Springer, Berlin 1972.
[193] *A. M. Reynard* and *L. F. Nellis*, Biochem. Biophys. Res. Commun. *48*, 1129 (1972).
[194] *A. M. Reynard, L. F. Nellis*, and *M. E. Beck*, Appl. Microbiol. *21*, 71 (1971).
[195] *D. Sompolinsky, Y. Zaidenzaig, R. Ziegler-Schlomowitz*, and *N. Abramova*, J. Gen. Microbiol. *62*, 351 (1970).
[196] *G. R. Craven, R. Gavin*, and *Th. Fanning*, Cold Spring Harbor Symp. Quant. Biol. *34*, 129 (1969).
[197] *A. I. Laskin* in *D. Gottlieb* and *P. D. Shaw:* Antibiotics. Springer, Berlin 1967, Vol. 1, p. 331.
[198] *E. F. Gale* u. *J. P. Folkes*, Biochem. J. *53*, 483 (1953).
[199] Surveys: a) *B. Weissblum* and *J. Davies*, Bacteriol. Rev. *32*, 493 (1968); b) *E. F. Gale*: The Molecular Basis of Antibiotic Action. Wiley, New York 1972, p. 315; c) *F. Lipmann*, Triangel *10*, 17 (1971).
[200] Surveys: a) *H. Matthaei, G. Sander, D. Swan, T. Kreuzer, H. Caffier*, and *A. Parmeggiani*, Naturwissenschaften *55*, 281 (1968); b) *G. Schreiber*, Angew. Chem. *83*, 645 (1971); Angew. Chem. internat. Edit. *10*, 638 (1971); c) *C. G. Kurland*, Annu. Rev. Biochem. *41*, 377 (1972); d) *P. Knolle*, Deut. Apoth.-Ztg. *113*, No. 2, 39 (1973).
[201] *M. Nirenberg* and *H. Matthaei*, Proc. Nat. Acad. Sci. USA *47*, 1588 (1961).
[202] *A. I. Laskin* and *W. May Chan*, Biochem. Biophys. Res. Commun. *14*, 137 (1964).
[203] *H. D. Summ* and *O. Christ*, Arzneimittelforsch. *17*, 1186 (1967).
[204] *H. D. Summ*, unpublished experiments.

Substitution Reactions Which Proceed *via* Radical Anion Intermediates

New synthetic methods (12)

By Nathan Kornblum[*]

A new type of substitution process at a saturated carbon atom is described. These reactions, which proceed *via* a chain sequence in which radical anions and free radicals are intermediates, are noteworthy for providing novel and powerful means of synthesis: they occur readily under mild conditions, they give excellent yields of pure products, and, in contrast to S_N2 displacements, they are rather insensitive to steric hindrance. As a consequence, radical anion processes are especially valuable for the preparation of highly branched structures. Many inorganic and organic anions readily enter into these displacements and, indeed, amines are also effective. Systems which undergo substitution *via* this electron transfer mechanism include benzylic, cumylic, strictly aliphatic, and heterocyclic molecules. It is of interest that a number of groups which do not behave as leaving groups in S_N2 displacements are readily displaced at room temperature from a saturated carbon atom *via* the radical anion-free radical pathway, *e.g.*, nitro, azide, sulfone, and ether groups.

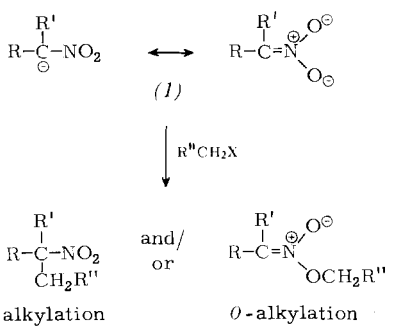
1. Introduction

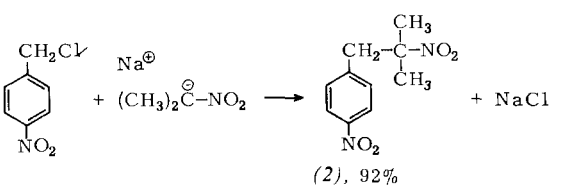
We deal here with substitution reactions at a saturated carbon atom which proceed *via* a multi-stage sequence involving radical anions and free radicals as intermediates. Apart from the intrinsic interest which attaches to a new type of substitution process, these reactions are noteworthy for their value in synthesis. Recognition of this new type of substitution reaction derived from a study, initiated in the 1950's, of the factors which control the course of ambident anion alkylations[1].

In this article we briefly describe how the discovery came to be made and then discuss a number of reactions for which there is compelling evidence that radical anions and free radicals are intermediates[2].

2. The *p*-Nitrobenzyl System

Treatment of the salt of an aliphatic nitro compound *(1)* with an alkyl halide may result in alkylation at carbon or at oxygen[**]. In general, oxygen alkylation with little, if any, concomitant carbon alkylation is observed[3, 4]. Consequently, the few instances of carbon alkylation known in the 1950's were of interest, and foremost among them was the reaction of *p*-nitrobenzyl chloride with the sodium salt of 2-nitropropane which gives a 92% yield of *C*-alkylated product[*].





(2), 92%

[*] Prof. Dr. N. Kornblum
Department of Chemistry, Purdue University
West Lafayette, Indiana 47907 (USA)

[**] Actually the *O*-alkylated product is not isolated; instead the carbonyl compound (R"CHO) derived from the alkyl halide and the oxime (RR'C=NOH) derived from the nitroalkane are obtained.

[*] A 6% yield of *p*-nitrobenzaldehyde is also produced; this, of course, comes from the *O*-alkylated product.

In contrast, the anion of 2-nitropropane undergoes exclusive oxygen alkylation on treatment with benzyl chloride or with *m*-nitrobenzyl chloride. Also striking is the fact that when the sodium salt of 2-nitropropane is treated with a series of benzylic halides substituted in the *para* position by CN, CF_3, $N^{\oplus}(CH_3)_3Cl^{\ominus}$, $CH_3C{=}O$, CH_3, and Br the result, in each case, is exclusively oxygen alkylation[4]. This was the position when we began our study of the alkylation of nitroalkane salts.

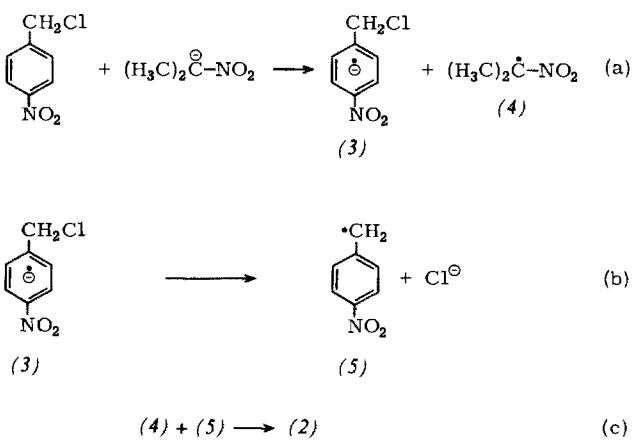
In 1961 it was found that the uniqueness of the *p*-nitrobenzyl system depends not only on the *p*-nitro group but also on the leaving group[5]. For example, when *p*-nitrobenzyl iodide is treated with the salt of 2-nitropropane the result is an 81% yield of *p*-nitrobenzaldehyde (*i.e.*, oxygen alkylation). As shown in Table 1, even in the *p*-nitrobenzyl system, carbon alkylation predominates only when the leaving group is a difficultly displaced one. It is also noteworthy that in the unsubstituted benzyl system there is no leaving group effect; benzyl chloride, bromide, iodide, and tosylate all give 82 to 84% yields of benzaldehyde and little, if any, *C*-alkylated product.

Table 1. Nature of the reaction of $p\text{-}O_2N{-}C_6H_4{-}CH_2X$ with the lithium salt of 2-nitropropane in DMF as a function of X.

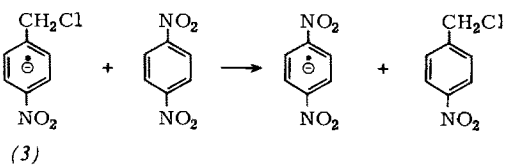
X	*C*-Alkylate, yield [%]	*O*-Alkylate, yield [%]
$N^{\oplus}(CH_3)_3Cl^{\ominus}$	93	0
C_6Cl_5COO	93	0
Cl	92	6
OTos	40	32
Br	17	65
I	7	81

Furthermore, whenever carbon alkylation in the *p*-nitrobenzyl system occurs to the essential exclusion of oxygen alkylation (*i.e.*, when the leaving group is $N^{\oplus}(CH_3)_3Cl^{\ominus}$, pentachlorobenzoate, or chloride) the reaction rate is at least one hundred times faster than for the corresponding unsubstituted benzyl compound. But, when oxygen alkylation preponderates the effect of a *para* nitro group on rate is small; *p*-nitrobenzyl iodide, for example, reacts with the lithium salt of 2-nitropropane only three times faster than benzyl iodide.

This array of facts led to the suggestion that oxygen alkylation of nitroalkane salts derives simply from a nucleophilic displacement by the oxygen of the nitroparaffin anion on the alkylating agent but that, in the *p*-nitrobenzyl series, if the leaving group is one which is difficultly displaced, a second mode of attack by the nitroparaffin anion has a chance to compete, and it is this second process which is productive of carbon alkylation[5]. Three years later, in 1964, it was proposed that carbon alkylation is a process which involves radical anions and free radicals as intermediates as shown in eqs. (a) to (c)[6].



A mechanistic sequence as novel as that proposed for the carbon alkylation of nitroalkane salts is not to be taken seriously in the absence of substantial experimental support. Actually, when first advanced it was backed by several significant lines of evidence which included rate and EPR studies[6, 2]. But the most impressive piece of evidence for the intermediacy of radical anions was provided by *Robert Kerber*, who was then a graduate student at Purdue. Since electron transfer from nitroarene radical anions to nitroarenes is rapid[7], it occurred to *Kerber* that an easily reduced nitroarene such as *p*-dinitrobenzene (*p*-DNB) might be able to take an electron away from the radical anion of *p*-nitrobenzyl chloride *(3)* before loss of chloride took place and thereby prevent carbon alkylation. The net effect of such intervention would be to retard carbon alkylation without affecting oxygen alkylation



(3)

and, as a consequence, the proportion of *O*-alkylate should increase at the expense of *C*-alkylate.

This proved to be a fertile idea. As shown in Table 2, when the lithium salt of 2-nitropropane is alkylated with *p*-nitrobenzyl chloride in the presence of aromatic nitro compounds, carbon alkylation is indeed suppressed[6]. Furthermore, the effectiveness of nitroaromatics in suppressing carbon alkylation decreases in the order *p*-DNB > *m*-DNB > $H_5C_6NO_2$, which is the order of their relative ease of one electron reduction[8].

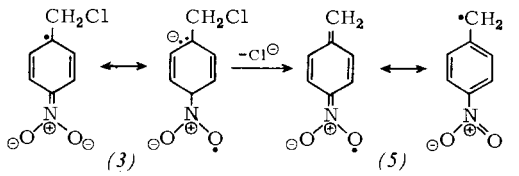
Table 2. Influence of nitroarenes on the reaction of *p*-nitrobenzyl chloride with the lithium salt of 2-nitropropane.

Added nitroarene (equiv.)	*C*-Alkylate, yield [%]	*O*-Alkylate, yield [%]
None	92	6
$PhNO_2$ (4)	84	7
m-DNB (1)	61	29
m-DNB (2)	40	48
p-DNB (0.2)	6	88
p-DNB (1)	2	72

It will be noted that the ability of *p*-DNB to enhance the proportion of *O*-alkylated product is ascribed not to facilitation of the oxygen alkylation process but, rather, to retardation of the carbon alkylation sequence. This view is borne out by the fact that the rate at which *p*-nitrobenzyl chloride reacts with the lithium salt of 2-nitropropane is reduced by a factor of ten when one equivalent of *p*-DNB is present.

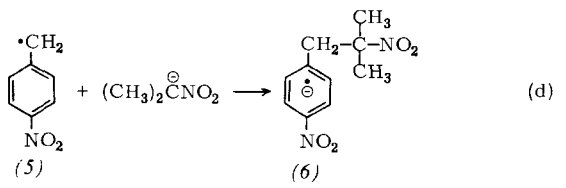
The most interesting feature of the mechanism [eqs. (a) to (c)] is recognition of a special property of the radical anion of *p*-nitrobenzyl chloride *(3)*, namely, by loss of chloride, it becomes a free radical *(5)*. Such expulsion of chloride is easy to understand if the structures for *(3)* and *(5)* are

written out in more detail. It then becomes apparent that ejection of chloride ion from *(3)* is, in essence, an elimination reaction, that the olefin produced is also a free radical, and, furthermore, that this olefin-free radical is nothing other than the *p*-nitrobenzyl radical.



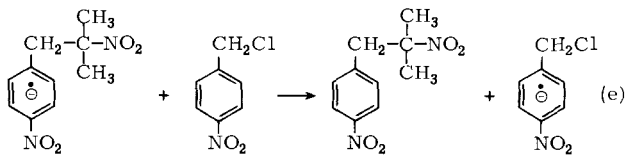
(3) *(5)*

Additional support for the view that carbon alkylation involves radical anions and free radicals was published in 1966. And, by this time, it had become apparent that carbon alkylation of nitroalkane salts is a chain reaction and that our mechanism needed to be modified accordingly. This was done by replacing eq. (c) of the original non-chain sequence by the two steps of eqs. (d) and (e)[9]. Simultaneously and independently *Russell* and *Danen* also recognized the necessity for converting the non-chain mechanism which had been proposed for this reaction into a chain sequence[10].



(d)

(5) *(6)*

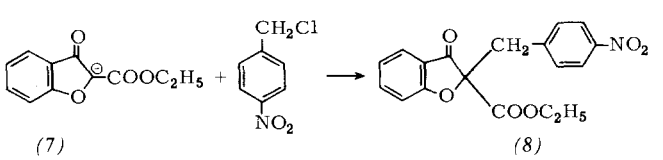


(e)

(6) *(2)* *(3)*

The key step of the chain mechanism [eqs. (a), (b), (d), and (e)] is the reaction of *p*-nitrobenzyl radical *(5)* with an anion to form a radical anion. Whereas there now exists a significant body of evidence for the view that radicals and anions can react to generate radical anions, this was rather a novel idea in 1966. Indeed, the possibility of a radical and an anion combining to produce a radical anion seems to have been recognized explicitly for the first time only in 1964[11].

Another early study involved the β-keto ester anion *(7)* which, on alkylation with *p*-nitrobenzyl chloride, gives an almost quantitative yield of the *C*-alkylate *(8)*—a result which is in contrast to what is observed with other benzylic halides[9]. Here again it transpires that alkylation



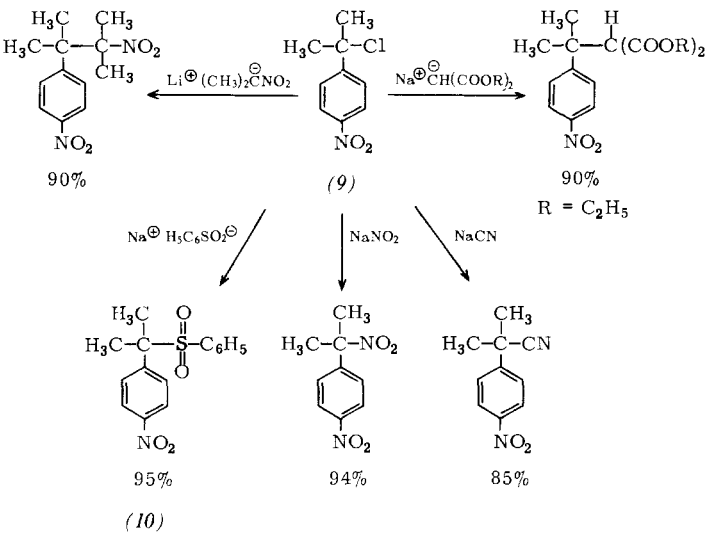
(7) *(8)*

of *(7)* is ordinarily an S_N2 process and gives the *O*-alkylate; but, when *p*-nitrobenzyl chloride with its relatively difficultly displaced leaving group and a nitro group in the *para* position is employed, the radical anion process becomes dominant. Furthermore, electron acceptors such as *p*-DNB and *m*-DNB suppress carbon alkylation; a chain mechanism fully analogous to that of eqs. (a), (b), (d), and (e) has been proposed[12].

3. The *p*-Nitrocumyl System

By far the most impressive evidence for the radical anion-free radical chain mechanism derives from the study of substitution reactions at a tertiary carbon. We turned to tertiary halides for several reasons. With primary and secondary halides the radical anion pathway and the S_N2 displacement process are in competition and it takes a difficultly displaced leaving group to provide an opportunity for the radical anion mechanism to predominate. The well known resistance of tertiary halides to S_N2 displacements at the tertiary carbon suggested that with tertiary halides radical anion substitution might be observed, free of competition by the S_N2 process. This proved to be the case[13]. The use of tertiary halides also made it possible to avoid experimental complications and mechanistic ambiguities which arise as a consequence of the relatively high acidity of the methylene hydrogens of some of the benzylic halides[*].

p-Nitrocumyl chloride *(9)* was the first tertiary halide studied, and Figure 1 presents some typical results[14]. These reactions all proceed at room temperature, are complete in minutes or hours, and the yields refer to pure products which have been isolated. Such facile substitution at a tertiary carbon atom is without precedent[**]. It has also been found that radical anion substitution at tertiary carbon can be brought about by primary, secondary, and tertiary amines[15]. Thus, the reaction of *p*-nitrocumyl chloride with piperidine results in a 91 % yield of the alkylated piperidine *(11)*.



90% *(9)* 90%

R = C_2H_5

95% 94% 85%

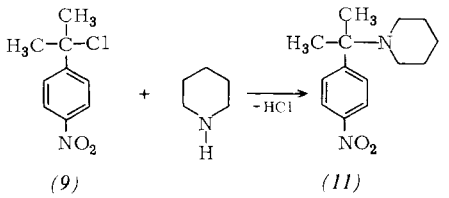
(10)

Fig. 1. Some substitution reactions of *p*-nitrocumyl chloride *(9)*.

With α,*p*-dinitrocumene an even more striking set of results is observed; some of these are shown in Figure 2. These

[*] For example, the reaction of sodium 1-methyl-2-naphthoxide with *p*-nitrobenzyl chloride gives, in addition to the *O*- and *C*-alkylated compounds, a 40 % yield of *p,p'*-dinitrostilbene (unpublished work of Dr. *D. H. Snow*).

[**] It is of interest that only with phenolic salts is there appreciable olefin formation. For example, *p*-nitrocumyl chloride *(9)* and sodium 1-methyl-2-naphthoxide give a 73 % yield of the ether *(14)* and a 17 % yield of *p*-nitro-α-methylstyrene.

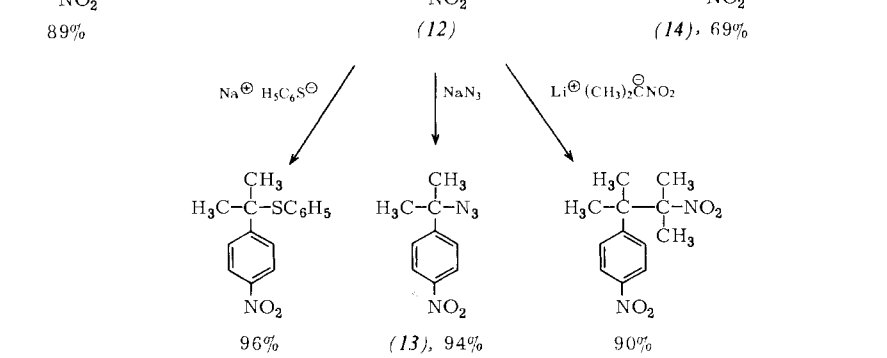


(9) (11)

reactions are noteworthy not only because they involve substitution at a tertiary carbon but also because the displacement of a nitro group from a saturated carbon atom is unprecedented; furthermore, they take place at room temperature and generally at rates not a great deal slower than those observed with *p*-nitrocumyl chloride. For instance, the reaction of *(12)* with the lithium salt of 2-nitropropane (Fig. 2) is complete in 2 h[16].

Actually, the aliphatic nitro group is but one of a number of functions which ordinarily do not behave as leaving groups and yet are readily displaced in these radical anion substitution processes: the reactions shown for compounds *(10)*, *(13)*, and *(14)* provide further examples of these extraordinary transformations. The facility with which they occur is indeed striking[17].

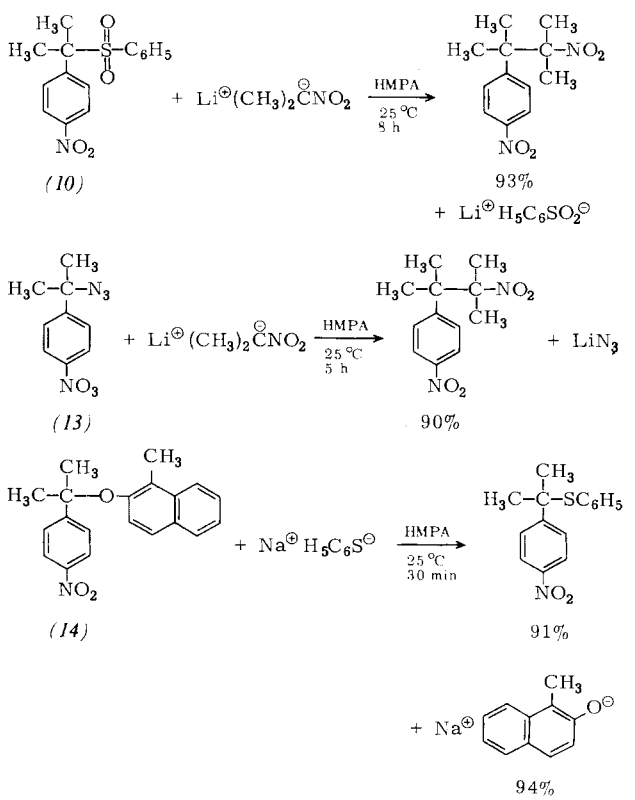
Two other points need to be emphasized. The *para* nitro group is essential for the reactions described in Figures 1 and 2; neither cumyl chloride nor α-nitrocumene undergoes substitution. Furthermore, when *p*-nitrocumyl chloride *(9)* and α,*p*-dinitrocumene *(12)* are treated with ambident anions, *i. e.*, with $NO_2^{\ominus}$, $(CH_3)_2C^{\ominus}NO_2$, and $C_6H_5SO_2^{\ominus}$, covalency is established at the more hindered of the two available positions—this despite the fact that substitution is occurring at a highly hindered carbon atom.



89% (12) (14), 69%

96% (13), 94% 90%

Fig. 2. Some substitution reactions of α,*p*-dinitrocumene *(12)*.

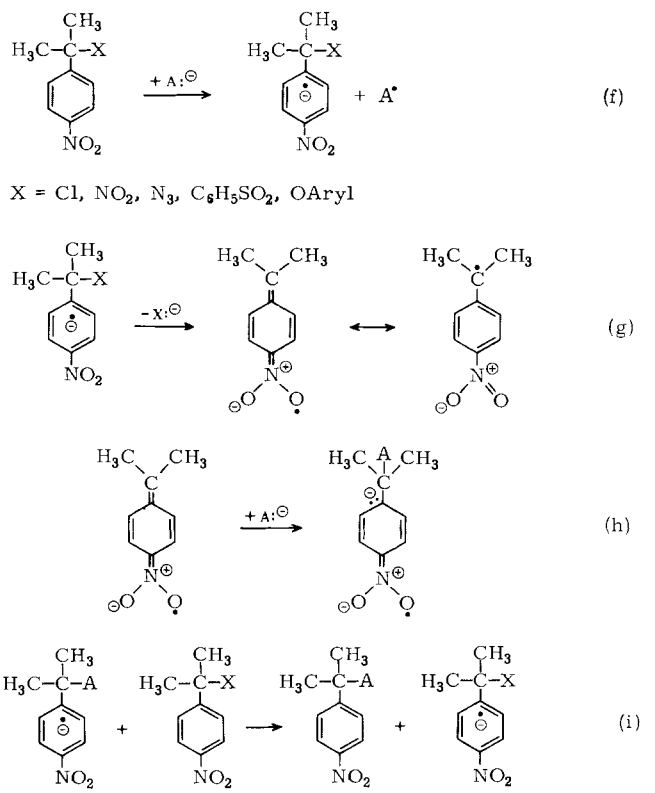


(10) 93%

(13) 90%

(14) 91%

94%



(f)

X = Cl, NO_2, N_3, $C_6H_5SO_2$, OAryl

(g)

(h)

(i)

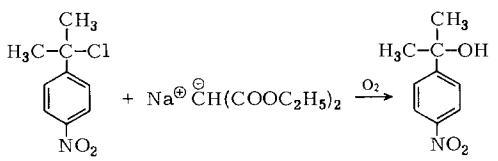
It is this lack of sensitivity to steric hindrance which makes radical anion substitution reactions so useful for the synthesis of highly branched compounds. These characteristics accord with the view[14] that the reactions shown in Figures 1 and 2, and those of compounds *(10)*, *(13)*, and *(14)*, proceed *via* the mechanistic sequence of eqs. (f) to (i). A *para* nitro group provides important additional delocalization for the odd electron and thereby facilitates radical anion formation. The insensitivity to steric hindrance is also readily understandable; it derives from minimal sensitivity to steric effects at each step of the chain sequence. The first step [eq. (f)] occurs at the unhindered nitroaromatic portion of the *p*-nitrocumyl system. The second step [eq. (g)] is an internal elimination and thus not subject to steric hindrance. The third stage [eq. (h)] involves addition to the planar system of a free radical; the combination of minimal steric hindrance and high reactivity associated with a free radical makes it easy for the reaction to take place. The last step [eq. (i)] is a one-electron transfer from a nitroaromatic radical anion to a nitroarene—a process known to be very rapid[7] and for which steric hindrance would again be expected to be minimal. The upshot is that substitution at a strongly hindered carbon atom occurs by a sequence of steps in which steric effects are minimized at every stage.

4. Concerning the Matter of Mechanism

The mechanism of eqs. (f) to (i) has been tested in a number of ways and some of these experiments are described in this section. They provide powerful support for the radical anion-free radical chain mechanism of eqs. (f) to (i).

4.1. The Effect of Oxygen

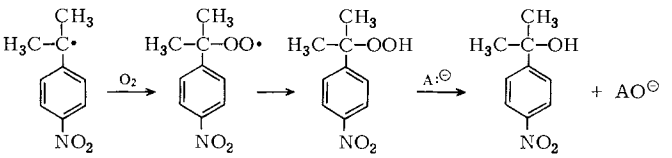
It was early recognized[6] that molecular oxygen interferes with the reaction of *p*-nitrobenzyl chloride with the lithium salt of 2-nitropropane, but it remained for studies in the *p*-nitrocumyl system to elucidate matters[18, 19]. Thus treatment of *p*-nitrocumyl chloride with sodiomalonic ester gives the *C*-alkylated product in 90% yield (Fig. 1)—provided the reaction is conducted under nitrogen. In contrast, if the reaction is carried out in the presence of oxygen, alkylation is completely suppressed and instead *p*-nitrocumyl alcohol *(15)* is produced in 88% yield. Oxygen does not convert *p*-nitrocumyl chloride into the alcohol in the absence of the malonate anion.



(9) *(15)*

In the same way, the reaction of α,*p*-dinitrocumene *(12)* with the sodium salt of *n*-butylmalonic ester gives an 89% yield of the *C*-alkylated product (Fig. 2) when conducted in a nitrogen atmosphere, but under oxygen the principal product (80% yield) is *p*-nitrocumyl alcohol *(15)*, and only a 6% yield of the *C*-alkylate is obtained. α,*p*-Dinitrocumene is, of course, completely stable to molecular oxygen in the absence of the *n*-butylmalonate anion.

The ability of oxygen to prevent substitution at the tertiary carbon of *p*-nitrocumyl chloride or α,*p*-dinitrocumene is not restricted to reactions employing such malonate ions. Oxygen not only suppresses substitution by the various other anions but also prevents alkylation of amines by *p*-nitrocumyl chloride[15]. Usually *p*-nitrocumyl alcohol *(15)* is obtained in place of the alkylation product. However, with sodium azide, and with piperidine, the hydroperoxide *(16)* is also isolated; indeed, the reaction of sodium azide with α,*p*-dinitrocumene under oxygen gives a 76% yield of the hydroperoxide[20].



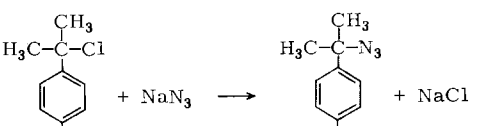
(16) *(15)*

These facts are easily understood on the basis of the proposed mechanism. Oxygen scavenges the *p*-nitrocumyl radicals, and the resulting peroxy radicals presumably are converted into *p*-nitrocumyl hydroperoxide *(16)* by hydrogen abstraction from the solvent. The various anions—except azide ion—readily reduce hydroperoxides to alcohols. The isolation, in excellent yields, of *p*-nitrocumyl alcohol and, in the azide and piperidine cases, of *p*-nitrocumyl hydroperoxide is consonant with the view that *p*-nitrocumyl radicals are intermediates in the various substitution reactions involving *p*-nitrocumyl chloride *(9)* and α,*p*-dinitrocumene *(12)*.

Furthermore, by using very small amounts of oxygen, evidence has been obtained for the chain character of these reactions[15, 19]. Thus, as shown in Figure 1, *p*-nitrocumyl chloride reacts with sodium benzenesulfinate to give the sulfone *(10)* in 95% yield. Under nitrogen at 25 °C this reaction is complete in 2 h; but with one mol % of oxygen present it proceeds only 1% in this time. Unambiguous retardation is also observed in reactions involving quinuclidine, sodiomalonic ester, the lithium salt of 2-nitropropane, and sodium azide.

4.2. The Effect of *m*- and *p*-Dinitrobenzene

In the *p*-nitrobenzyl system *p*-dinitrobenzene (*p*-DNB) prevents carbon alkylation of the 2-nitropropyl anion but does not interfere with the S_N2 process which gives rise to oxygen alkylation (Table 2). However, with a tertiary halide such as *p*-nitrocumyl chloride competition from S_N2 displacement processes is virtually non-existent. If, then, the radical anions of the chain sequence [eqs. (f) to (i)] were intercepted by a powerful one electron acceptor, *e.g.* *p*-DNB, the radical anion process would be inhibited and no reaction at all would be observed. This proves to be the case[21]. Thus the reaction *(9)* → *(13)* is 65% complete in 75 s but if 10 mol % of *p*-DNB is present no reaction occurs in this time.



(9) *(13)*

The reaction of sodium nitrite with *p*-nitrocumyl chloride *(9)* (Fig. 1) is also inhibited by *p*-DNB. If no *p*-DNB is present it proceeds 93% to completion in 20 min but in the presence of 10 mol % of *p*-DNB no reaction whatsoever takes place in this time.

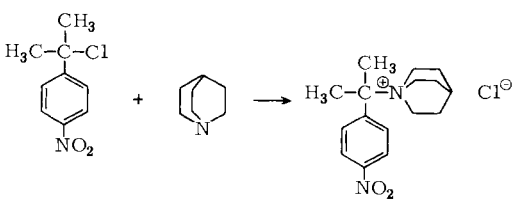
Whereas the reaction of *p*-nitrocumyl chloride with sodium benzenesulfinate (Fig. 1) is 83% complete in 5 min, if 10 mol % of *m*-DNB is present only 19% reaction occurs. Here, as elsewhere[6, 9], *m*-DNB is a less effective inhibitor than *p*-DNB, and this is consistent with the fact that *m*-DNB undergoes one electron reduction less readily than *p*-DNB[8].

These and a number of other experiments employing *p*-DNB and *m*-DNB support the view that radical anions are intermediates in substitution reactions of the *p*-nitrocumyl system. And they provide unambiguous evidence for the chain character of these processes.

4.3. The Effect of Di-*tert*-Butyl Nitroxide (Di-*tert*-butylaminyl Oxide)

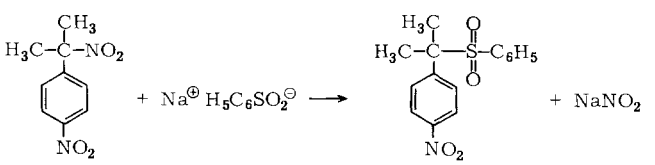
The mechanism of eqs. (f) to (i) invokes the *p*-nitrocumyl radical as part of a chain carrying sequence. Since di-*tert*-butyl nitroxide [di-*tert*-butylaminyl oxide $(C_4H_9)_2NO$] is known to be a free radical scavenger[22] inhibition ought to be observed when reactions of *p*-nitrocumyl chloride or α,*p*-dinitrocumene are conducted in its presence. This is precisely what happens. Thus the reaction of *p*-nitrocumyl chloride with the lithium salt of 2-nitropropane (Fig. 1) is 90% complete in 30 min but if 5 mol % of di-*tert*-butyl nitroxide is present only 3% reaction occurs.

Another example involves the reaction of quinuclidine with *p*-nitrocumyl chloride *(9)* to give the salt *(17)* which, after 5 h is 61% complete; but if 5 mol% of di-*tert*-butyl nitroxide is present only 4% reaction occurs in this time.



(9) *(17)*, 90%

And whereas the reaction of *(12)* with sodium benzenesulfinate goes 48% to completion in 20 min, if 5 mol % of nitroxide is present there is no reaction whatsoever in this time.



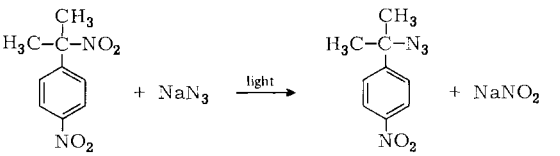
(12) *(10)*, 96%

In all, eight different reactions have been studied. In every case a small amount of di-*tert*-butyl nitroxide inhibits the reaction[23]. This is readily intelligible on the basis that the *p*-nitrocumyl radical is an intermediate and that these are chain reactions[24].

4.4. The Effect of Light

That light may speed up a radical anion substitution process was first realized during a study of the reactions of *p*-nitrobenzyl chloride[10]. Subsequently, numerous instances of light effects have been found, some of them very large[14, 15, 16, 19, 20, 22]. All that is required is illumination by diffuse daylight or by ceiling lights[*].

One of the most dramatic examples of a light effect involves α,*p*-dinitrocumene and sodium azide which, in the dark, do not react at all within 48 h. However, when they are exposed to room light for 30 min transformation into the azide *(13)* is 63% complete. And if the reaction flask is held about 15 cm from two ordinary 20 watt fluorescent lamps then the



(12) *(13)*, 94%

reaction goes to completion in less than 10 min[20]. These rather primitive observations have now been upgraded by a more sophisticated photochemical study[25]. It turns out that the reaction *(12)* → *(13)* has a quantum yield of 570. Even more striking is the finding that the reaction of *p*-nitrocumyl chloride *(9)* with sodium azide to give *(13)* has a quantum yield of 6000. With such quantum yields there can be no doubt that these are chain reactions[**].

4.5. Entrainment

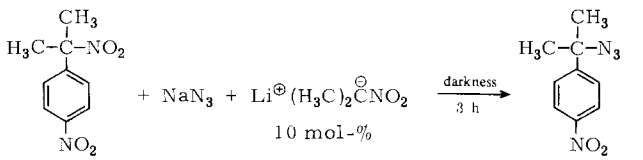
The view that substitution reactions of *p*-nitrocumyl chloride *(9)* and α,*p*-dinitrocumene *(12)* are chain processes suggested that those anions which react readily are the ones which find it easy to transfer one electron to the *p*-nitrocumyl system and thereby initiate the chain sequence of eqs. (f) to (i). Conversely, those anions which react slowly are the ones which have difficulty entering into the initiation step [eq. (f)].

The mechanism of eqs. (f) to (i) assigns not one, but two, roles to the anion. In the chain-propagating step [eq. (h)] the anion adds to the *p*-nitrocumyl radical in a manner reminiscent of the first stage of the Michael reaction; since this is part of a chain-propagating sequence it should be a rapid process. Thus, one would predict that *p*-nitrocumyl radicals can be intercepted not only by the anions used to produce them but also by other anions. In other words, even those anions which react slowly with *p*-nitrocumyl chloride should be able to compete for *p*-nitrocumyl radicals [eq. (h)]. If this is so, a catalytic amount of a reactive nucleophile should be capable of inducing the reaction of a less reactive (or nonreactive) nucleophile with *p*-nitrocumyl chloride or α,*p*-dinitrocumene. This prediction has been amply fulfilled[26].

[*] It should be emphasized that quite often light is *not* necessary for the reaction to proceed but in many instances it does provide significant acceleration.

[**] *Wade*'s study [25] of the wavelength dependence of the quantum yields suggests that photochemical initiation involves charge-transfer complexes derived from the nucleophile and *p*-nitrocumyl chloride (or α,*p*-dinitrocumene).

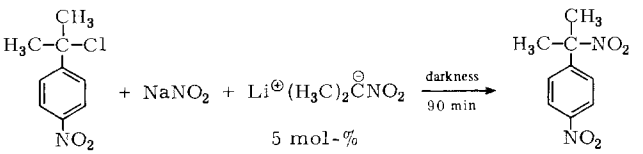
One of the more striking examples of entrainment involves α,*p*-dinitrocumene *(12)* and sodium azide which do not react at all in the dark within 48 h (Section 4.4). In contrast, even in the dark the lithium salt of 2-nitropropane reacts readily with α,*p*-dinitrocumene, the reaction being 87% complete in 3 h (Fig. 2). When α,*p*-dinitrocumene (1 mol) is treated with sodium azide (2 mol) in the presence of the lithium salt of 2-nitropropane (0.1 mol) all the α,*p*-dinitrocumene is consumed in 3 h, and a 97% yield of pure *p*-nitrocumyl azide *(13)* is obtained. Thus, the 2-nitropropyl anion transforms sodium azide from a reagent which does not react to one which reacts completely.



(12) *(13)*, 97%

The reaction of α,*p*-dinitrocumene with sodium benzenesulfinate provides another clear example of entrainment. In the dark only 8% reaction occurs in 96 h. However, when 5 mol % of the lithium salt of 2-nitropropane is present it goes to completion in 4 h and gives a 95% yield of *p*-nitrocumyl phenyl sulfone *(10)*.

Entrainment is not restricted to reactions employing α,*p*-dinitrocumene *(12)*. Thus, although *p*-nitrocumyl chloride *(9)* and sodium nitrite fail to react during 90 min in the dark, when 5 mol % of the lithium salt of 2-nitropropane is added the reaction goes to completion in 90 min and a 93% yield of α,*p*-dinitrocumene *(12)* is isolated.



(9) *(12)*, 93%

The radical anion chain mechanism of eqs. (f) to (i) provides a simple explanation for what would otherwise be an inexplicable phenomenon: the entraining anion initiates chains and the entrained anion carries them along[26].

4.6. Reactions Induced by One Electron Transfer Reagents

If the entrainment processes described in Section 4.5 do indeed derive from facile one electron transfer by the entraining anion then other one electron transfer agents should also be capable of inducing these substitution reactions. This proves to be the case[27].

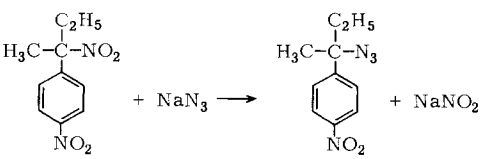
Thus α,*p*-dinitrocumene and sodium azide do not react at all in the dark, even after 48 h (see Section 4.4). But if 5 mol % of naphthalenesodium, which is a one electron transfer agent[28], is added they react completely in less than an hour to give *p*-nitrocumyl azide *(13)* in 97% yield. Sodium hyperoxide, $Na^{\oplus}O_2^{\ominus}$, also induces this reaction. Even as little as 3 mol % of sodium trimesitylborane, which is also a one electron transfer agent[29], results in a 92% yield of *p*-nitrocumyl azide in 30 min. Finally, a solution of sodium metal in hexamethylphosphoramide (HMPA), which is thought to contain solvated electrons[30, 29], produces *p*-nitrocumyl azide in 87% yield within 30 min when present at the 4 mol % level.

Similar results are obtained with *p*-nitrocumyl chloride. For example, in the dark this chloride and sodium nitrite do not react in 90 min. But if 12 mol % of naphthalenesodium is present the chloride is consumed within an hour and an 89% yield of pure α,*p*-dinitrocumene is isolated. A solution of sodium in HMPA (20 mol %) brings about complete reaction of *p*-nitrocumyl chloride with sodium nitrite in 90 min and an 85% yield of α,*p*-dinitrocumene is obtained.

The fact that a variety of one electron transfer agents, and a solution of electrons in HMPA, induce substitution processes in the *p*-nitrocumyl system is consonant with the view that these reactions are initiated by one electron transfer and provides further support for the radical anion-free radical chain mechanism [eqs. (f) to (i)].

4.7. Stereochemistry of Substitution

If these reactions involve free radical intermediates then substitution processes in which the aliphatic nitro group of optically active *(18)* is displaced should give completely racemic products. This is precisely what is observed[25]. When optically active *(18)* is treated with sodium azide in HMPA it is rapidly and cleanly converted to the azide *(19)* and this azide is *racemic*. In the same way, treatment of optically active *(18)* with sodium benzenesulfinate gives an excellent yield of the corresponding racemic sulfone. Substitution of the aliphatic nitro group of *(18)* by thiophenoxide



(18) *(19)*

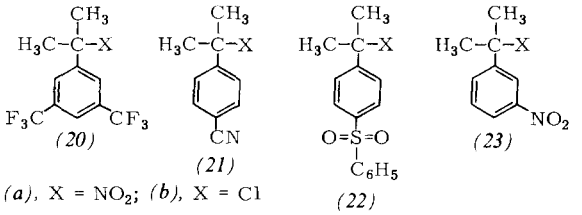
ion or by the anion of 2-nitropropane also occurs readily and, again, the products are racemic. Finally, it is of interest that optically active *(18)* is racemized by sodium nitrite.

5. Other Systems

In order to establish what other types of compounds are capable of undergoing substitution reactions *via* the one electron transfer pathway the study of a variety of aromatic, aliphatic, and heterocyclic compounds has been initiated.

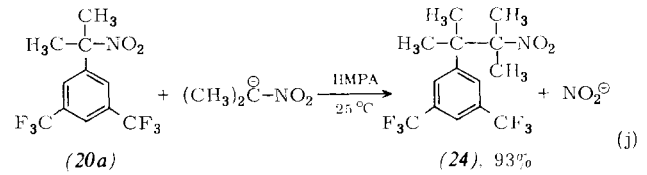
5.1. Aromatic Systems

Among the systems being studied are *(20)* to *(23)*. Although this work is incomplete, and the understanding of the chemistry of these systems is in a less than satisfactory state, some things are clear. For one, a number of synthetically valuable reactions occur at room temperature. But complications which do not exist in the *p*-nitrocumyl system may intrude here, and as a consequence the very high yields of pure products which are almost effortlessly obtained in the *p*-nitrocumyl system are not as yet routinely obtainable with systems *(20)* to *(23)*.

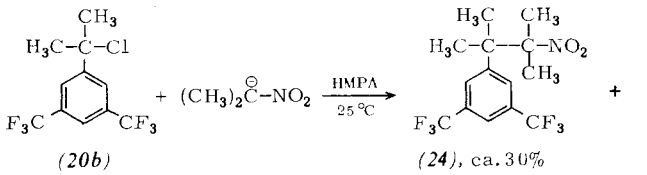


(a), X = NO_2; *(b)*, X = Cl

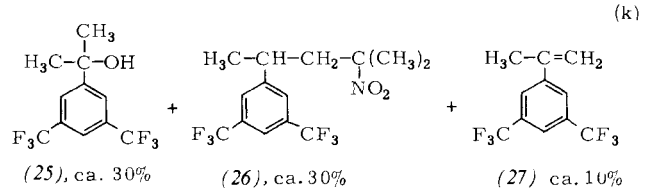
To illustrate: reaction (j) results in a 93% yield of pure *C*-alkylate *(24)*, but reaction (k) gives only a *ca.* 30% yield[31]. This difference is believed to derive from competition, in the case of the chloride, by two other processes:



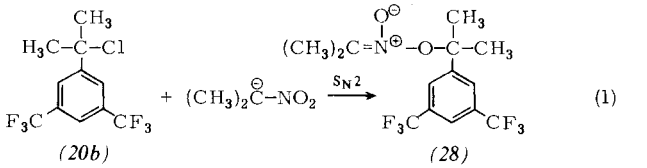
(j)



(k)



1) An S_N2 displacement[13] by the 2-nitropropane anion [eq. (1)]; this would produce the *O*-alkylated product which, on work-up, would probably hydrolyze to the alcohol *(25)*.



(1)

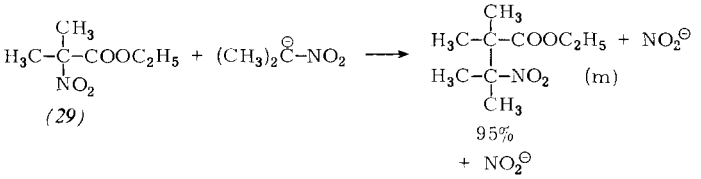
2) Dehydrohalogenation of the chloride *(20b)* by the nitroalkyl anion to give the olefin *(27)* followed by Michael addition of 2-nitropropane to the olefin. This Michael addition is known to take place readily to yield *(26)*[31].

The use of some of the diagnostics described in Section 4 supports the view that the *C*-alkylated product *(24)* obtained in reactions (j) and (k) is produced by a radical anion pathway but that the by-products *(25)* to *(27)* do not arise from a radical anion process. The other aromatic systems [*(21)*, *(22)*, *(23)*] also appear to be capable of undergoing substitution *via* radical anions but the scope and limitations of these processes have not yet been delineated.

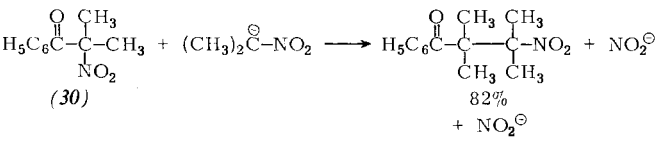
5.2. Aliphatic Systems

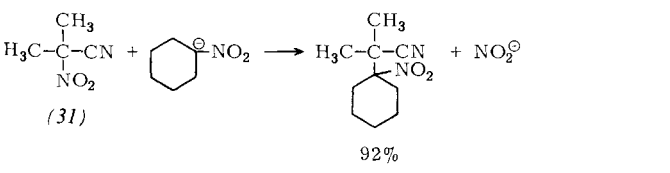
In 1970 a new reaction, the displacement of a nitro group from α-nitro esters, α-nitro ketones, α-nitro nitriles, and α,α-dinitro compounds by nitroalkyl anions, was described[32].

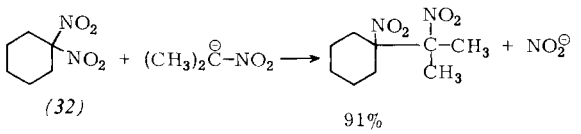
These transformations are especially interesting because they involve purely aliphatic systems; some typical examples are the reactions of compounds *(29)* to *(32)*. These reactions take place at room temperature in a matter of minutes or hours, and they make readily accessible very highly branched compounds which would be difficult to prepare by other means.



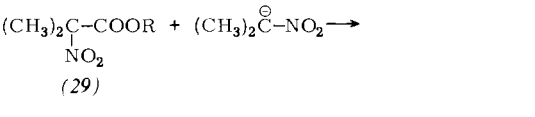
(m)



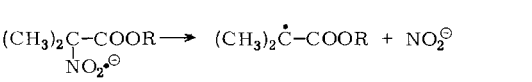




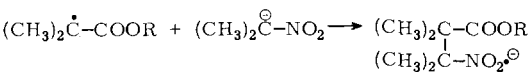
The mechanism of these displacements has been investigated[33]. With α-nitro esters there is a pronounced light effect, and a recent study of reaction (m) has shown that the quantum yield is *ca.* 220 when 400 nm light is employed[25]. Thus, the average chain length is at least 220. This fact, in conjunction with those given below, has led to the proposal that the mechanism is that described by eqs. (n) to (q).



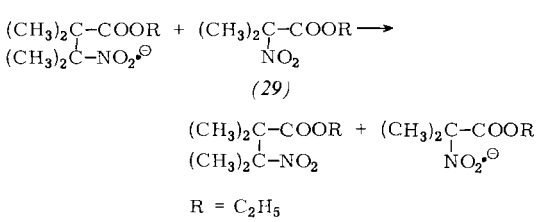
(n)



(o)



(p)



(q)

R = C_2H_5

Table 3 summarizes what happens when the reaction (m) is subjected to the influence of small amounts of inhibitors. It will be seen that free radical scavengers are effective in stopping the reaction. For example, 5 mol % of galvinoxyl[24] produces a dead period of 2.5 h after which the reaction begins; without galvinoxyl, the reaction proceeds to 83 % completion in this time. *p*-Dinitrobenzene, a diagnostic for radical anions[22], is also a powerful inhibitor. But most interesting of all is the observation that even nitrobenzene inhibits this reaction, a fact which accords with the view that nitroaliphatic radical anions are intermediates[33].

Table 3. Influence of inhibitors on the reaction of ethyl α-nitroisobutyrate with the lithium salt of 2-nitropropane.

Inhibitor 5 mol %	Dead time [h]	Control reaction [%] [a]
Galvinoxyl [b]	2.5	83
p-Benzoquinone	3	88
Di-*tert*-butyl nitroxide	11	100
p-Dinitrobenzene	4	96
Nitrobenzene	1	40
Nitrobenzene [c]	4	95

[a] Extent of reaction in the specified time without inhibitor.
[b] 2,6-Di-*tert*-butyl-4-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadienylidenemethyl)phenoxyl.
[c] 94 mol %.

In the same way, the reaction of α-nitroisobutyrophenone *(30)* with the 2-nitropropyl anion is completely inhibited for 30 min by 5 mol % of either *p*-dinitrobenzene or galvinoxyl; in the absence of these inhibitors 35 % reaction takes place in 30 min. Di-*tert*-butyl nitroxide (5 mol %) stops this reaction for 10 h; without nitroxide the reaction is complete in this time. It is concluded, then, that displacement of the nitro group from the α-nitro ketone proceeds by a chain sequence completely analogous to that of eqs. (n) to (q).

The reaction of 2-nitroisobutyronitrile *(31)* with the 2-nitropropyl anion is inhibited by *p*-dinitrobenzene, galvinoxyl, *p*-benzoquinone, and di-*tert*-butyl nitroxide at the 5 mol % level.

$$(CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}CN + (CH_3)_2C\text{–}NO_2 \longrightarrow (CH_3)_2\underset{\underset{(CH_3)_2C\text{–}NO_2}{|}}{C}\text{–}CN + NO_2^{\ominus}$$

(31) 90%

Clearly, it is a chain process. A mechanism fully analogous to that of eqs. (n) to (q), involving the $(CH_3)_2C(CN)NO_2^{\ominus}$ radical anion and the $(CH_3)_2C$—CN radical, is easily envisioned.

The displacement of a nitro group from an α,α-dinitro compound by a nitroalkyl anion is a very rapid process. In DMSO, reaction (r) is complete in 2 min, but if 5 mol % of *p*-dinitrobenzene is present, it proceeds only to the extent of 10 % in this time. In DMF the rate is decreased somewhat—now the reaction requires 90 min to go to completion; but if the solution contains 5 mol % of galvinoxyl the reaction is completely inhibited for at least 90 min. Manifestly, we are dealing with a chain reaction, and, once again, it is reasonable to presume that radical anions and free radicals are intermediates and that the mechanism corresponds to that of eqs. (n) to (q)[33].

$$(CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}NO_2 + (CH_3)_2\overset{\ominus}{C}\text{–}NO_2 \longrightarrow (CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{—}\underset{\underset{NO_2}{|}}{C}(CH_3)_2 + NO_2^{\ominus} \quad (r)$$

(33) *(34)*, 82%

The proposal that an aliphatic nitro group is capable of accepting one electron and that the resulting radical anion, by loss of nitrite ion, gives a free radical [eqs. (n) and (o)] is derived from the pioneering work of *A. K. Hoffmann et al.*[34]. However, where the earlier workers employed metallic sodium or an electric current as the source of electrons, the transformations of compounds *(29)* to *(33)* use nitroalkyl anions. It is remarkable that such a "low pressure" source of electrons as a nitroalkyl anion is able to transfer one electron to an aliphatic nitro group and thereby initiate the chain sequence of eqs. (n) to (q).

Nitroalkyl anions are not the only nucleophiles which are able to displace a nitro group from an α,α-dinitro compound. Thus reaction (s) occurs at 25 °C and, although a relatively slow process, gives an 81 % yield of the α-nitro sulfone *(35)*[35]. This displacement by a sulfinate ion is speeded up by light and inhibited by 10 mol % of di-*tert*-butyl nitroxide.

$$(CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}NO_2 + H_5C_6SO_2^{\ominus} \xrightarrow[25\,^{\circ}C]{3\ \text{days}} (CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}SO_2C_6H_5 + NO_2^{\ominus} \quad (s)$$

(33) *(35)*, 81%

The anion *(36)* also reacts with 2,2-dinitropropane *(33)* at 25 °C. Here again the reaction is greatly accelerated by light; it is also catalyzed by a small amount of nitrobenzene-potassium (the radical anion of nitrobenzene)[36]. There can be little doubt that the last two reactions are also radical anion-free radical chain processes.

$$(CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}NO_2 + H_5C_2\overset{\ominus}{C}(COOC_2H_5)_2 \longrightarrow$$

(33) *(36)*

$$(CH_3)_2\underset{\underset{NO_2}{|}}{\overset{\overset{C_2H_5}{|}}{C}}\text{–}C(COOC_2H_5)_2 + NO_2^{\ominus}$$

65%

Thus far, all the reactions described in this section involve the displacement of a nitro group from an aliphatic molecule. It has been known for some time, however, that α-halo nitro compounds, on treatment with nucleophiles, undergo an alternative type of substitution in which the halogen rather than the nitro group is displaced. Thus, 2-chloro-2-nitropropane, 2-bromo-2-nitropropane, and 2-iodo-2-nitropropane all react with the nitropropyl anion to give 2,3-dimethyl-2,3-dinitrobutane *(34)*[37]. Another early example is the reaction of 2-chloro-2-nitropropane with the anion *(36)*[38]. In recent years a number of cases have been reported in which the halogen atom of α-chloronitroalkanes, α-bromonitroalkanes, and α-iodonitroalkanes is displaced. Among them are the transformations of compounds *(37)* to *(39)*[35,36,39].

$$(CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}X + (CH_3)_2\overset{\ominus}{C}\text{–}NO_2 \longrightarrow (CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{—}\underset{\underset{NO_2}{|}}{C}(CH_3)_2 + X^{\ominus}$$

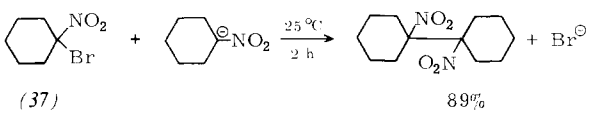
X = Cl, Br, I *(34)*

$$(CH_3)_2\underset{\underset{NO_2}{|}}{C}\text{–}Cl + H_5C_2\overset{\ominus}{C}(COOC_2H_5)_2 \longrightarrow$$

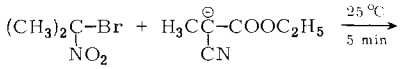
(36)

$$(CH_3)_2\underset{\underset{NO_2}{|}}{\overset{\overset{C_2H_5}{|}}{C}}\text{—}C(COOC_2H_5)_2 + Cl^{\ominus}$$

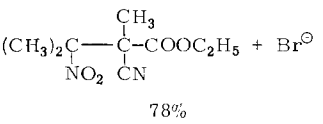
68%



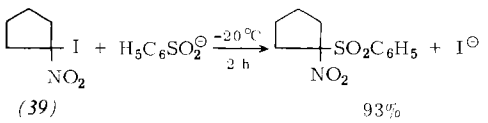
(37) 89%



(38)

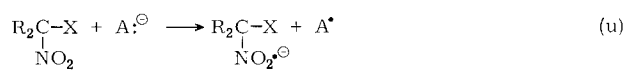


78%



(39) 93%

These substitution reactions of α-halo nitro compounds are, in a number of cases, catalyzed by light. Furthermore, various of these processes have been shown to be inhibited by small amounts of di-*tert*-butyl nitroxide, *p*-dinitrobenzene, and triphenylmethyl radicals. They are, therefore, regarded as proceeding *via* the mechanism of eqs. (u) to (x).

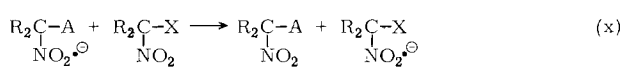


(u)

X = Cl, Br, I

(v)

(w)

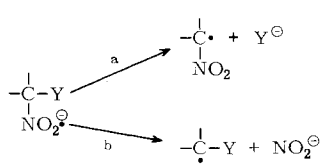


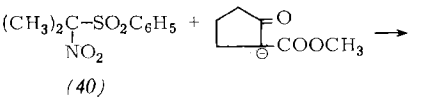
(x)

α-Nitro sulfones in which the carbon bearing the nitro and sulfone groups is devoid of hydrogen atoms have become available thanks to the transformation exemplified by eq. (t)[35]. It has recently been found that α-nitro sulfones such as *(40)* to *(43)* react readily with a variety of nucleophiles at room temperature and that it is the sulfone group which is displaced[40,41].

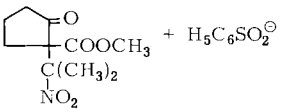
These new reactions all show the characteristics of radical anion-free radical chain processes: many of them are strongly accelerated by light and they are inhibited by small amounts of di-*tert*-butyl nitroxide, *p*-dinitrobenzene, and *m*-dinitrobenzene. The mechanism of eqs. (u) to (x) [X = Ar—$SO_2^{\ominus}$] provides a simple basis for understanding these facts.

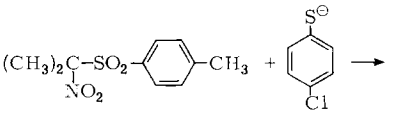
We see then that the radical anion derived from an α-substituted nitroalkane may fragment in two ways:



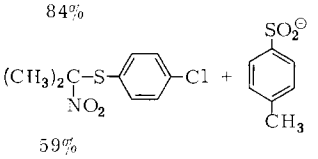


(40)

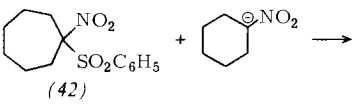




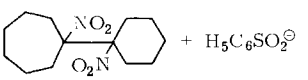
(41) 84%



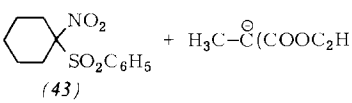
59%



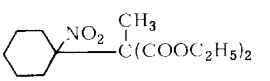
(42)



85%



(43)



87%

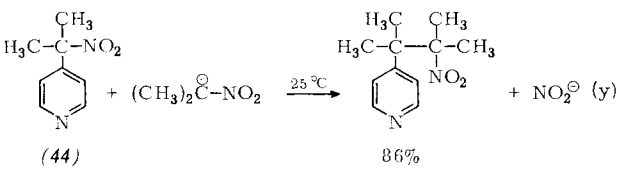
With Y = Cl, Br, I, Ar—SO_2, the halide or sulfinate ion is formed (path a) whereas when Y = COOR, C(O)—R, CN, NO_2, a nitrite ion is expelled (path b).

In sum, a variety of radical anion processes are already known in purely aliphatic systems. While it is true that in each case a nitro compound is involved, it seems reasonable to assume that other functions which can delocalize one electron, *e.g.*, the cyano group, will give rise to analogous substitution processes.

5.3. Heterocyclic Systems

Very little is known about the ability of heterocyclic systems to enter into radical anion substitution at a saturated carbon attached to the heterocyclic nucleus. The only heterocycles to have been studied are some substituted pyridines, and the investigation is far from complete[42].

The nitropyridine *(44)* reacts cleanly with the 2-nitropropyl anion according to eq. (y); light greatly accelerates the reaction and 5 mol % of either *m*-dinitrobenzene or di-*tert*-butyl nitrox-

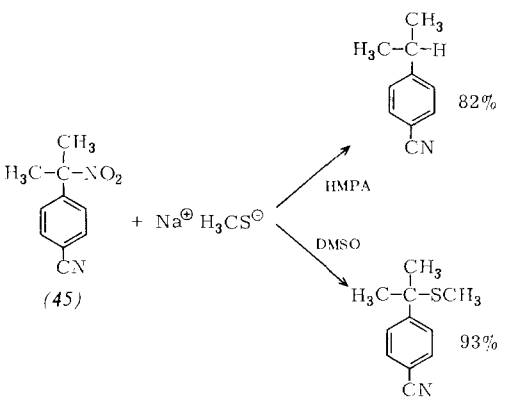


(44) 86% (y)

ide serves as an effective inhibitor. There can be little doubt that this is a radical anion process. But it is by no means established that reaction (y) reflects the ability of a pyridine ring to accept one electron readily enough to sustain a radical anion-free radical chain process. Actually, preliminary work suggests that the ability of *(44)* to react with the 2-nitropropyl anion *via* the electron transfer pathway may depend chiefly, or exclusively, on the nitro group in *(44)* rather than on the pyridine ring[42].

6. Related Processes

It has recently been found[43] that tertiary nitro compounds such as *(45)* on treatment with the sodium methanethiolate may undergo clean replacement of the nitro group by hydrogen, or by thiomethyl, depending on the solvent. Although

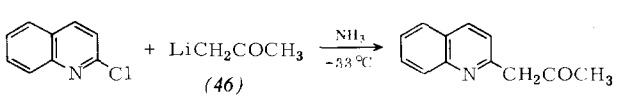


a number of questions remain to be answered, it appears likely that these transformations involve radical anion intermediates.

While this paper is primarily concerned with electron transfer substitution at a saturated carbon it should be noted that since 1970 *Bunnett et al.* have described a number of examples of substitution at an aromatic carbon atom which appear to proceed *via* a chain mechanism involving radical anions and free aryl radicals[44].

ArX + electron donor → $[ArX]^{\ominus}$ + residue
$[ArX]^{\ominus} \rightarrow Ar\bullet + X^{\ominus}$
$Ar\bullet + Y^{\ominus} \rightarrow [ArY]^{\ominus}$
$[ArY]^{\ominus} + ArX \rightarrow ArY + [ArX]^{\ominus}$
X = Cl, Br, I, SC_6H_5, $N^{\oplus}(CH_3)_3A^{\ominus}$, $O{-}PO(OC_2H_5)_2$
Y = NH_2, carbanions, SC_6H_5

Still more recently, *Wolfe et al.*[45] have shown that in liquid ammonia at −33 °C the chlorine of 2-chloroquinoline is readily displaced by dialkali metal salts of benzoylacetone and by the lithio enolate of acetone *(46)*. *Wolfe*'s evidence clearly supports his assignment of a radical anion-free radical chain



mechanism to these processes. Furthermore, in 1973 *Zoltewicz* and *Oestreich*[46] reported that replacement of the bromine of 4-bromoisoquinoline by sodium thiophenoxide is changed from an ionic to a radical anion-free radical chain pathway merely on adding sodium methoxide.

7. Summary

Nucleophilic substitution at a saturated carbon atom may occur *via* a multi-stage pathway in which radical anions and free radicals are intermediates. These reactions take place rapidly under mild conditions and give excellent yields of pure products. In contrast to S_N2 displacements, electron transfer substitution reactions are rather insensitive to steric hindrance and, consequently, they are especially effective for the synthesis of highly branched compounds.

It would be incorrect to regard S_N2 displacements as electron transfer processes. The S_N2 reaction is distinct and different from the transformations described in this review—there is, in fact, often a competition between these two processes. That this is so becomes especially clear when the nucleophile is an ambident anion[*].

I wish to express sincere appreciation to my students and coworkers not only for the experimental work on which this paper is based but, also, for the fact that they have made significant contributions to the studies herein described.—Over the years this work has received generous support from a number of sources: The National Science Foundation, Eli Lilly and Company, The Petroleum Research Fund of the American Chemical Society, The Hoffman-La Roche Foundation, and the DuPont Company.—This manuscript was written during my tenure as a visiting professor in the Organic Chemistry Department of the Swiss Federal Institute of Technology, Zürich. It gives me great pleasure to thank the staff of the Organic Chemistry Department for providing a congenial and stimulating environment.

Received: March 12, 1975 [A 85 IE]
German version: Angew. Chem. *87*, 797 (1975)

[1] *N. Kornblum, R. A. Smiley, R. K. Blackwood,* and *D. C. Iffland,* J. Am. Chem. Soc. *77*, 6269 (1955).
[2] For a more detailed description of the historical aspects see *N. Kornblum,* Proc. Int. Congr. Pure Appl. Chem., 23rd, *4*, 81 (1971).
[3] *L. Weisler* and *R. W. Helmkamp,* J. Am. Chem. Soc. *67*, 1167 (1945).
[4] *H. B. Hass* and *M. L. Bender,* J. Am. Chem. Soc. *71*, 1767, 3482 (1949).
[5] *N. Kornblum, P. Pink,* and *K. V. Yorka,* J. Am. Chem. Soc. *83*, 2779 (1961).
[6] *R. C. Kerber, G. W. Urry,* and *N. Kornblum,* J. Am. Chem. Soc. *86*, 3904 (1964); *87*, 4520 (1965).
[7] *S. I. Weissman,* Z. Elektrochem. *64*, 47 (1960); *R. L. Ward,* J. Chem. Phys. *32*, 410 (1960); *M. T. Jones* and *S. I. Weissman,* J. Am. Chem. Soc. *84*, 4269 (1962).
[8] *A. H. Maki* and *D. H. Geske,* J. Am. Chem. Soc. *83*, 1852 (1961).
[9] *N. Kornblum, R. E. Michel,* and *R. C. Kerber,* J. Am. Chem. Soc. *88*, 5660, 5662 (1966).
[10] *G. A. Russell* and *W. C. Danen,* J. Am. Chem. Soc. *88*, 5663 (1966).
[11] *N. Kornblum,* cited by *H. Feuer,* Tetrahedron Suppl. *1*, 107 (1964).
[12] The claim [9] that $CuCl_2$ at very low concentrations also suppresses carbon alkylation has been disputed by *G. S. Greene* (Ph. D. Thesis, Purdue University, 1968); this discrepancy requires clarification.
[13] When these studies were initiated there were few, if any, well authenticated examples of S_N2 displacements at a tertiary carbon atom. Since that time a few cases have been reported: *A. Miotti* and *A. Fava,* J. Am. Chem. Soc. *88*, 4274 (1966); *F. G. Bordwell* and *T. G. Mecca, ibid. 94*, 2119 (1972). Also see: *R. A. Sneen* and *P. S. Kay, ibid. 94*, 6983 (1972); *C. A. Grob, K. Seckinger, S. W. Tam,* and *R. Traber,* Tetrahedron Lett. *1973*, 3051. We have found that if matters are arranged so that the radical anion process is disfavored, *e.g.*, by the presence of inhibitors, then an S_N2 displacement by azide ion at the tertiary

[*] Lest this cautionary note appear somewhat gratuitous, attention must be drawn to a recent publication entitled "Evidence for an Electron-Transfer Component in a Typical Nucleophilic Displacement Reaction" [*S. Bank* and *D. A. Noyd,* J. Am. Chem. Soc. *95*, 8203 (1973)] which makes the completely unwarranted proposal that S_N2 reactions ought to be considered as having an electron transfer component.

carbon of *p*-nitrocumyl chloride can be observed (unpublished work of Dr. *P. A. Wade*). But, ordinarily the S_N2 displacement does not compete with the radical anion process when *p*-nitrocumyl chloride is treated with a nucleophile. However, with cumyl chlorides which enter into radical anion reactions less readily than *p*-nitrocumyl chloride competition from the S_N2 displacement at a tertiary carbon may occur (see below). We are indebted to Dr. *J. W. Manthey* and to Professor *F. G. Bordwell* for drawing our attention to the possibility of S_N2 displacements in cumylic systems.

[14] *N. Kornblum, T. M. Davies, G. W. Earl, N. L. Holy, R. C. Kerber, M. T. Musser*, and *D. H. Snow*, J. Am. Chem. Soc. *89*, 725 (1967); *N. Kornblum* and *M. M. Kestner*, unpublished work.

[15] *N. Kornblum* and *F. W. Stuchal*, J. Am. Chem. Soc. *92*, 1804 (1970).

[16] *N. Kornblum, T. M. Davies, G. W. Earl, G. S. Greene, N. L. Holy, R. C. Kerber, J. W. Manthey, M. T. Musser*, and *D. H. Snow*, J. Am. Chem. Soc. *89*, 5714 (1967).

[17] Unpublished work by Drs. *P. A. Wade* and *R. T. Swiger*.

[18] *N. Kornblum, G. W. Earl, N. L. Holy, J. W. Manthey, M. T. Musser, D. H. Snow*, and *R. T. Swiger*, J. Am. Chem. Soc. *90*, 6221 (1968).

[19] *R. T. Swiger*, Ph. D. Thesis, Purdue University, June 1970.

[20] *J. W. Manthey*, Ph. D. Thesis, Purdue University, August 1969.

[21] *Leung Cheng*, unpublished work.

[22] *N. Kornblum, S. D. Boyd*, and *N. Ono*, J. Am. Chem. Soc. *96*, 2580 (1974), and references cited therein.

[23] *H. W. Pinnick*, Ph. D. Thesis, Purdue University, January 1972.

[24] The stable free radical galvinoxyl, an efficient scavenger of free radicals [*P. D. Bartlett* and *T. Funahashi*, J. Am. Chem. Soc. *84*, 2600 (1962)] also inhibits the reaction *(12)* → *(10)*. If 5 mol % is added no reaction occurs in 30 min; without galvinoxyl the reaction goes 57 % to completion in this time (Dr. *M. M. Kestner*, unpublished).

[25] *P. A. Wade*, Ph. D. Thesis, Purdue University, May 1973. We are indebted to Professor *H. A. Morrison* for valuable assistance in this photochemical work.

[26] *N. Kornblum, R. T. Swiger, G. W. Earl, H. W. Pinnick*, and *F. W. Stuchal*, J. Am. Chem. Soc. *92*, 5513 (1970).

[27] *M. M. Kestner*, Ph. D. Thesis, Purdue University, May 1973.

[28] *J. F. Garst*, Accounts Chem. Res. *4*, 400 (1971).

[29] *S. D. Darling, O. N. Devgan*, and *R. E. Cosgrove*, J. Am. Chem. Soc. *92*, 696 (1970).

[30] *G. Fraenkel, S. H. Ellis*, and *D. T. Dix*, J. Am. Chem. Soc. *87*, 1406 (1965).

[31] *B. N. Newton*, Ph. D. Thesis, Purdue University, January 1972.

[32] *N. Kornblum, S. D. Boyd*, and *F. W. Stuchal*, J. Am. Chem. Soc. *92*, 5783 (1970).

[33] *N. Kornblum* and *S. D. Boyd*, J. Am. Chem. Soc. *92*, 5784 (1970).

[34] *A. K. Hoffmann, W. G. Hodgson, D. L. Maricle*, and *W. H. Jura*, J. Am. Chem. Soc. *86*, 631 (1964); also see *H. Sayo, Y. Tsukitani*, and *M. Masui*, Tetrahedron *24*, 1717 (1968).

[35] *N. Kornblum, M. M. Kestner, S. D. Boyd*, and *L. C. Cattran*, J. Am. Chem. Soc. *95*, 3356 (1973).

[36] *G. A. Russell, R. K. Norris*, and *E. J. Panek*, J. Am. Chem. Soc. *93*, 5839 (1971).

[37] *L. W. Seigle* and *H. B. Hass*, J. Org. Chem. *5*, 100 (1940).

[38] *E. E. van Tamelen* and *G. Van Zyl*, J. Am. Chem. Soc. *71*, 835 (1949).

[39] *N. Kornblum, S. D. Boyd, H. W. Pinnick*, and *R. G. Smith*, J. Am. Chem. Soc. *93*, 4316 (1971).

[40] *N. Kornblum, S. D. Boyd*, and *N. Ono*, J. Am. Chem. Soc. *96*, 2580 (1974).

[41] *J. J. Zeilstra* and *J. B. F. N. Engberts*, Rec. Trav. Chim. Pays-Bas. *92*, 954 (1973).

[42] *J. K. Doty, H. Feuer*, and *N. Kornblum*, unpublished work.

[43] *N. Kornblum, S. C. Carlson*, and *R. G. Smith*, unpublished work.

[44] *J. K. Kim* and *J. F. Bunnett*, J. Am. Chem. Soc. *92*, 7643 (1970); *J. F. Bunnett* and *B. F. Gloor*, J. Org. Chem. *39*, 382 (1974); *J. F. Bunnett*, J. Chem. Educ. *51*, 312 (1974).

[45] *J. F. Wolfe, J. C. Greene*, and *T. Hudlicky*, J. Org. Chem. *37*, 3199 (1972); *J. V. Hay, T. Hudlicky*, and *J. F. Wolfe*, J. Am. Chem. Soc. *97*, 374 (1975).

[46] *J. A. Zoltewicz* and *T. M. Oestreich*, J. Am. Chem. Soc. *95*, 6863 (1973).

Mechanism of Ozonolysis

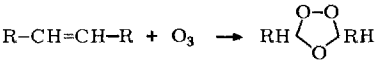
By Rudolf Criegee[*]

The formation of ozonides (1,2,4-trioxolanes) from alkenes and ozone can be described as a succession of three [2+3] cycloadditions or cycloreversions involving primary ozonides (1,2,3-trioxolanes) and aldehyde or ketone oxides as decisive intermediates, all of which have finite lifetimes. There is no warranted experimental basis for assuming an alterna ive mechanism.

1. Introduction

The oxidative cleavage of unsaturated compounds with ozone in solution, which was first studied in detail by *Harries*[1] at the turn of the century, is, in many respects an unusual type of reaction. With very few exceptions, a double bond is cleaved quantitatively under extremely mild conditions—usually at or below −78 °C in dilute solution in the absence of acids or bases. The products of this cleavage are aldehydes and/or ketones or their peroxidic derivatives, or—in the case of aldehydes—their oxidation products, the carboxylic acids. The product pattern obtained in individual cases depends not only on the constitution of the starting compounds but also on the reaction conditions, especially the solvent used and the method of workup, which can be carried out purely hydrolytically, reductively, or oxidatively.

One group of possible reaction products includes the so-called "ozonides", which were shown more than three decades ago by *Rieche*[2] to have the structure of the 1,2,4-trioxolanes *(1)*. These are cyclic peroxides, a large number of which are known today as distillable liquids or crystalline compounds. The "exotic" nature of ozone cleavage or "ozonolysis" is at once apparent when one considers the formation of these ozonides. Not only is the double bond of the alkene cleaved but also the ozone molecule itself, the two resulting fragments of which form an ether bridge and a peroxide bridge, respectively, between the two C atoms of the alkene.



(1)

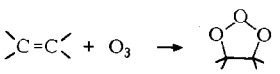
Few other reactions have so compellingly warranted attention as regards the mechanism involved. We have been studying this question since 1949. Essential contributions have been made by other groups, too [3].

[*] Prof. Dr. R. Criegee
Institut für Organische Chemie der Universität
75 Karlsruhe, Richard-Willstätter-Allee (Germany)

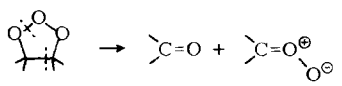
2. Three-Step Mechanism of Ozonolysis

It is clear from the start that ozonolysis cannot proceed as a one-step reaction. As we currently believe (and as we had already suggested in a lecture delivered at the IUPAC Congress in New York in 1951), to our knowledge the reaction proceeds in three discrete steps, all of which, according to *Huisgen*'s terminology[4], are 1,3-dipolar reactions ([2+3] additions or reversions). Let us first of all look at these postulated steps and then, in the following and later Sections, we shall deal with illustrative examples and confirmatory evidence of their participation in ozonolysis.

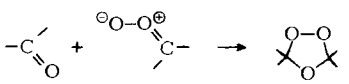
Reaction A: Formation of a "primary ozonide"



Reaction B: Decomposition of the primary ozonide into carbonyl compound + "carbonyl oxide"

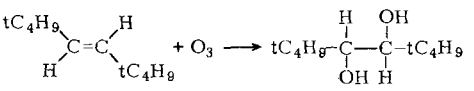


Reaction C: Addition of the "carbonyl oxide" to the carbonyl compound



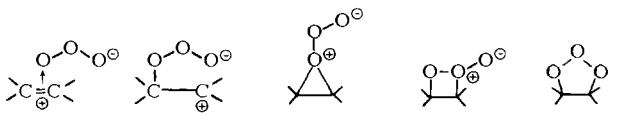
3. Primary Ozonides

Addition compounds of ozone and olefin have already been postulated on numerous occasions as the primary intermediate products of ozonolysis, but it was not until 1958 before *Schröder*[5] succeeded in detecting such a compound. On ozonization of *trans*-2,2,5,5-tetramethyl-3-hexene *(2)* in pentane at −78 °C crystals are formed which decompose exothermally on warming to about −40 °C and do not reappear on subsequent cooling. The constitution with still intact C—C single bond could be confirmed by low-temperature reduction with isopropylmagnesium chloride: the racemic diol *(3)* was formed.



(2) *rac. (3)*

There are five conceivable ways in which we can formulate an olefin-ozone adduct, namely those depicted in *(4)*—*(8)*.



(4) *(5)* *(6)* *(7)* *(8)*

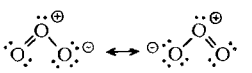
π-complex σ-complex peroxy-epoxide oxy-1,2-dioxetane 1,2,3-trioxolane

Of these, only the dioxetane derivative *(7)* and the 1,2,3-trioxolane *(8)* are likely to favor formation of a 1,2-diol on reduction. Formula *(7)*, which was first proposed almost half a century ago by *Staudinger*[6] for the then hypothetical primary ozonides, was recently favored by *Story*[7]. However, according to *Bailey*[8] the NMR spectrum of the primary ozonide of *(2)*[5] indicates equivalence of the chemical environs at both C atoms, which would not be so in the case of *(7)*. *Story*'s apparent evidence for *(7)*, namely the reduction of a primary ozonide with pinacoline to give a 1,2-dioxetane[9], was later recognized as being experimentally erroneous[10].

Other instances of the detection of primary ozonides have been reported; those derived from aliphatic *trans*-olefins are stable only below −110 °C, those from corresponding *cis*-olefins only below −130 °C[11].

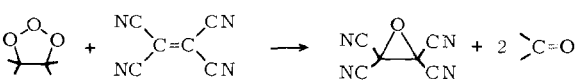
While the primary ozonides are, in general, 1,2,3-trioxolanes *(8)* there are also indications for the existence of π complexes of formula *(4)*. *Bailey* was able to detect such complexes in the reaction of ozone with electron-rich arenes at −150 °C[12]. They absorb visible light, but in contrast to the deep-blue of ozone they are violet, red, or yellow. At higher temperatures they decompose into their components. It is possible that they are also formed from olefins and ozone if sufficiently low temperatures are used. It is still questionable, however, whether they play any further part in the process of ozonization.

σ-Complexes *(5)* or peroxy-epoxides *(6)* must be assumed as primary products in the few ozonizations in which the double bond is not completely cleaved but epoxides or their secondary products are formed. This is the case in sterically very strongly hindered olefins, *e. g.* in 1-mesityl-1-phenylethylene[13] or in adamantylideneadamantane[14]. Probably the intermediates *(5)* or *(6)* in these cases immediately lose an oxygen molecule and thus give the epoxides. The addition of ozone, which, in accordance with the principle resonance formulas



is a typical dipole[15], proceeds stereospecifically, as is evident from the configuration of the diols formed on reduction.

Since resonance stabilization of the ozone molecule is missing in the primary ozonides *(8)* they are not only thermally much more labile but are also stronger oxidizing agents than ozone towards some substrates. For example, tetracyanoethylene (TCNE) is stable toward ozone at −78 °C but, according to *Günther*[16], is oxidized by primary ozonides to the (previously unknown) TCNE epoxide *(9)*. The primary ozonide is converted smoothly into the carbonyl compound.



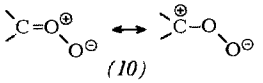
(8) TCNE *(9)*

Isolation of the primary ozonide is unnecessary, ozonization of the olefin in the presence of one equivalent of TCNE suffices. The reaction has twofold significance: On the one hand it is helpful for recognizing primary ozonides and estimating their stability, and on the other hand one can obtain carbonyl compounds as products by this "reductive ozoniza-

tion" even in cases where otherwise rearrangements to anomalous ozonization products occur (see Section 4.3).

4. Carbonyl Oxides

Primary ozonides are stable at or above −78 °C only in exceptional cases. In order to explain the diversity of decomposition products it was assumed at a very early stage[17] that decomposition into a carbonyl compound (aldehyde or ketone) and a carbonyl oxide (aldehyde oxide or ketone oxide) *(10)* takes place in accordance with the Reaction B given in Section 2. In this decomposition an O—O and a C—C bond cleave, while the (stronger) C—O bonds remain intact. Of the decomposition products the aldehydes and ketones are stable compounds, whereas the carbonyl oxides *(10)*, thus far unknown in substance, are energy-rich species but have the possibility of resonance stabilization. The structures of the carbonyl oxides are analogous to those of the amine



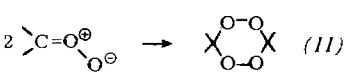
(10)

oxides, nitrile oxides or sulfoxides, but only the nitrile oxides have comparable resonance possibilities.

Which type of reactions can the carbonyl oxides (earlier also called peroxidic zwitterions) undergo that will lead to their final stabilization? These reactions will be described in the following.

4.1. Dimerization

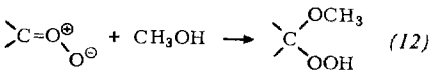
Primarily with olefins bearing four substituents at the double bond, but also in other cases, one obtains as ozonization products the "dimeric keto- (or aldehyde-) peroxides" *(11)* (1,2,4,5-tetraoxanes)[18]. They are most readily rationalized as dimers of the carbonyl oxides.



(11)

4.2. Reactions with Proton-Active Substances

Ozonization of olefins in the presence of alcohols[17, 18], ammonia[19], hydrocyanic acid[20], hydrogen peroxide[21], *etc.* leads to products, which arise formally—and in our opinion also in reality—by addition of the respective reagent to the carbonyl oxide. A typical example is the ozonization in methanol as solvent, in which the geminal methoxyhydroperoxides *(12)* are formed.

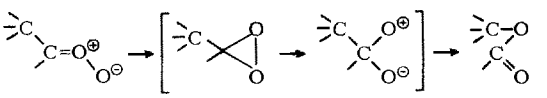


(12)

Ozonolysis in methanol is also of preparative importance, since in this case not only is the formation of dimeric peroxides avoided but also that of oligomeric ozonides, which can sometimes considerably interfere with the ozonization in inert solvents. If the carbonyl oxides were not zwitterions, but singlet diradicals as proposed by *Goddard*[23], then methanol should not add as H—OCH_3 but as H—CH_2OH; this however, has never been observed.

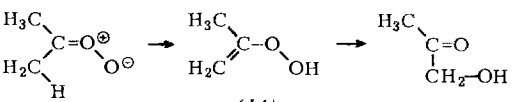
4.3. Rearrangements

There are a series of cases in which ozonization leads not only to oxidative rupture of the double bond but also of an adjacent C—C single bond. This "anomalous ozonization"[22] can be explained in terms of a peroxide rearrangement of the carbonyl oxide. Whether this proceeds *via* a dioxirane *(13)* as intermediate[23] is undecided. The products in these cases are esters, lactones, or (in the case of α,β-unsaturated ketones) also acid anhydrides.



(13)

α-Hydroxyacetone is sometimes observed as by-product in the ozonolysis of olefins bearing an isopropylidene group. This can also be explained in terms of an—albeit different type—rearrangement of a carbonyl oxide, here of acetone oxide. The two-step rearrangement ought to involve formation of a very unstable vinyl hydroperoxide *(14)* as intermediate[24, 25].



(14)

4.4. Reaction with Aldehydes or Ketones

The most important and most frequent reaction of the carbonyl oxides is their combination with an aldehyde or a ketone to give an "ozonide". This could be a monomeric ozonide having the 1,2,4-trioxolane structure, formed according to Reaction C in Section 2 by cycloaddition, or also an (in inert solvents usually insoluble) oligomeric ozonide. Very little is known about the constitution[26] of the latter, so they will not be considered any further here. In section 5 we shall review the arguments that favor formation of the monomeric ozonides according to Reaction C.

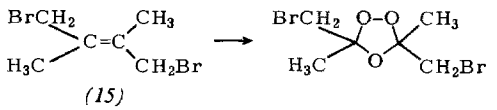
5. Formation of Monomeric Ozonides

5.1. Scope of Formation of Monomeric Ozonides

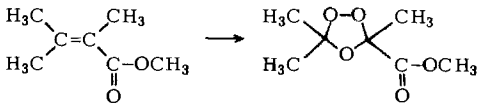
Monomeric ozonides are obtained from alkenes only if at least one H atom is present at the double bond[27], whereas tetraalkyl-substituted ethylenes afford only oligomers, dimeric peroxides, and/or rearrangement products[18]. This is understandable, since in the last mentioned cases the carbonyl oxides must be accompanied by ketones, whose activity in a cycloaddition is certainly much smaller than that of the aldehydes. Hence the zwitterion (carbonyl oxide) has time for alternative reactions.

One can, of course, also "force" keto groups to add to carbonyl oxides. One possible way of doing this is by increasing the reactivity of a keto group by neighboring substituents. Suitable substituents for this purpose are electron-withdrawing groups such as halogen atoms or ester groups. Thus monomeric ozonides could be obtained both from 1,4-dibromo-2,3-dimethyl-2-butene *(15)* as well as from 2,3-dimethylcrotonate

(16), although both starting compounds carry four substituents at the double bond[28]. Bromoacetone and pyruvate, respectively, must be assumed as intermediates.



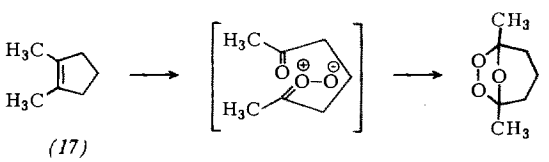
(15)



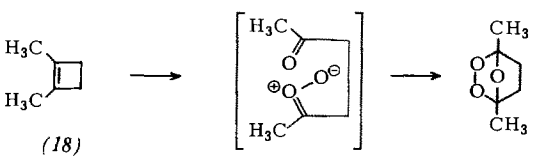
(16)

A keto group can also be reactive, however, if for steric reasons there is a particularly great tendency for its C atom to change from sp^2- into sp^3-hybridization. This is so, *e. g.* in the case of adamantanone, which has proved to be a good dipolarophile toward several carbonyl oxides[14].

The third possibility for the addition of a keto group to a carbonyl oxide group is when both groups are in one molecule, so that the cycloaddition will be an intramolecular reaction, which is far more preferred than an intermolecular reaction. Here, it is necessary to use a *cyclic* olefin with a tetrasubstituted double bond as starting material. Indeed, cyclopentenes such as *(17)*[29] and cyclobutenes such as *(18)*[30] give monomeric ozonides in excellent yields.



(17)



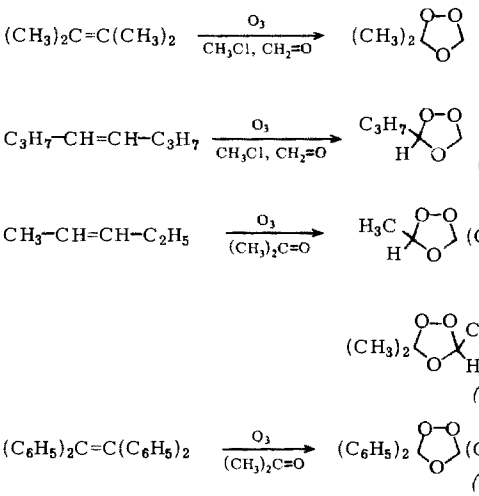
(18)

If, on the other hand, the double bond is present in a six- or higher-membered ring no monomeric but only oligomeric ozonides are obtained[18]. Apparently, in these cases the cycloaddition is not favored since the monomeric ozonide would then contain, *inter alia*, an eight- or higher-membered ring and such rings are generally formed only with difficulty.

5.2. Ozonization in the Presence of "Foreign" Aldehydes or Ketones

If the carbonyl oxides have a finite lifetime they must also be able to add to an aldehyde or reactive ketone admixed prior to the ozonization, for the latter ought to be able to compete for the carbonyl oxide with any aldehyde (or ketone) formed during ozonization. This is especially so when an aldehyde is added and a ketone is formed from the olefin. Furthermore, admixed aldehydes or ketones can be added in larger concentration, and in the extreme case they can be used as solvent. Examples of such intermolecular competing reactions are those which lead to the ozonides *(19)*—*(23)*[31,32,25].

In these and other cases ozonides of olefins not employed in the experiment are obtained.



(19)

(20)

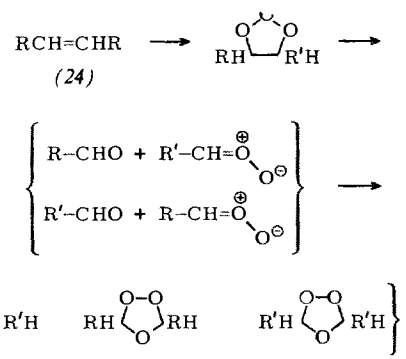
(21)

(22)

(23)

5.3. Cross-Ozonizations

Primary ozonides of unsymmetric olefins *(24)* can fundamentally decompose in two different ways, so that two aldehydes or ketones and two carbonyl oxides are formed. These can afford by cycloaddition three ozonides, namely the unsymmetrical ozonide corresponding to the starting olefin in addition to two symmetrical ozonides.

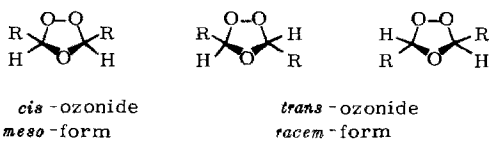


(24)

Since the time it became possible to separate similar ozonides by thin layer chromatography or the lower members by gas chromatography[33], the expected "crossed-ozonides" have been detected and isolated from the "normal" ozonides in many cases[34-36].

5.4. *cis/trans* Isomeric Ozonides

In a 1,2,4-trioxolane ring, substituents can be present in the *cis* or *trans* positions. Using the above mentioned methods of separation it has been possible to isolate numerous pairs of *cis/trans* isomeric ozonides[33,36]. In some of these cases the configuration could be unequivocally assigned. Symmetrically disubstituted trioxolanes are *meso*-forms in the *cis*-ozonide, racemates in the *trans*-ozonide. Optically active ozonides can be obtained only from the latter. *Murray*[37] achieved this by partial destruction of the one enantiomer with brucine,



cis - ozonide
meso - form

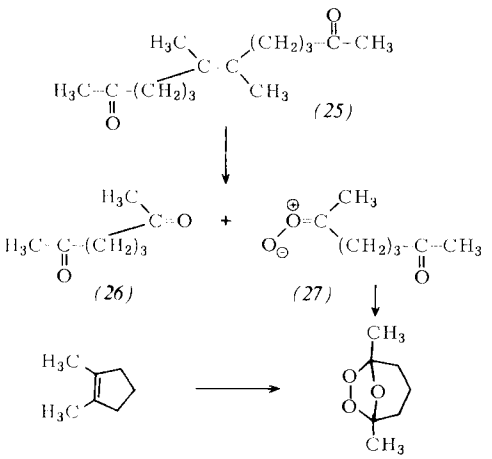
trans - ozonide
racem - form

and *Korber*[38] by chromatography of the racemates on optically active cellulose-2½ acetate

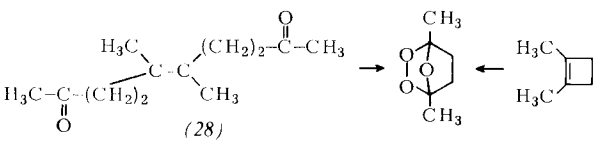
The *cis*-ozonides have longer retention times than the *trans*-ozonides in column- and gas-chromatography, so a less tedious albeit not as well founded determination of configuration can be carried out in this way[38].

5.5. Competition between Inter- and Intramolecular Ozonide Formation

When olefins bearing keto groups are ozonized there is the possibility that such keto groups interfere in the ozonide formation. As long ago as the fifties *Lohaus*[39] ozonized the unsaturated diketone *(25)*. Here, decomposition of the primary ozonide ought to lead to the ketocarbonyl oxide *(27)* as well as the diketone *(26)*. The carbonyl oxide group now has the choice of forming an ozonide ring intermolecularly with a keto group of the diketone or intramolecularly with the keto group in its own molecule. The intramolecular reaction predominates; the same ozonide as is formed from 1,2-dimethylcyclopentene is obtained in good yield.

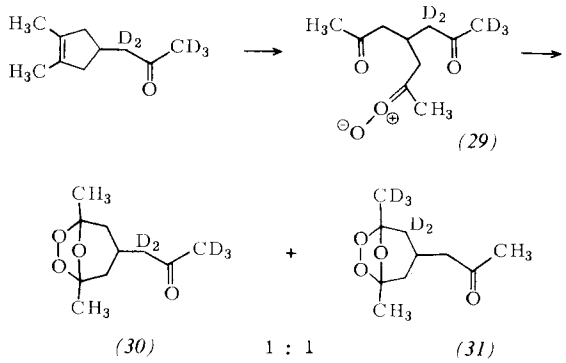


Later, *Griesbaum*[40] was able to obtain the ozonide of 1,2-dimethylcyclobutene from the unsaturated diketone *(28)* having one less methylene group in each of the two chains (see also Section 5.1).



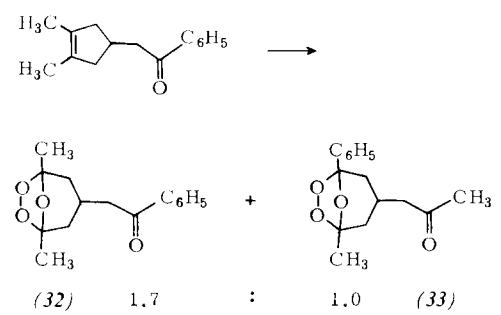
5.6. Intramolecular Competing Reactions

When a cyclic olefin having a sidechain containing a keto group is ozonized one expects intermediary formation of a molecule having one carbonyl oxide and two keto groups, both of which can cycloadd to the carbonyl oxide group. Mrs. *Banciu* has carried out experiments of this type[41]. The first example was (3,4-dimethyl-3-cyclopentenyl)acetone. In this case the intermediate product to be expected on ozonization is symmetrical with respect to the zwitterion group. In order to be able to distinguish between the two keto groups the H atoms adjacent to the keto group of the starting material were deuterated. The two possible reaction products can now be differentiated NMR-spectroscopically. Both ozonides—*(30)* and *(31)*—are formed in exactly equal amounts.

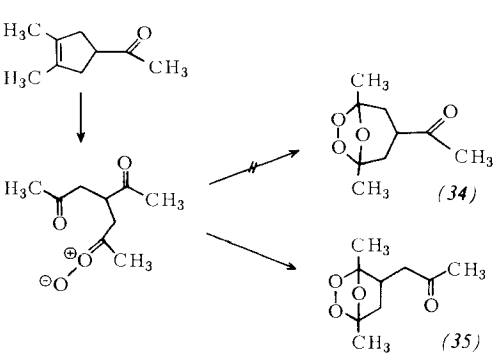


Accordingly, both keto groups react equally rapidly with the carbonyl oxide. Hence there is no preference for the keto group which is formed along with the carbonyl oxide group on cleavage of the primary ozonide. Reaction of these two groups with one another in a partial solvent cage is therefore ruled out, as is also a direct intramolecular rearrangement of the primary ozonide into the ozonide. Rather, the intermediate *(29)* must have a finite lifetime so that the carbonyl oxide has time to choose between the two alternative possibilities.

The starting compound can be varied in many different ways so as to obtain further information about the possible choices open to the carbonyl oxide group. Only two further examples will be mentioned here. One concerns the ozonolysis of the phenacyl derivative corresponding to the acetonyl compound. An acetyl and a benzoyl group compete in the intermediate. Here also there are two—in this case separable—reaction products *(32)* and *(33)*, which, however, are not formed in equal amounts. As regards cycloaddition the acetyl group proved to be 1.7 times more reactive than the benzoyl group.



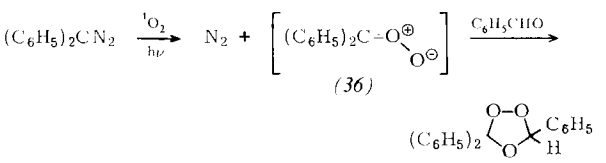
In the second example 4-acetyl-1,2-dimethylcyclopentene was ozonized. In this case two acetyl groups situated in different positions to the carbonyl group compete with each other in the intermediate. In one case a cyclopentene ozonide *(34)*



should have been formed, and in the other a cyclobutene ozonide (*35*). The result was surprising: the cyclobutene derivative was formed exclusively, although it should be thermodynamically more labile because of greater ring strain. The reaction must therefore be kinetically controlled.

5.7. Ozonides from Diazo Compounds

In all experiments described so far the carbonyl oxide was formed by spontaneous decomposition of a primary ozonide. On photo-oxidation of diphenyldiazomethane, *Murray*[42] was able to detect a short-lived product which in the presence of benzaldehyde affords the ozonide of triphenylethylene. This short-lived intermediate can only be benzophenone oxide (*36*).



Murray's experiments provide evidence, which is independent of all ozonolysis results, that ozonides can arise by addition of a carbonyl compound to a carbonyl oxide.

6. Objections to the "Three-Step Mechanism"

Having dealt with the arguments supporting the validity of the proposed ozonolysis mechanism, we should not overlook a number of serious objections to this mechanism or at least to its representing the sole route from olefins to ozonides. The principal objections come from the stereoselectivity of ozonization and the incorporation of labeled oxygen into the trioxolane ring of ozonides.

6.1. Stereoselectivity of Ozonolysis

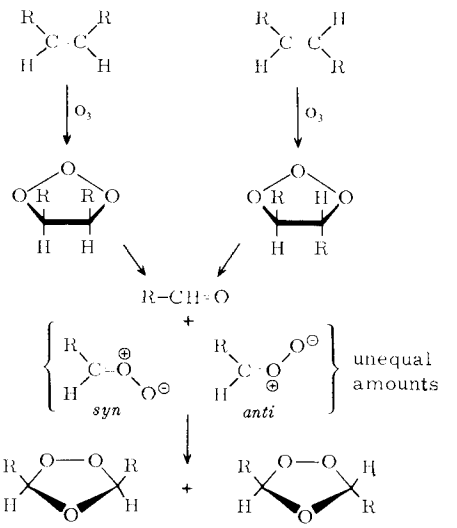
The mechanism developed in Sections 1 to 5 requires, *inter alia*, that the primary ozonide decomposes entirely into two fragments in the second reaction step. A *cis* olefin should then give the same fragments as the isomeric *trans* olefin. These fragments are transformed by cycloaddition into the ozonides which can likewise exist in *cis/trans* isomeric forms.

The mechanism developed is incapable of predicting whether the reunification of the fragments leads to a *cis* or a *trans* ozonide or to a mixture of the two.

In any case the ozonide composition should be independent of whether the *cis* or *trans* olefin is used as starting material. However, as first established by *Schröder*[33], and later by *Story* and *Murray*[43], and other workers[44, 36], this is not always the case. The geometry of the olefin can indeed exert a considerable influence on the composition of the ozonide mixture, especially when bulky groups such as *tert*-butyl or isopropyl are attached to the double bond of the olefin. This applies not only to the composition of the "normal" ozonides but in the same way to that of "crossed ozonides".

In order to interpret these findings, *Story* and *Murray*[45] developed an alternative mechanism of ozonolysis. Although it explains the stereochemical results, their proposal contains a number of improbable *ad hoc* assumptions, *e.g.* insertion of an aldehyde group into an O—O bond of the primary ozonide. A detailed discussion is unnecessary however, since another explanation developed by *Bailey*[46, 47] requires no fundamentally new mechanism.

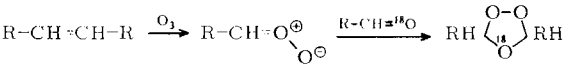
According to *Bailey*, carbonyl oxides having two unlike substituents (*e.g.* H and *tert*-butyl) should be able to exist in *syn/anti* isomeric forms, similar to those of oximes. This hypothesis states that *cis/trans* isomeric primary ozonides having a bulky substituent at each of the two carbon atoms should afford unequal amounts of *syn* and *anti* carbonyl oxide and, moreover, that these stereoisomeric carbonyl oxides add in unequal amounts to aldehydes to form *cis* and *trans* ozonide.



Prerequisite for this hypothesis is that the primary ozonides are nonplanar immediately prior to decomposition and that the preferred conformations of the five-membered ring depend upon the position and size of the substituents. Likewise, the ozonides should be formed in preferred nonplanar conformations.

6.2. Incorporation of Labeled Oxygen into the Ozonide Ring

Ozonization of an olefin in the presence of an [O^{18}]aldehyde should afford an ozonide having a labeled oxygen atom. The three-step mechanism would require, in accord with Reaction C (Section 2) also in the modified form of *Bailey*, that the labeled O atom is always incorporated exclusively as the ether bridge of the ozonide.



In principle, it is possible to deduce the site of the heavy oxygen atom from the fragments observed in the mass spectra of ozonides. *Story* and *Murray*[48] were the first to perform such studies. They came to the surprising conclusion that a considerable proportion of the label was located in the peroxide bridge and not in the ether bridge. This would indicate that part of the O—O bridge is generated from the aldehydic oxygen atom with formation of a new O—O bond. The mechanism due to *Story* and *Murray* mentioned in Section 6.1 would account for these findings.

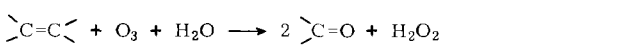
Independent studies performed in recent years, first by *Fliszár*[49] and later by *Kuczkowski*[50], have shown that the heavy ozonides prepared in the above manner from ethylene, propylene, 1-butene, 2,5-dimethyl-3-hexene, and stilbene all contain

the ^{18}O label exclusively, or at least to an extent far in excess of 90%, in the ether bridge. No explanation for the different results of *Story* and *Murray* has yet become available. At any rate, there is no definite experimental evidence requiring an alternative mechanism.

7. Concluding Remarks

In conclusion, let us recapitulate how the action of ozone on olefins leads to complete oxidative cleavage of the double bond and furthermore to cleavage of the ozone molecule into an ether and a peroxide fragment.

Even the initial step, addition of ozone to the double bond, amounts to an oxidation of the olefin to the oxidation state of a 1,2-diol. At the same time, the —O—O—O— unit, which is still able to perform oxidation, is anchored to the organic molecule. Since the three O atoms are bonded relatively loosely to each other in the primary ozonide owing to lack of resonance, one of the O—O bonds is easily ruptured. However, stable or stabilized molecules (and not energy-rich radicals or ions) can only arise if the C—C bond is broken simultaneously. As a result of this cleavage, the two C atoms which were originally double bonded attain the oxidation state of ketones or aldehydes while the ozone molecule is reduced to a derivative of hydrogen peroxide. The ozonide is finally decomposed by water. The overall reaction is described by the equation



Of course, many details still remain open. Let us mention a few.

For instance, what is the structure of the oligomeric ozonides and how are they formed? Do they really contain O—O—O units alongside ether and peroxide groups, as proposed by *Greenwood*[26]?

With suitably substituted cyclobutenes, *endo/exo* isomeric ozonides have been found on numerous occasions[51, 41]. How can their configuration be established and what determines their relative proportions?

Will it become possible to at least detect a carbonyl oxide spectroscopically, or even to isolate one?

The products of ozonolysis are strongly solvent dependent. Can this dependence be correlated with any solvent parameters?

What is the course of gas phase ozonolysis of olefins[2, 52, 53]? Are primary ozonides again formed initially? If so, do they also decompose to aldehyde and carbonyl oxide, or is a diradical $>\dot{C}—O\dot{O}$ formed instead?

Can the view recently expressed by *Goddard*[23] that the so called carbonyl oxides are singlet diradicals also in solution be confirmed or disproved? Solution of this problem will be of crucial importance for our understanding of the events occurring during the ozonolysis of olefins.

In 1844, that is 131 years ago, and four years after the discovery of ozone by *Schönbein*, no less than six pages were devoted to ozone by *Otto* in his "Lehrbuch der Chemie"[54]. He closed this section with the exclamation: A highly productive field for further research! I consider this statement to have lost none of its validity.

Received: February 28, 1975 [A 76 IE]
German version: Angew. Chem. 87, 765 (1975)

[1] *C. Harries*, Liebigs Ann. Chem. *343*, 311 (1905).
[2] *A. Rieche, R. Meister*, and *H. Sauthoff*, Liebigs Ann. Chem. *553*, 246 (1942).
[3] Older summaries: a) *P. S. Bailey*, Chem. Rev. *58*, 925 (1958); b) *R. W. Murray*, Accounts Chem. Res. *1*, 313 (1968).
[4] *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. internat. Edit. *2*, 565 (1963).
[5] *R. Criegee* and *G. Schröder*, Chem. Ber. *93*, 689 (1960).
[6] *H. Staudinger*, Ber. Deut. Chem. Ges. *58*, 1088 (1925).
[7] *P. R. Story, J. A. Alford, J. R. Burgess*, and *W. C. Ray*, J. Amer. Chem. Soc. *93*, 3042, 3044 (1971).
[8] *P. S. Bailey, J. A. Thompson*, and *B. A. Shoulders*, J. Amer. Chem. Soc. *88*, 4098 (1966).
[9] *P. R. Story, E. A. Whited*, and *J. A. Alford*, J. Amer. Chem. Soc. *94*, 2143 (1972).
[10] *K. R. Kopecky, R. A. Lockwood, J. E. Filby*, and *R. W. Reid*, Can. J. Chem. *51*, 468 (1973); *P. S. Bailey, T. P. Carter, C. M. Fischer*, and *J. A. Thompson*, *ibid. 51*, 1278 (1973).
[11] *F. L. Greenwood*, J. Org. Chem. *30*, 3108 (1965); *L. J. Durham* and *F. L. Greenwood*, *ibid. 33*, 1629 (1968); *F. L. Greenwood* and *L. J. Durham*, *ibid. 34*, 3363 (1969).
[12] *P. S. Bailey, J. W. Ward, T. P. Carter, Jr., E. Nieh, C. M. Fischer*, and *A.-I. Y. Khashab*, J. Amer. Chem. Soc. *96*, 6136 (1974).
[13] *P. S. Bailey* and *A. G. Lane*, J. Amer. Chem. Soc. *89*, 4473 (1967).
[14] *H. Keul*, Chem. Ber. *108*, 1207 (1975).
[15] Cf. however: *P. J. Hay, T. H. Dunning*, and *W. A. Goddard*, Accounts Chem. Res. *6*, 368 (1973).
[16] *R. Criegee* and *P. Günther*, Chem. Ber. *96*, 1546 (1963).
[17] *R. Criegee* and *G. Wenner*, Liebigs Ann. Chem. *564*, 9 (1949).
[18] *R. Criegee* and *G. Lohaus*, Liebigs Ann. Chem. *583*, 6 (1953).
[19] *M. J. Fremery* and *E. K. Fields*, J. Org. Chem. *29*, 2240 (1964).
[20] *E. K. Fields*, Advan. Chem. Ser. *51*, 99 (1965).
[21] *J. C. Robertson* and *W. J. Verzino*, J. Org. Chem. *35*, 545 (1970).
[22] See [3a], Page 947ff.
[23] *W. R. Ward* and *W. A. Goddard*, J. Amer. Chem. Soc. *97*, 2819 (1975).
[24] *P. R. Story* and *J. R. Burgess*, J. Amer. Chem. Soc. *89*, 5726 (1967); *90*, 1094 (1968).
[25] *R. Criegee* and *H. Korber*, Chem. Ber. *104*, 1812 (1971).
[26] *F. L. Greenwood* and *H. Rubinstein*, J. Org. Chem. *32*, 3369 (1967).
[27] *R. Criegee, A. Kerckow*, and *H. Zinke*, Chem. Ber. *88*, 1878 (1955).
[28] *R. Criegee, S. S. Bath*, and *B. von Bornhaupt*, Chem. Ber. *93*, 2891 (1960).
[29] Example: *R. Criegee* and *G. Lohaus*, Chem. Ber. *86*, 1 (1952).
[30] Example: *R. Criegee* and *K. Noll*, Liebigs Ann. Chem. *625*, 1 (1959).
[31] *R. Criegee, G. Blust*, and *H. Zinke*, Chem. Ber. *87*, 766 (1954).
[32] *R. W. Murray, P. S. Story*, and *L. D. Loan*, J. Amer. Chem. Soc. *87*, 3025 (1965).
[33] *G. Schröder*, Chem. Ber. *95*, 733 (1962).
[34] *G. Riezebos, J. C. Grimmelikhuysen*, and *D. A. van Dorp*, Rec. Trav. Chim. Pays-Bas *82*, 1234 (1963).
[35] *L. D. Loan, R. W. Murray*, and *P. R. Story*, J. Amer. Chem. Soc. *87*, 737 (1965).
[36] *O. Lorenz* and *C. R. Parks*, J. Org. Chem. *30*, 1976 (1965).
[37] *R. W. Murray, R. D. Youssefyeh*, and *P. R. Story*, J. Amer. Chem. Soc. *88*, 3655 (1966).
[38] *R. Criegee* and *H. Korber*, Chem. Ber. *104*, 1807 (1971).
[39] *G. Lohaus*, Chem. Ber. *87*, 1708 (1954).
[40] *K. Griesbaum*, Chem. Ber. *101*, 463 (1968).
[41] *R. Criegee* and *A. Banciu*, Chem.-Ztg. *98*, 161 (1974); *R. Criegee, A. Banciu*, and *H. Keul*, Chem. Ber. *108*, 1642 (1975).
[42] *R. W. Murray* and *A. Suzui*, J. Amer. Chem. Soc. *95*, 3343 (1973); *R. W. Murray* and *D. P. Higley*, *ibid. 95*, 7886 (1973).
[43] *R. W. Murray, R. D. Youssefyeh*, and *P. R. Story*, J. Amer. Chem. Soc. *88*, 3143 (1966).
[44] *F. L. Greenwood* and *B. J. Haske*, Tetrahedron Lett. *1965*, 631.
[45] *P. R. Story, R. W. Murray*, and *R. D. Youssefyeh*, J. Amer. Chem. Soc. *88*, 3144 (1966); *R. W. Murray, R. D. Youssefyeh*, and *P. R. Story*, *ibid. 89*, 4473 (1967).
[46] *N. L. Bauld, J. A. Thompson, C. E. Hudson*, and *P. S. Bailey*, J. Amer. Chem. Soc. *90*, 1822 (1968).
[47] *R. P. Lattimer, R. L. Kuczkowski*, and *C. W. Gillis*, J. Amer. Chem. Soc. *96*, 348 (1974).
[48] *P. R. Story, C. E. Bishop, J. R. Burgess, R. W. Murray*, and *R. D. Youssefyeh*, J. Amer. Chem. Soc. *90*, 1907 (1968); *P. R. Story, C. E. Bishop, J. R. Burgess*, and *J. B. Olson*, Advan. Chem. Ser. *77*, 46 (1968); *R. W. Murray* and *R. Hagen*, J. Org. Chem. *36*, 1103 (1971).
[49] *S. Fliszár, J. Carles*, and *J. Renard*, J. Amer. Chem. Soc. *90*, 1364 (1968).

[50] C. W. Gillies and R. L. Kuczkowski, J. Amer. Chem. Soc. 94, 7609 (1972); C. W. Gillies, R. P. Lattimer, and R. L. Kuczkowski, ibid. 96, 1536 (1974); R. P. Lattimer and R. L. Kuczkowski, ibid. 96, 6205 (1974).
[51] R. Criegee and R. Rusckbäschel, Chem. Ber. 103, 50 (1970).
[52] L. A. Hull, I. C. Hisatsune, and J. Heicklen, Can. J. Chem. 51, 1504 (1973).
[53] R. Atkinson, B. J. Finlayson, and N. J. Pitts, J. Amer. Chem. Soc. 95, 7592 (1973); B. J. Finlayson, N. J. Pitts, and R. Atkinson, ibid. 96, 5356 (1974); N. J. Pitts and B. J. Finlayson, Angew. Chem. 87, 18 (1975); Angew. Chem. internat. Edit. 14, 1 (1975).
[54] F. J. Otto: Lehrbuch der Chemie. 2nd edit., Vol. 2, 1st half. Vieweg, Braunschweig 1844, p. 653.

COMMUNICATIONS

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

Dilithium-Nickel-Olefin Complexes. Novel Bimetal Complexes Containing a Transition Metal and a Main Group Metal

By *Klaus Jonas*[*]

During investigations on the reactions between nickel(0) complexes and organometallic compounds of Group IB to IIIB elements, which have already been reported in part[1,2], it was found that binary olefin complexes such as all-*trans*-1,5,9-cyclododecatrienenickel(0)[3] [CDT·Ni] or bis(1,5-cyclooctadiene)nickel(0)[3] [$(COD)_2Ni$] can also undergo reaction with elemental lithium to form crystalline adducts.

The deep red solution formed by CDT·Ni in a mixture of tetrahydrofuran and *N,N,N',N'*-tetramethylethylenediamine gradually becomes lighter in color, *e.g.*, on stirring with lithium sand. If the excess of lithium sand is removed by filtration and diethyl ether added to the reaction mixture, the yellow adduct *(2)* crystallizes out on cooling to −40 °C.

$$\text{CDT·Ni} + 2\ \text{Li} + 2\ (CH_3)_2N(CH_2)_2N(CH_3)_2 \xrightarrow[0\,^\circ C]{\text{THF}} \left[\text{CDT·Ni}\left\{\text{Li·}(CH_3)_2N(CH_2)_2N(CH_3)_2\right\}_2\right]$$

(1)

The CDT ligand in complex *(1)* is present as unchanged all-*trans*-1,5,9-cyclododecatriene, as is evident from the reaction of *(1)* both with cyclooctatetraene (COT) and with COT and an excess of 1,5-cyclooctadiene. In the former case CDT·Ni is regenerated alongside $Li_2(COT)$ while in the second the excess of COD quantitatively displaces the cyclododecatriene from the nickel.

[*] Dr. K. Jonas
Max-Planck-Institut für Kohlenforschung
433 Mülheim/Ruhr, Kaiser-Wilhelm-Platz 1 (Germany)

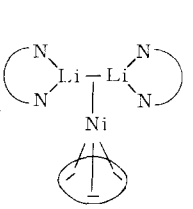
The novel compound *(1)* displays a slight electrical conductivity in tetrahydrofuran, apparently due to partial dissociation. On the other hand, *(1)* is also readily soluble in nonpolar solvents such as pentane or benzene. Molecular-weight determination in benzene gives the value expected for *(1)* (exp. 455, calc. 466). This finding contraindicates a largely ionic structure, such as is characteristic of alkali metal-transition metal carbonyl compounds, which are composed of alkali metal cations and carbonylmetalate anions.

$$(1) \xrightarrow{+1\ COT} Li_2(COT) + 2\ (CH_3)_2N(CH_2)_2N(CH_3)_2 + \text{CDT·Ni}$$

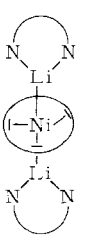
$$(1) \xrightarrow[+1\ COT]{+2\ COD} Li_2(COT) + 2\ (CH_3)_2N(CH_2)_2N(CH_3)_2 + (COD)_2Ni + \text{CDT}$$

The ^{1}H-NMR spectrum of *(1)* in [D_8]-THF at −20 °C contains two singlets at $\tau = 7.77$ and 7.9 for the protons of the amine. Three groups of signals of approximately equal intensity occur at $\tau = 8.2$, 9.33, and 9.72 for the protons of the cyclododecatriene bound to the nickel. All the protons of the CDT ligand in complex *(1)* are more strongly shielded than in CDT·Ni^0, whose spectrum consists of only two signals at $\tau = 5.7$ (=CH) and 7.7 ($-CH_2$).

The two most likely structures of *(1)* are shown as *(1a)* and *(1b)*.



(1a)



(1b)

In both cases adduct formation can be attributed to the tendency of the coordinatively unsaturated CDT·Ni^0 (16 electron shell) to achieve a noble gas configuration in which the two additional electrons come from the two lithium atoms. With regard to the hybridization of the nickel, structure *(1a)* appears more likely than *(1b)*. In *(1a)* the ligands are arranged tetrahedrally around the Ni atom. The two Li atoms jointly occupy a coordination site of the nickel. This kind of tetrahedral arrangement around the central atom is also suspected in [CDT·Ni(CO)][3] and the corresponding monophosphane adducts [CDT·Ni(PR_3)][3,4]. However, consideration of models permits better correlation of the ^{1}H-NMR spectrum of *(1)* with *(1b)*[5].

On reaction of lithium sand with coordinatively saturated bis(1,5-cyclooctadiene)nickel(0) (18 electron shell), the

$(COD)_2Ni$, which is sparingly soluble in tetrahydrofuran, goes into solution and the diamagnetic adduct *(2)* crystallizes out on cooling: in other words, an Li_2Ni-olefin complex is formed preferentially in this case too.

$$(COD)_2Ni + 2\ Li \xrightarrow[0\,^\circ C]{THF} \underset{(2)}{\left[(COD)_2NiLi_2 \cdot 4\ THF\right]}$$

$$(2) + I_2 \longrightarrow (COD)_2Ni + 2\ LiI + 4\ THF$$

Treatment of *(2)* with iodine regenerates bis(cyclooctadiene)Ni^0 with formation of LiI. The complexed olefin of *(2)* can be displaced unchanged as 1,5-cyclooctadiene by CO. The ^{1}H-NMR spectrum of *(2)* in [D_8]-THF is temperature dependent. At $-40\,^\circ C$ a signal appears, alongside others, at $\tau = 4.59$ which is assignable to the protons attached to a free COD double bond, which can also be recognized as a free double bond from a band at $1635\,cm^{-1}$ in the IR spectrum (THF, $0\,^\circ C$). A coordination site of the nickel in *(2)* is clearly occupied by a "Li_2" ligand instead of by a double bond. A free double bond can no longer be detected in the ^{1}H-NMR spectrum at $0\,^\circ C$. It appears plausible that all four double bonds of the two COD ligands participate in bonding to the nickel only on a time-average basis (fluctional system) so that, as in *(1)*, an 18-electron shell is also established in complex *(2)*.

(2) reacts particularly readily with monoolefins such as ethylene or dienes such as butadiene and 1,3-dimethylbutadiene which displace the cyclooctadiene to form new complexes while retaining the bimetal unit Li_2Ni.

Received: July 10, 1973 [Z 924c IE]
German version: Angew. Chem. *87*, 809 (1975)
Publication delayed at author's request

[1] *K. Fischer, K. Jonas*, and *G. Wilke*, Angew. Chem. *85*, 620 (1973); Angew. Chem. internat. Edit. *12*, 565 (1973).
[2] *K. Fischer, K. Jonas, P. Misbach, R. Stabba*, and *G. Wilke*, Angew. Chem. *85*, 1002 (1973); Angew. Chem. internat. Edit. *12*, 943 (1973).
[3] *B. Bogdanović, M. Kröner*, and *G. Wilke*, Liebigs Ann. Chem. *699*, 1 (1966).
[4] *K. Jonas*, Dissertation, Universität Bochum 1968.
[5] *Note added in proof* (October 16, 1975): Arrangement *(1b)* has meanwhile been confirmed by X-ray structure analysis (*D. J. Brauer* and *C. Krüger*, to be published).

Conversion of Ammonia into Ketimine Ligands—a Simple Method for Synthesis of Ketimine Complexes[1]

By *Dieter Sellmann* and *Ernst Thallmair*[*]

Complexes containing aldimine or ketimine ligands $R^1R^2C{=}NH$ (R^1, R^2 = H, alkyl or aryl) can be prepared from metal compounds and ketimines, oximes, diazo derivatives or other nitrogen compounds. Starting from ketimines one is then limited to aromatic ketimines, which can be isolated in substance *e. g.* diphenylmethanimine[2]. As far as we know, the condensation of ammonia complexes with carbonyl compounds has not been observed previously:

$$L_xM{-}NH_3 + O{=}CR^1R^2 \rightarrow L_xM{-}NH{=}CR^1R^2 + H_2O$$

This reaction could become important in respect of the catalytic oxidation of ammonia to hydrazine by air *via* ketazine intermediates: ketazines from which hydrazine can be liberated hydrolytically may be prepared by aerial oxidation of ketimines[3], the direct synthesis of the required ketimines from free ammonia and ketones, however, is beset with difficulties[4].

We have found a simple synthesis of the ketimine skeleton from complex-bound NH_3 and ketones: $(OC)_5CrNH_3$ *(1)* with an excess of acetone in the presence of a drying agent ($MgSO_4$) affords the imine complex *(2)*[5] in 75% yield.

$$(1) + \text{Acetone} \xrightarrow{56\,^\circ C/4\,h} \underset{(2)}{(OC)_5CrNH{=}C(CH_3)_2} + H_2O$$

(2) can also be obtained at room temperature; addition of bases increases the reaction rate. We therefore assume that the anion of *(1)*, $[(OC)_5CrNH_2]^-$, takes part in the formation of *(2)*.

This type of reaction can be applied to other aliphatic ketones, *e. g.* $(OC)_5CrNH{=}C_6H_{10}$ *(3)* can be obtained from *(1)* and cyclohexanone in 78% yield after 5 h at $55\,^\circ C$.

No ketimine, but only polymolecular products therefrom can be isolated when lower aliphatic ketones such as acetone are condensed with free ammonia[4]. The formation of *(2)* and *(3)* shows that this condensation can be stopped after the first step by use of complex-bound ammonia since the ketimine skeleton that is unstable in the free state is stabilized by the complex formation.

Experimental:

(1) (1.00 g, 4.8 mmol) is heated in acetone (30 ml) together with $KOCH_3$ (30 mg) and $MgSO_4$ (2 g) for 4 h at the boiling point. After filtration and evaporation of the filtrate a yellow oil remains, whence pure crystalline *(2)* (0.89 g, 75%) is obtained by chromatography in pentane/toluene (1 : 1) on SiO_2 (column: $l = 80$, $\varnothing = 1.5$ cm; Merck silica gel 60, grain size 0.063–0.200 mm) at $-20\,^\circ C$.

Received: June 12, 1975 [Z 269 IE]
German version: Angew. Chem. *87*, 772 (1975)
Publication delayed at authors' request

CAS Registry numbers:
(1), 15228-27-0; *(2)*, 28394-70-9; *(3)*, 28294-78-2; acetone, 67-64-1; cyclohexanone, 108-94-1; $MgSO_4$, 7487-88-9

[*] Priv.-Doz. Dr. D. Sellmann and Dipl.-Chem. E. Thallmair
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[1] Reactions of Complex-bound Ligands, Part 17. Lecture at Düsseldorf, April 9, 1975. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 16: *D. Sellmann* and *E. Kleinschmidt*, Angew. Chem., Angew. Chem. internat. Edit., in the press.
[2] *A. Misono, T. Osa*, and *S. Koda*, Bull. Chem. Soc. Jap. *41*, 373 (1968).
[3] Cf. *Th. Kauffmann*, Angew. Chem. *86*, 321 (1974); Angew. Chem. internat. Edit. *13*, 291 (1974).
[4] Cf. *S. Patai*: The Chemistry of the Carbon-Nitrogen Double Bond. Wiley-Interscience, London 1970, p. 61.
[5] *E. O. Fischer* and *L. Knauss*, Chem. Ber. *103*, 1262 (1970).

7-Oxanorbornadiene—3-Oxaquadricyclane[**]

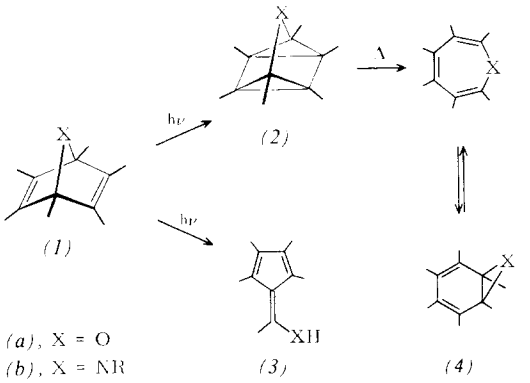
By *Horst Prinzbach* and *Horst Babsch*[*]

Owing to the unavailability of the unsubstituted 7-heteronorbornadienes, the synthesis of 3-oxa- *(2a)* and 3-azaquad-

[*] Prof. Dr. H. Prinzbach and Dipl.-Chem. H. Babsch
Lehrstuhl für Organische Chemie der Universität
78 Freiburg, Albertstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Dr. *H. Fritz* for ^{13}C measurements, and to Dr. *W. J. Richter* for some MS measurements.

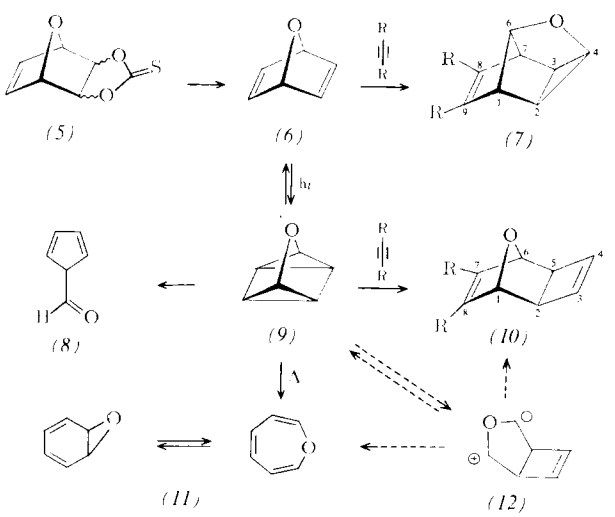
ricyclanes *(2b)*, and thus of oxepins *(4a)*[1a] and azepines *(4b)*[1b] from 7-oxa- *(1a)* and 7-azanorbornadienes *(1b)* has hitherto been limited to specifically substituted derivatives. Hence no conclusive treatment of fundamental mechanistic questions relating to the photoreactions *(1)*→*(2)*+*(3)*[2], cycloaddition reactions to *(2)*, and isomerizations *(2)*→*(4)*



was possible. We have now developed a preparatively utilizable entry to the oxa parent system *(6)* which also possesses interest in the field of inositol chemistry[3].

The mixture of *endo*- and *exo*-thiocarbonates *(5)* is readily accessible from furan and vinylene carbonate[4a] *via* a saponification step and reaction with *N,N'*-thiocarbonyldiimidazole[4b]. Degradation to *(6)* by the method of Corey-Winter[5] is admittedly complicated by the retro-Diels-Alder decomposition to furan and dioxolenethione[4b]; however, on heating in excess triethyl phosphite to 110 °C (overall conversion after *ca.* 120 h) compound *(6)* is favored over furan in the ratio of *ca.* 3:1 (ratio *ca.* 1:4 at 150 °C). Compound *(6)* is distilled off and purified by filtration through a short SiO_2 column [*ca.* 60% yield, colorless liquid, b.p. 129 °C; ^{1}H-NMR ($CDCl_3$): τ = 2.91 (m, 4H), 4.55 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ = 144.7 (C-2(3,5,6)), 82.5 ppm (C-1(4)); MS: *m/e* = 94 (M^+), 68 ($M^+ - C_2H_2$)].

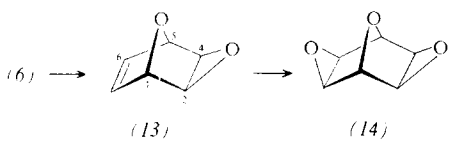
On irradiation in the presence of acetone (λ > 280 nm (Pyrex vessel)) *(6)* undergoes rapid and quantitative [2π+2π] cy-



cloaddition to form 3-oxaquadricyclane *(9)*; the di-π-methane rearrangement [leading eventually to *(8)* or its tautomers][2], which is of significance for derivatives of *(6)* on sensitized excitation, cannot be detected (^{1}H-NMR, TLC). Compound *(9)*, which is isolated as a colorless liquid [b.p. *ca.* 50 °C/50 torr; ^{1}H-NMR (C_6D_6): τ = 5.83 (m, 2H); 8.49 (m, 4H); ^{13}C-NMR (C_6D_6): δ = 62.4 (C-2(4)), 16.3 ppm (C-1(5,6,7)] is expectedly acid-labile and isomerizes, *e.g.* on heating in $CDCl_3$, slowly to the tautomeric mixture *(8)*. This rearrangement is complete within minutes in the presence of silver tetrafluoroborate (C_6H_6, 20 °C). On exclusion of acid, *e.g.* on heating in benzene, *(9)* undergoes thermal stabilization without any competition to give benzene oxide/oxepin *(11)*[6]. Having a tentative half-life of *ca.* 25 min (^{1}H-NMR) at 100 °C (benzene), the isomerization is clearly faster than in the case of the 1,5-dicarboxylic ester ($t_{1/2}$ *ca.* 174 min at 100 °C (benzene))[1a]; hence the influence of the substituents differs from that observed in the carbocyclic series[7]. The third possible mode of isomerization *viz.* 2σ→2π cleavage to form *(6)* is accomplished quantitatively by addition of the complex $PdI_2[(C_6H_5)_3Sb]_2$ (benzene, 20 °C).

Compound *(6)* reacts smoothly with dienophiles to give the [2+2+2] adducts, *e.g.* with dimethyl acetylendicarboxylate (DMAD) at 100 °C forming *(7)* whose structure is verified *inter alia* by spectral comparison with analogous 5-methylenetetracycles[8] [^{1}H-NMR ($CDCl_3$): τ = 5.30 (st, 4-H, $J_{2,4}$ = 3.8, $J_{4,6} \approx 0.8$ Hz), 5.78 (m, 6-H, $J_{1,6} \approx 2.5$ Hz), 6.20 (s, $2OCH_3$), 6.95 (m, 1(7)-H), 8.15 (m, 2(3)-H)].

On reaction of *(9)* with DMAD it is confirmed that addition does not occur until the temperature range of thermolysis to *(11)* has been reached; between 80 and 100 °C reaction in excess DMAD affords approximately equal proportions of the tricyclic compound *(10)* [^{1}H-NMR ($CDCl_3$): τ = 3.71 (s, 3(4)-H), 5.18 (s, 2(5)-H), 6.19 (s, $2OCH_3$), 7.10 (s, 1(6)-H)] and the known [4+2] adduct of benzene oxide *(11)*[6], both processes probably proceeding *via* the ylide *(12)*[1a, 9].



The utility of *(6)* as a synthon in inositol chemistry[3] can be demonstrated by way of its oxidation by *m*-chloroperbenzoic acid. Reaction in the molar ratio 1:1 ($CDCl_3$, Na_2HPO_4, 0 °C) selectively affords the *exo*-epoxide *(13)* [^{1}H-NMR ($CDCl_3$): τ = 3.49 (s, 6(7)-H), 5.28 (s, 1(5)-H), 6.19 (s, 2(4)-H] while excess peracid quantitatively leads to the *exo,exo*-bisepoxide *(14)* [1,2:3,6:4,5-trisanhydro-*cis*-inositol, colorless needles, m.p. 118 °C, ^{1}H-NMR ($CDCl_3$): τ = 5.53 (s, 2H), 6.50 (s, 4H)]. The MS fragmentation pattern of the latter largely resembles that of the isomeric *cis*-trioxatris-σ-homobenzene (*cis*-"benzene trioxide")[10].

Received: August 5, 1975 [Z 294 IE]
German version: Angew. Chem. 87, 772 (1975)

CAS Registry numbers:
exo-(5), 56648-90-9; *endo-(5)*, 56648-91-0; *(6)*, 6569-83-1; *(7)*, 56598-50-6; *(8)*, 56598-51-7; *(9)*, 16151-91-0; *(10)*, 6568-11-2; *(11)*, 1488-25-1; *(11)*, tautomer, 291-70-3; *(13)*, 56648-92-1; *(14)*, 56598-52-8; furan, 110-00-9; vinylene carbonate, 872-36-6; *N,N'*-thiocarbonyldiimidazole, 6160-65-2

[1] a) *W. Eberbach, M. Perroud-Argüelles, H. Achenbach, E. Druckrey*, and *H. Prinzbach*, Helv. Chim. Acta *54*, 2579 (1971); *R. K. Bansal, A. W. McCulloch, P. W. Rasmussen*, and *A. G. McInnes*, Can. J. Chem. *53*, 138 (1975); b) *H. Prinzbach, G. Kaupp, R. Fuchs, M. Joyeux, R. Kitzing*, and *J. Markert*, Chem. Ber. *106*, 3824 (1973); references cited therein.
[2] *D. Stusche* and *H. Prinzbach*, Chem. Ber. *106*, 3817 (1973).
[3] *H. Prinzbach, R. Keller*, and *R. Schwesinger*, Angew. Chem. *87*, 626 (1975); Angew. Chem. internat. Edit. *14*, 632 (1975), references cited therein; cf. *C. R. Kowarski* and *S. Sarel*, J. Org. Chem. *38*, 117 (1973).
[4] a) *M. S. Newman* and *R. W. Addor*, J. Am. Chem. Soc. *77*, 3789 (1955); b) *W. K. Anderson* and *R. H. Dewey*, *ibid.* *95*, 7161 (1973).
[5] *E. J. Corey* and *R. A. E. Winter*, J. Am. Chem. Soc. *85*, 2677 (1963).
[6] *E. Vogel, W. A. Böll*, and *H. Günther*, Tetrahedron Lett. *1965*, 609.
[7] *D. S. Kabakoff, J.-C. G. Bünzli, J. F. M. Oth, W. B. Hammond*, and *J. A. Berson*, J. Am. Chem. Soc. *97*, 1510 (1975).

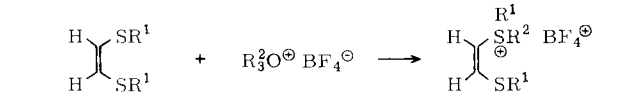
[8] *H. Prinzbach, W. Auge,* and *M. Basbudak*, Chem. Ber. *106*, 1822 (1973).
[9] *E. Haselbach* and *H.-D. Martin*, Helv. Chim. Acta *57*, 472 (1974).
[10] *R. Schwesinger* and *H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. internat. Edit. *11*, 942 (1972).

cis- and *trans*-Vinylenedisulfonium Salts[**]

By *Heinz Braun* and *Anton Amann*[*]

Whereas some vinylenediphosphonium salts have already been reported[1] corresponding disulfonium salts have, to our knowledge, not yet been described. We now wish to communicate the synthesis of *cis*- and *trans*-vinylenedisulfonium salts.

On reaction with oxonium tetrafluoroborates *(2)* (molar ratio 1:1) in dichloromethane at room temperature, the *cis*-dithioethers *(1)*[2] afford the *cis*-monosulfonium salts *(3)* in yields between 80 and 90%. Compounds *(3a)* and *(3b)*

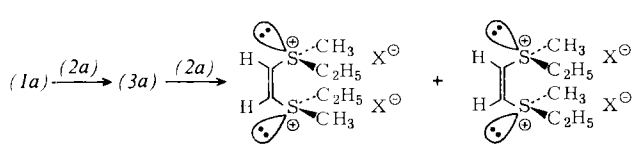


(1a), $R^1 = C_2H_5$ *(2a)*, $R^2 = CH_3$ *(3a)*, $R^1 = C_2H_5$, $R^2 = CH_3$
(1b), $R^1 = CH_2C_6H_5$ *(2b)*, $R^2 = C_2H_5$ *(3b)*, $R^1 = R^2 = C_2H_5$
(3c), $R^1 = CH_2C_6H_5$, $R^2 = CH_3$
(3d), $R^1 = CH_2C_6H_5$, $R^2 = C_2H_5$

are thus obtained as oils which appears to be pure on NMR spectroscopy; they were analyzed as trinitrobenzenesulfonates (dec. 110—112 °C and 101—103 °C respectively). *(3c)* (dec. 113—116 °C) and *(3d)* (dec. 93—95 °C) are obtained in crystalline form.

In contrast to *(1)*, the stereochemistry of the monosulfonium salts *(3)* can be deduced from the coupling constants of the olefinic protons (Table 1). Since no isomerization of the double bond occurs under the conditions given for the formation of *(3)*, the monoalkylation by *(2)* of compounds analogous to *(1)* offers a simple method of elucidating their stereochemistry.

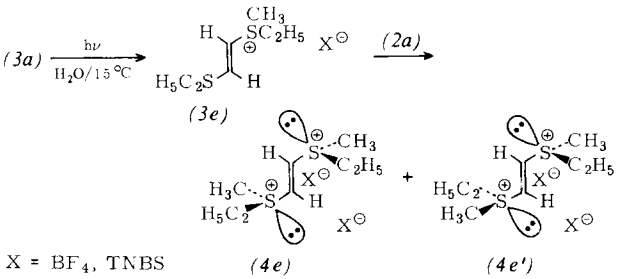
Even when an excess of alkylating agent *(2)* was used, the reaction of *(1a)* with *(2b)* and of *(1b)* with *(2a)* and *(2b)* gave only the monoalkylated compounds *(3b)*, *(3c)*, and *(3d)*, respectively. However, alkylation of *(1a)* with *(2a)* in the molar ratio 1:2 gives a crystalline mixture of the diastereomeric *cis*-disulfonium salts *(4a)*[3] and *(4a')*.



(4a) *(4a')*
X = BF_4, PF_6, TNBS

Surprisingly, the isomers *(4a)* and *(4a')* give identical ^{1}H-NMR spectra in the 60 MHz range (Table 1). The appearance of separate signals for *(4a)* and *(4a')* in the ^{13}C-NMR spectrum establishes the presence of a diastereoisomeric mixture[6].

(3a) undergoes photochemical[4] isomerization to *(3e)*[5], which was obtained in sterically pure form as crystalline picryl sulfonate (dec. 140—142 °C).



X = BF_4, TNBS *(4e)* *(4e')*

On reaction with *(2a)* compound *(3e)* yields a mixture of the diastereoisomeric *trans*-salts *(4e)*[3] and *(4e')*.

The *trans*-vinylenedisulfonium salts are less soluble in acetone than their *cis*-isomers and have higher decomposition points. The ^{1}H-NMR spectra (Table 1) of the *cis*- and *trans*-salts *(4)* are very similar; more extensive differences are observed in the ^{13}C-NMR spectra[6].

In the case of *(4)* the protons of the vinylene group can be replaced by deuterium with retention of stereochemistry[7]. Reaction with methoxide ions proceeds highly stereoselectively to give methoxyvinylsulfonium salts[7].

cis-Ethyl(2-ethylthiovinyl)methylsulfonium tetrafluoroborate *(3a)*

Compound *(1a)* (7.40 g, 0.05 mol) is added under nitrogen at room temperature to a suspension of *(2a)* (7.40 g, 0.05 mol) in anhydrous dichloromethane (70 ml). After one hour's stirring the resulting clear solution is freed from solvent in a rotary evaporator. The residue is treated with a small volume (2—3 ml) of anhydrous methanol and then extracted several times with anhydrous ether (total volume 100 ml) to remove *(1a)* from the ether-insoluble *(3a)*. The ethereal solutions are decanted from the heavy oil. Removal of the residual ether at 30 °C/0.01 torr affords 11.00 g (88%) of a pale yellow oil, which was shown to be pure by NMR spectroscopy.

trans-Ethyl(2-ethylthiovinyl)methylsulfonium tetrafluoroborate *(3e)*

Compound *(3a)* (4.40 g, 0.018 mol) is dissolved in N_2-saturated water (480 ml) and irradiated with exclusion of oxygen for 15 h at 15 °C[4]. After concentration to a volume of 10—15 ml (rotary evaporator, bath temp. 30—40 °C) the mixture is extracted three times with dichloromethane (total volume 30 ml). Drying of the combined organic phases with sodium sulfate and removal of solvent affords 3.60 g (80%) of a pale yellow oil, which was shown to consist of *(3e)* with <5% of *(3a)* by NMR spectroscopy.

Table 1. ^{1}H-NMR data [a] of some sulfonium salts.

Cpd.	S^+—CH=	=CH—S	S^+—CH_3	S^+—CH_2—CH_3		S—CH_2—CH_3	
(3a) [b]	3.92 d	2.17 d	7.07 s	6.6 [d]	8.60 t	7.00 q	8.67 t
(3e) [c]	4.07 d	2.13 d	7.08 s	6.68 q	8.63 t	7.00 q	8.67 t
(4a)/*(4a')*	2.14 s	—	6.76 s	6.28 q	8.48 t	—	—
(4e)/*(4e')*	2.19 s	—	6.80 s	6.32 q	8.51 t	—	—

[a] 60 MHz, τ values in D_2O with sodium trimethylsilylpropanesulfonate as internal standard: [b] $^3J_{cis} = 8.5$ Hz; [c] $^3J_{trans} = 14.7$ Hz [5]; [d] methylene protons are diastereotopic.

[*] Dr. H. Braun and A. Amann
Organisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

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

cis-S,S'-Diethyl-S,S'-dimethylvinylenedisulfonium bis(tetrafluoroborate) (4a)/(4a')

To a suspension of *(2a)* (20.7 g, 0.14 mol) in anhydrous dichloromethane (100 ml) is added *(1a)* (10.4 g, 0.07 mol) under nitrogen, and the mixture is warmed (bath temperature 50 °C) for 3 h in the absence of moisture. After cooling the crystals are filtered off and recrystallized from anhydrous methanol; 17.4 g (70 %) of colorless crystals of m. p. 117—119 °C (dec.) is obtained.

trans-S,S'-Diethyl-S,S'-diethylvinylenedisulfonium bis(tetrafluoroborate) (4e)/(4e')

Analogous reaction of *(2a)* (1.20 g, 8.1 mmol) and *(3e)* (2.00 g, 8.0 mmol) in anhydrous dichloromethane (40 ml) for 3 h at 50 °C affords 2.46 g (85 %) of colorless crystals of m. p. 161—162 °C (dec.).

Received: July 11, 1975 [Z 295a IE]
German version: Angew. Chem. *87*, 773 (1975)

CAS Registry numbers:
(1a), 14044-67-8; *(1b)*, 16906-37-9; *(2a)*, 420-37-1; *(2b)*, 368-39-8; *(3a)*, 56554-01-9; *(3b)*, 56554-03-1; *(3c)*, 56554-05-3; *(3d)*, 56554-07-5; *(3e)*, 56554-09-7; *(4a)*, 56586-76-6; *(4a')*, 56586-78-8; *(4e)*, 56586-80-2; *(4e')*, 56586-82-4

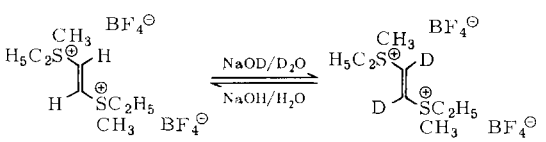
[1] *H. Christol, H. J. Cristau*, and *J. P. Joubert*, Bull. Soc. Chim. Fr. *1974*, 1421; and references cited therein; *H. Christol, H. J. Cristau, J. P. Joubert*, and *M. Soleiman*, C. R. Acad. Sci. *C 279*, 167 (1974).
[2] Review: *L. Brandsma, H. J. T. Bos*, and *J. F. Arens* in *H. G. Viehe*: Chemistry of Acetylenes. Marcel Dekker, New York 1969.
[3] Only the (*R,R*)-enantiomer is shown. TNBS = 2,4,6-trinitrobenzenesulfonate.
[4] High-performance photoreactor, O. Fritz GmbH; Hg high-pressure lamp TQ 150, Hanau.
[5] *G. K. Helmkamp, B. A. Olsen*, and *J. R. Kokinen*, J. Org. Chem. *30*, 1623 (1965).
[6] *H. Braun* and *A. Amann*, unpublished.
[7] *H. Braun* and *A. Amann*, Angew. Chem. *87*, 775 (1975); Angew. Chem. internat. Edit. *14*, 756 (1975).

Stereoselective Reactions of Vinylenedisulfonium Salts[**]

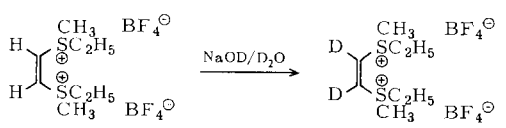
By *Heinz Braun* and *Anton Amann*[*]

In recent years cumulated phosphorus ylides have become the center of exceptional interest[1]. Meanwhile the intermediate occurrence of corresponding sulfur ylides has been deduced indirectly from the structure of reaction products[2]. However, to our knowledge neither the isolation of nor direct evidence for a cumulated sulfonium ylide has yet been published.

Careful addition of a dilute sodium deuterioxide solution to a solution of *(1)*[3] or *(3)*[3] in deuterium oxide until pH ≈6 results in a complete H/D exchange of the vinylenic protons, as shown by NMR. The stereochemistry of the C=C double bond is retained in the process.



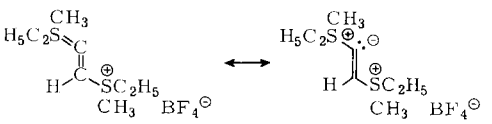
(1) *(2)*



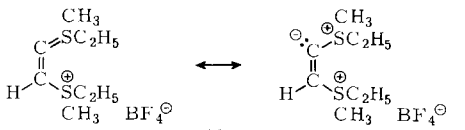
(3) *(4)*

Under analogous conditions we have established the reversibility of the reaction by treatment of *(2)* with sodium hydroxide/water. At pH ≈6 no H/D exchange is detectable for the α protons of the S^+ alkyl groups, *i.e.* the olefinic protons are more acidic than those of the alkyl groups. At higher pH values decomposition occurs with liberation of ethyl methyl sulfide.

We interpret this experiment as proof of the cumulated sulfonium ylides *(5)* and *(6)* which are configurationally stable under the conditions of H/D exchange.



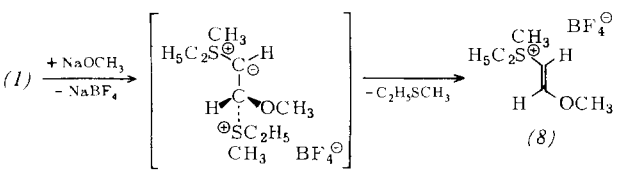
(5)



(6)

Since proton abstraction does not lead to isomerization in the case of *(1)* and *(3)*, we have examined whether *(1)* and *(3)* give stereochemically distinguishable products on treatment with bases.

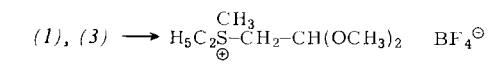
With equimolar amounts of sodium methoxide, compound *(1)* affords—possibly *via* the ylidic intermediate *(7)*[4]—the *trans*-vinylsulfonium salt *(8)* in a stereospecific reaction. The *cis*-isomer *(10)* cannot be detected in the reaction mixture (NMR). As a by-product (< 10 %) compound *(9)* is



(7)

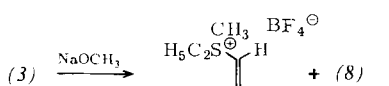
(8)

observed[5], which can be formed from *(8)* by base-catalyzed addition of methanol. Compound *(9)* was also synthesized from *(1)* and from *(3)* with an excess of sodium methoxide and analyzed as the tetraphenylborate (m. p. 119 °C).



(9)

Also in the case of *(3)*, nucleophilic substitution proceeds in a highly stereoselective manner with retention. Reaction with sodium methoxide affords a mixture of > 90 % *(10)* and < 10 % *(8)* as a colorless oil.



(10)

Recrystallization from water and acetone/ether respectively afforded *(10)* as the 2,4,6-trinitrobenzenesulfonate and tetraphenylborate in pure form.

[*] Dr. H. Braun and A. Amann
Organisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

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

trans-Ethyl(2-methoxyvinyl)methylsulfonium tetrafluoroborate (8)

To a solution of *(1)* (1.20 g, 3.4 mmol) in anhydrous methanol (10 ml) at 0 °C is added a 0.4 M sodium methoxide solution (8.5 ml) dropwise over a period of 3 h. After concentration of the clear neutral solution in a rotary evaporator (bath temp. 30—40 °C), the residue is freed from remaining solvent and from ethyl methyl sulfide at 0.01 torr (bath temp. 30—40 °C). The reaction product is taken up in dichloromethane and sodium tetrafluoroborate filtered off. Removal of solvent leaves 0.68 g (90 %) of colorless oil consisting of >90 % *(8)* and <10 % *(9)* (NMR spectrum).—*(8)* is obtained as the 2,4,6-trinitrobenzenesulfonate if a concentrated aqueous solution of *(8)/(9)* is treated with trinitrobenzenesulfonic acid until precipitation is complete and the precipitate recrystallized three times from water; yield 80 %, pale yellow crystals of m. p. 136—137 °C (dec.).

cis-Ethyl(2-methoxyvinyl)methylsulfonium tetrafluoroborate (10)

To a stirred suspension of *(3)* (10.00 g, 0.08 mol) in anhydrous methanol (100 ml) at −40 °C is added dropwise a 1 M sodium methoxide solution (28.0 ml) over a period of 3 h. The neutral colorless solution is stirred for another 12 h at −40 °C and worked up in the same manner as *(8)* to give 5.85 g (95 %) of an almost colorless oil consisting of >90 % *(10)* and <10 % *(8)* (NMR spectrum).—The 2,4,6-trinitrobenzenesulfonate (yield 70 %) forms pale yellow crystals of m. p. 134—135 °C (dec., from water).

Received: July 11, 1975 [Z 295b IE]
German version: Angew. Chem. 87, 775 (1975)

CAS Registry numbers:
(1), 56553-75-4; *(3)*, 56553-776; *trans*-ethyl(2-methoxyvinyl)methylsulfonium tetrafluoroborate, 56553-79-8; *trans*-ethyl(2-methoxyvinyl)-methylsulfonium 2,4,6-trinitrobenzenesulfonate, 56553-80-1; *(9)*, as tetraphenylborate, 56553-82-3; *cis*-ethyl(2-methoxyvinyl)methylsulfonium tetrafluoroborate, 56553-84-5; *cis*-ethyl(2-methoxyvinyl)-methylsulfonium 2,4,6-trinitrobenzenesulfonate, 56553-85-6

[1] Reviews: *C. N. Matthews* and *G. H. Birum*, Acc. Chem. Res. 2, 373 (1969); *H. J. Bestmann* and *R. Zimmermann*, Fortschr. Chem. Forsch. *1971*, 130; *R. W. Saalfrank*, Tetrahedron Lett. *1973*, 3985; further references cited therein; *H. J. Bestmann, G. Schmid.* and *D. Sandmeier*, Angew. Chem. 87, 34 (1975); Angew. Chem. internat. Edit. *14*, 53 (1975); further references cited therein.

[2] *D. Michelot, G. Linstrumelle*, and *S. Julia*, J. C. S. Chem. Commun. *1974*, 10.

[3] *H. Braun* and *A. Amann*, Angew. Chem. 87, 773 (1975); Angew. Chem. internat. Edit. *14*, 755 (1975).

[4] Concerning mechanism of vinylic substitution, cf. *W. D. Stohrer*, Tetrahedron Lett. *1975*, 207; and further references cited therein.

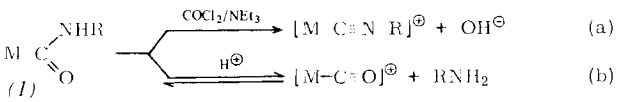
[5] *A. R. Firestone*, DOS 2004814 (1970), Merck and Co., Inc.; Chem. Abstr. 73, 77385u (1970).

Transformation of Carbonyl into Isocyanide Ligands *via* Carbamoyl Intermediates[**]

By *Wolf Peter Fehlhammer* and *Andreas Mayr*[*]

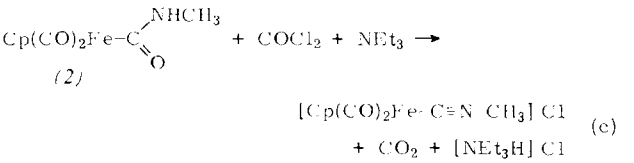
In the chemistry of the isocyanides R—NC, their *synthesis on a complex* which is feasible under particularly mild conditions possesses a number of advantages: isocyanides that are incapable of existence in the free state are only accessible in this manner. On a protecting metal further reactions of the substituent group R can take place without the NC group being attacked. Furthermore, there is *activation on coordination*[1] which can be utilized for (metal-catalyzed) α-additions to the isocyanide function.

We have been able to place oxidative addition of isocyanide dichlorides to metal complexes alongside the long-known alkylation of cyano complexes as a further isocyanide synthesis on a complex[2]. In this communication we report a versatile new process that appears to be of general validity.



(a) (b)

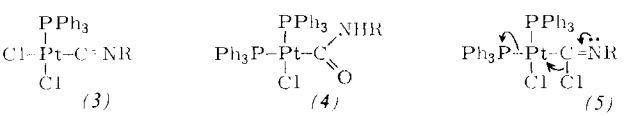
Carbamoylmetal compounds *(1)*, which can be regarded as metalated formamides, can be smoothly converted into the corresponding isocyanide complexes by treatment with acyl halides in the presence of base[3] (a). In contrast, protic acids effect reversal of the formation of *(1)* from a metal carbonyl and a primary amine (b)[4]. The reaction solution must therefore contain at least sufficient amine base to bind all the HCl formed (c). An excess of phosgene, and consequently an acid solution after hydrolysis, does not have a detrimental effect on the yield.



(c)

Heating, which is often additionally required for elimination of water from formamides (a), M = H, proves to be superfluous; removal of OH^- from carbamoyl complexes *(1)* proceeds sufficiently rapidly even below 0 °C: a C—H bond rupture, as in formamides is not required here and the C=O bond [ν(CO) ≈ 1600 cm^{-1}] is weakened relative to that in formamide [ν(CO) ≈ 1700 cm^{-1}].

The preparation of *(3a)* [IR (KBr): 2200 vs [ν(NC)]; 1744, 1733 vs [ν(C=O)]; 340, 304 m cm^{-1} [ν($PtCl_2$)]. 98 % yield, 273 °C (dec.)] from the carbamoyl complex *(4a)*[5] also underlines the utility of the method for the synthesis of functional isocyanides on a complex. In this case the substitution of triphenylphosphane suggests a reaction path *via* the intermediate *(5a)* which is stabilized by chlorine migration to the metal[6]. An analogous methyl isocyanide-platinum complex *(3b)* was obtained from *(4b)*[7].



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

The conversion of a carbonyl into an isocyanide ligand without isolation of the carbamoyl intermediate can be achieved in a particularly simple manner—although so far only in yields of ≤10 %—by mixing pentacarbonyliron, an excess of primary amine, and phosgene at 0 °C, hydrolysis, and extraction of the reaction product $Fe(CO)_4CNR$ with light petroleum. Attempts to optimize this "one-flask" reaction are in progress.

$[\eta^5$—$C_5H_5(CO)_2Fe$—$CNCH_3]PF_6$:

Phosgene is passed for 5 min into a solution of *(2)*[8] (0.4 g, 1.7 mmol) and triethylamine (0.48 ml, 3.5 mmol) in methylene

[*] Dr. W. P. Fehlhammer and Dipl.-Chem. A. Mayr
Institut für Anorganische Chemie der Universität
8 München 2, Meiserstrasse 1 (Germany)

[**] Isonitrile Syntheses at a Metal, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft. – Part 1: ref. [2].

chloride (10 ml). After removal of the solvent the residue is extracted with water (10 ml). The methyl isocyanide complex can be isolated from the extract by precipitation with a concentrated solution of NH_4PF_6 (0.3 g = 1.9 mmol); yield after recrystallization from acetone/ether: 0.33 g (54%).

Received: July 15, 1975 [Z 299 IE]
German version: Angew. Chem. 87, 776 (1975)

CAS Registry numbers:
(2), 33218-94-9; *(3a)*, 56943-27-2; *(3b)*, 33989-94-5; *(4a)*, 56943-28-3; *(4b)*, 56994-63-9; $[\eta^5\text{-}C_5H_5(CO)_2Fe{-}CNCH_3]PF_6$, 56943-25-0; $COCl_2$, 75-44-5

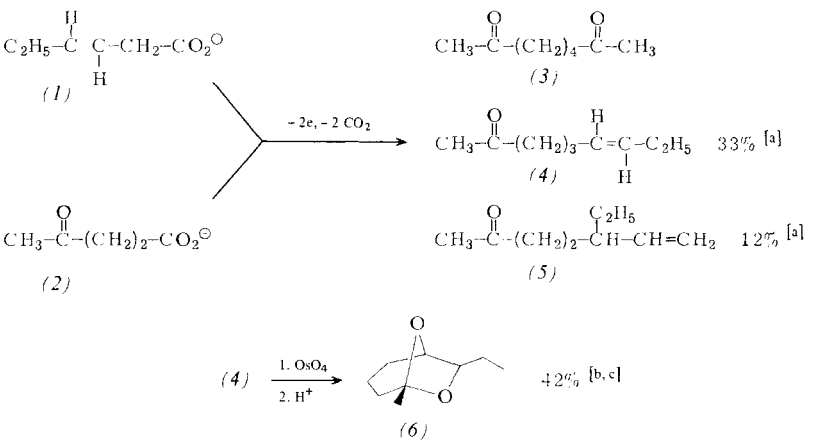
[1] *K. Bartel, A. Mayr*, and *W. P. Fehlhammer*, Lecture delivered at Chemiedozententagung, Düsseldorf 1975.
[2] *W. P. Fehlhammer, A. Mayr*, and *B. Olgemöller*, Angew. Chem. *87*, 290 (1975); Angew. Chem. internat. Edit. *14*, 369 (1975).
[3] *I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer*, and *K. Offermann*, Angew. Chem. 77, 492 (1965); Angew. Chem. internat. Edit. 4, 472 (1965).
[4] *R. J. Angelici*, Acc. Chem. Res. 5, 335 (1972).
[5] *W. P. Fehlhammer, K. Bartel*, and *W. Petri*, J. Organometal. Chem. *87*, C 34 (1975).
[6] We postulate the same intermediate for the the reaction of $Pt(PPh_3)_4$ with isocyanide dichlorides, cf. ref. [2].
[7] *C. R. Green* and *R. J. Angelici*, Inorg. Chem. *11*, 2095 (1972).
[8] *L. Busetto* and *R. J. Angelici*, Inorg. Chim. Acta *2*, 391 (1968).

Synthesis of Brevicomin by Kolbe Electrolysis[1][**]

By *Jochen Knolle* and *Hans J. Schäfer*[*]

Kolbe electrolysis of carboxylic acids is a simple versatile method for forming C—C linkages[2]. Mixed Kolbe dimerization of *trans*-3-hexenoic acid *(1)* and levulinic acid *(2)* opens an abbreviated entry[3a,c] to brevicomin[3a] (*exo*-7-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane) *(6)*, the sex attractant of the western pine beetle *Dendroctonus brevicomis*.

Electrolysis of *(1)*[4] and *(2)* affords, besides the symmetrical dimer 2,7-octanedione *(3)*, the unsymmetrical coupling products *trans*-6-nonen-2-one *(4)* and 5-ethyl-6-hepten-2-one *(5)*; *(4)* can be converted into brevicomin *(6)* by *cis*-hydroxylation and ketalization (cf. Scheme 1).



Scheme 1. [a] Yield determined by gas chromatography, based on *(1)*; [b] isolated yield: *(4)* → *(6)*; [c] spectroscopic data in agreement with literature values [3b].

trans-6-Nonen-2-one (4): After addition of potassium methoxide (0.1 mol), *(1)* (0.5 mol) and *(2)* (0.1 mol) are electrolyzed in methanol (120 ml) at platinum electrodes at a current density of 166 mA/cm² until consumption of 0.56 F. The fraction of the crude product (23.74 g) having b. p. 75—80 °C/12 torr (5 is separated into *(4)* and *(5)* by gas chromatography 30, 25%, 130 °C).

Brevicomin (6): *(4)* (2.3 mmol) and OsO_4 (2.36 mmol) stirred at room temperature for 24 h in pyridine (10 ml). crude product (380 mg) is dissolved in methanol (3 ml) water (2 ml) and acidified relative to Congo red. Bulb distillation at 90 °C/11 torr yields 0.97 mmol of *(6)*.

Received: July 21, 1975 [Z 30
German version: Angew. Chem. 87, 777 (

CAS Registry numbers:
(1), 1577-18-0; *(2)*, 123-76-2; *(4)*, 56889-98-6; *(5)*, 56889-99-7; *(6)*, 20290-99-7

[1] Anodic Oxidation of Organic Compounds, Part 15.—Part 14: *M. F* and *H. J. Schäfer*, Angew. Chem. *87*, 173 (1975); Angew. Chem. inte Edit. *14*, 247 (1975).
[2] *B. C. L. Weedon*, Adv. Org. Chem. *1*, 1 (1960).
[3] a) *R. M. Silverstein, R. G. Brownlee, T. E. Bellas, D. L. Wood, L. E. Browne*, Science *159*, 889 (1968); b) *R. M. Silverstein*, J. C Ed. *45*, 794 (1968); c) *T. E. Bellas, R. G. Brownlee*, and *R. M. Silver* Tetrahedron *25*, 5149 (1969); *H. H. Wassermann* and *E. H. Barbe* Am. Chem. Soc. *91*, 3674 (1969); *B. P. Mundy, R. D. Otzenberger, A. R. De Bernardis*, J. Org. Chem. *36*, 2390 (1971); *K. B. Lypko B. P. Mundy*, and *D. Geeseman*, Synth. Commun. *3*, 453 (1973) *Mori*, Tetrahedron *30*, 4223 (1974).
[4] *S. E. Boxer* and *R. P. Linstead*, J. Chem. Soc. *1931*, 740.

Thermal Diastereoisomerization of 3-Methyl-6-eth denebicyclo[3.1.0]hexane: Orthogonal *versus* Pla Trimethylenemethane[**]

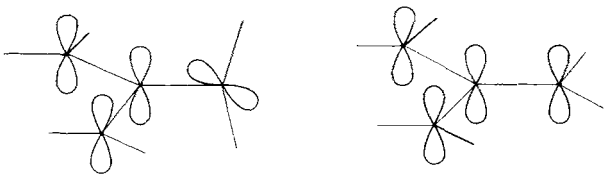
By *Wolfgang R. Roth* and *Gerhard Wegener*[*]

Stereochemical studies by *Doering et al.*[1] have shown t the structurally degenerate rearrangement of methylenecy propane proceeds *via* inversion at the migrating carbon at and that orbital symmetry control can be ruled out for process. The reaction was formulated in terms of an orthogc methyleneallyl diradical *(1)*, which is stabilized with resp to the planar trimethylenemethane *(2)* in the singlet st by *ca.* 25 kcal/mol according to MINDO/2 calculation and even by 52 kcal/mol (31.6 and 32.6 kcal/mol on inclus

[*] Prof. Dr. H. J. Schäfer and Dipl.-Chem. J. Knolle
Organisch-chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)
[**] This work was supported by the Arbeitsgemeinschaft Industrieller Forschungsvereinigungen and the Fonds der Chemischen Industrie.

[*] Prof. Dr. W. R. Roth [+] and Dipl.-Chem. G. Wegener
Abteilung für Chemie der Universität
4630 Bochum, Postfach 2148 (Germany)
[+] To whom correspondence should be addressed.
[**] This work was supported by the Deutsche Forschungsgemeinsc and the Fonds der Chemischen Industrie.

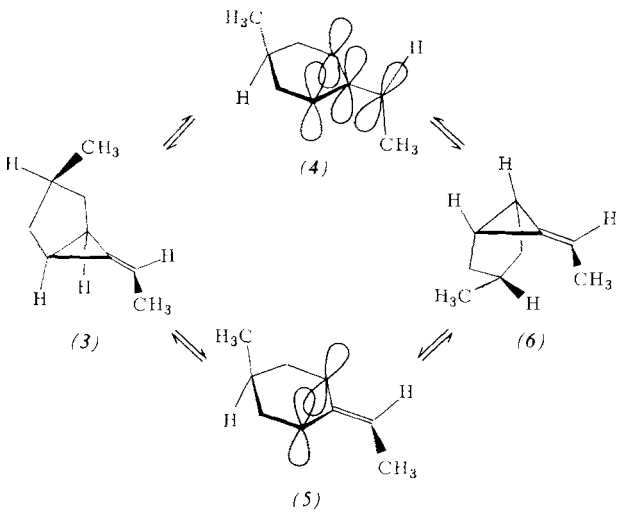
of Jahn-Teller splitting) according to *ab initio* calculations[3]. A much smaller energy difference (2.8 kcal/mol) was calculated by *Yarkony* and *Schaefer*[4].



(1) *(2)*

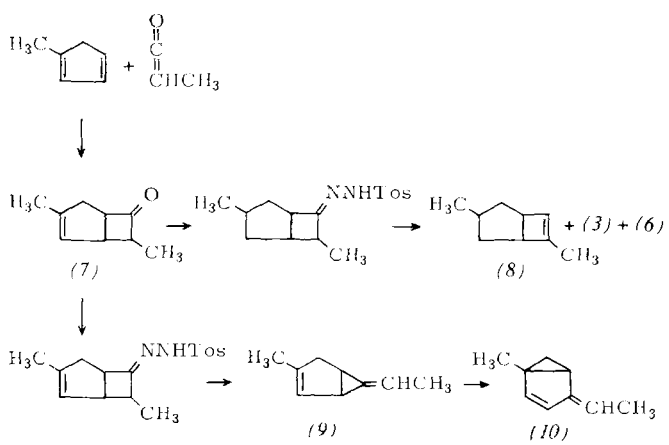
If these calculations are valid then the diastereoisomerization of methylenecyclopropane would also be expected to proceed *via* the orthogonal diradical *(1)*.

We have tested this prediction for the mutual thermal isomerization of optically active *syn*- *(3)* and *anti*-3-methyl-6-ethylidenebicyclo[3.1.0]hexane *(6)*. In this case racemization will occur if an intermediate diradical *(4)* analogous to *(1)* is involved, whereas optical integrity will be retained if the diradical *(5)* analogous to *(2)* is formed.



(3) *(4)* *(5)* *(6)*

Compounds *(3)* and *(6)* were prepared by addition of methylcyclopentadiene to methylketene, catalytic hydrogenation of the [2+2] adduct *(7)*, and pyrolysis of the lithium salt of its tosylhydrazone to give a 5:4:1 mixture of 3,6-dimethylbicyclo[3.2.0]hept-6-ene *(8)*, the *syn* compound *(3)*, and the *anti* compound *(6)*. The structures of *(3)* and *(6)* are established by their spectroscopic properties and with regard to the position of the methyl group on C^3 also by transformation (methyllithium/THF) of the tosylhydrazone of *(7)* into 1-methyl-4-ethylidenebicyclo[3.1.0]hex-2-ene *(10)*, which in turn is related to 3-methyl-6-ethylidenebicyclo[3.1.0]hex-2-ene *(9)* by way of a vinylcyclopropane rearrangement[5].



(7) *(8)* *(9)* *(10)*

Partial enantiomerization of *(3)* and *(6)* by *Brown*'s method[6] led to rotations of $[\alpha]_{365} = (+)\,2.05$ and $(+)\,2.02°$, respectively.

The diastereoisomers *(3)* and *(6)* undergo mutual interconversion in the gas phase with partial loss of their optical integrity. The reaction is accompanied by the racemization of the reactants. From the rates for the rearrangement ($k_{36} = 5.3 \times 10^{-5}$, $k_{63} = 0.64 \times 10^{-5}\,s^{-1}$), the rates for the racemization ($k_{33} = 3.2 \times 10^{-5}$, $k_{66} = 0.88 \times 10^{-5}\,s^{-1}$), and the optical activity of the rearranged products, all determined at 164.4 °C, a stereospecificity of 9.8 % was calculated for diastereoisomerization at this temperature.

These observations can be interpreted by a kinetic model in which a two-step reaction—with *(4)* as intermediate—competes with stereospecific rearrangement *via* the planar diradical *(5)*. The transition states of the two reactions should then differ by about 2.3 and 2.7 kcal/mol in their Gibbs energy (cf. Fig. 1).

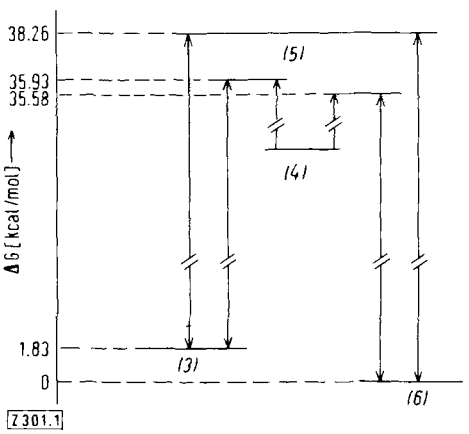


Fig. 1. Gibbs energy changes in the rearrangement *(3)*⇌*(6)* at 164.4 °C.

Hence the greater stability of the orthogonal as against the planar diradical is confirmed, although the energy difference is not in the same order of magnitude as postulated by *Dewar*[2] and *Salem*[3].

Support for the assumption of competing reaction pathways is provided by the considerable increase in stereoselectivity with rising temperature. The two-step route should have a smaller A factor and thus become less significant at higher temperature. The resulting non-linear relation between $\ln(k_1 + k_{-1})$ and T^{-1} cannot be observed in the temperature range accessible for kinetic measurements (140—195 °C) since the expected deviations lie within the limits of experimental error. The activation parameters for the rearrangement *(3)*⇌*(6)* were determined as $E_a = 35.55 \pm 0.16$ kcal/mol, $A = 3.0 \times 10^{13}\,s^{-1}$. The temperature dependence of the equilibrium constant $K = [6]/[3]$ affords $\Delta H = -2.49 \pm 0.02$ kcal/mol, $\Delta S = 1.50 \pm 0.05$ cal K^{-1} mol^{-1}.

Received: July 21, 1975 [Z 301 IE]
German version: Angew. Chem. 87, 777 (1975)

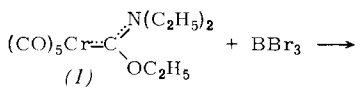
CAS Registry numbers:
(3), 56943-29-4; *(6)*, 56978-18-8; *(7)*, 56908-33-9; *(7)*-tosylhydrazone, 56908-34-0; *(8)*, 56908-35-1; *(10)*, 56908-36-2

[1] *W. v. E. Doering* and *L. Birladeanu*, Tetrahedron 29, 499 (1973).
[2] *M. J. S. Dewar* and *J. W. Wasson*, J. Am. Chem. Soc. 93, 3081 (1971).
[3] *W. J. Hehre, L. Salem*, and *M. R. Willcott*, J. Am. Chem. Soc. 96, 4328 (1974).
[4] *D. R. Yarkony* and *H. F. Schaefer III*, J. Am. Chem. Soc. 96, 3754 (1974); *W. Th. Borden, ibid.* 97, 2906 (1975).
[5] *M. Rey, U. A. Huber*, and *A. S. Dreiding*, Tetrahedron Lett. 1968, 3583.
[6] *H. C. Brown, N. R. Ayyangar*, and *G. Zweifel*, J. Am. Chem. Soc. 86, 1071 (1964); *W. R. Moore, H. W. Anderson*, and *S. O. Clark, ibid.* 95, 835 (1973).

trans-Bromo(diethylaminocarbyne)tetracarbonylchromium[1]

By *Ernst Otto Fischer*, *Gottfried Huttner*, *Willi Kleine*, and *Albin Frank*[*]

In order to elucidate the influence of a hetero atom having a lone pair located in α position relative to the carbyne carbon atom of the CR ligand, on the triple bond transition metal—$C_{carbyne}$ we have synthesized *trans*-bromo(diethylaminocarbyne)tetracarbonylchromium *(2)*. In contrast to *trans*-$BrW(CO)_4[CN(C_2H_5)_2]$[2], reaction according to



(1)

$$(CO)_5Cr{\equiv}C{-}N(C_2H_5)_2 + BBr_3 \longrightarrow BrCr(CO)_4[CN(C_2H_5)_2] + CO + \{BBr_2OC_2H_5\}$$

(2)

was only successful when performed in methylene chloride. The composition and configuration of the orange complex *(2)* were established by total elemental analysis, the mass spectrum [M^+: $m/e = 329$, relative to ^{81}Br and ^{52}Cr; ion source TO4, 50 eV] and IR and NMR data[3] (four equivalent CO ligands). The long wave shift of the most intense ν_{CO} band by 60 cm^{-1} relative to alkyl- and arylcarbyne complexes of chromium[4] in the IR spectrum and the upfield shift of the carbyne carbon in the ^{13}C-NMR spectrum of *(2)* indicate a considerable increase in electron density at the metal.

The *trans* arrangement of the ligands $CN(C_2H_5)_2$ and Br in the pseudooctahedral chromium complex *(2)* has been confirmed by an X-ray study[5] (Fig. 1).

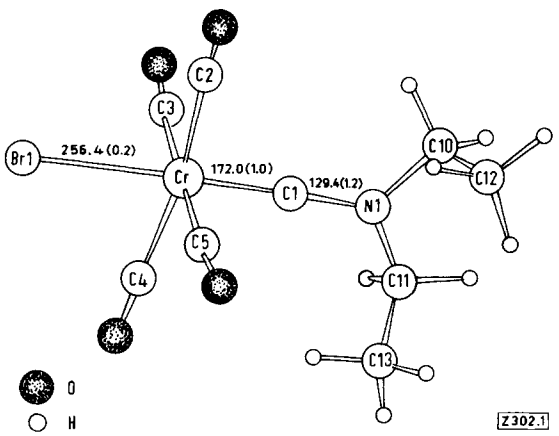
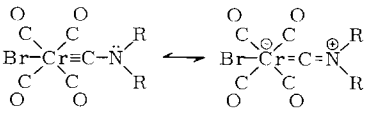


Fig. 1. Molecular structure of *trans*-bromo(diethylaminocarbyne)tetracarbonylchromium *(2)*.

The Cr—C distance in the linear metal-carbyne fragment Cr—C(1)—N(1) is 172 ± 1 pm, *i.e.* not significantly larger than the corresponding distances in analogous methyl- or phenylcarbyne complexes[4, 6]. The length of the bond from the carbyne carbon atom C(1) to the trigonal-planar nitrogen atom N(1) amounts to 129 ± 1 pm, which is hardly greater than the C=N double bond length in diacetyl dioxime (127 ± 2 pm[7]); this indicates a significant contribution of the resonance formula *(2b)* to the electron distribution, as had previously been deduced from spectroscopic data for the tungsten compound[2]. However, the increase in bond length expected for Cr—C(1) in *(2b)* could not be observed.

[*] Prof. Dr. E. O. Fischer, Doz. Dr. G. Huttner, Dipl.-Chem. W. Kleine, and Dipl.-Chem. A. Frank
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)



(2a) *(2b)*

Procedure:

All operations performed in solvents freed from water and oxygen under N_2. BBr_3 (1.3 g, 5 mmol) is added dropwise to a stirred solution of *(1)*[8] (1.6 g, 5 mmol) in CH_2Cl_2 (30 ml). After 30 min the reaction mixture is evaporated to dryness at −20 °C and the reddish brown residue chromatographed in pentane/ether (4 : 1) on a cooled column ($l = 25$, diam. 2.5 cm) of silica gel at −20 °C. Following an initial yellow zone containing *(1)* and $Cr(CO)_6$, orange *(2)* is eluted with methanol. The eluate is evaporated to dryness, dissolved in ether, filtered, precipitated with pentane, and then recrystallized from ether/pentane (−80 °C). M. p. 47 °C; yield 1.3 g (*ca.* 80%).

Received: August 1, 1975 [Z 302 IE]
German version: Angew. Chem. 87, 781 (1975)

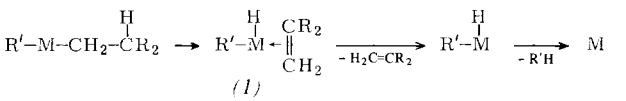
CAS Registry numbers:
(1), 28471-37-6; *(2a)*, 57091-06-2; *(2b)*, 57091-07-3; BBr_3, 10294-33-4

[1] Transition Metal-Carbyne Complexes, Part 10.—Part 9: *E. O. Fischer* and *K. Weiss*, Chem. Ber., in press.
[2] *E. O. Fischer*, *G. Kreis*, *F. R. Kreissl*, *W. Kalbfus*, and *E. Winkler*, J. Organometal. Chem. *65*, C 53 (1974).
[3] IR (in CH_2Cl_2; ν_{CO}): 2094 s (A_1), 1990 vs (E), 2020 m sh (B_1) cm^{-1}. ^1H-NMR (in CD_2Cl_2; τ-values): 6.66 q NCH_2CH_3, 8.76 t NCH_2CH_3. ^{13}C-NMR (in CD_2Cl_2; −20 °C; δ in ppm rel. TMS): 264.12 Cr*C*, 211.24 *C*O, 46.71 NCH_2CH_3, 14.13 NCH_2CH_3.
[4] *E. O. Fischer* and *U. Schubert*, J. Organometal. Chem. *100*, 59 (1975).
[5] Data: 1609 structure factors, Syntex P21; solution: Syntex-XTL, $R_1 = 0.047$.
[6] *G. Huttner*, *H. Lorenz*, and *W. Gartzke*, Angew. Chem. *86*, 667 (1974); Angew. Chem. internat. Edit. *13*, 609 (1974).
[7] *L. Merritt* and *E. Lanterman*, Acta Crystallogr. *5*, 811 (1952).
[8] *E. O. Fischer* and *H. J. Kollmeier*, Angew. Chem. *82*, 325 (1970); Angew. Chem. internat. Edit. *9*, 309 (1970).

Tetraisopropylchromium[**]

By *Jörn Müller* and *Walter Holzinger*[*]

σ-Organyl-transition metal compounds bearing hydrogen on the β-C atom are considered to be extremely labile and generally decompose at low temperatures preferably according to the reaction scheme[1, 2]:



(1)

Thus compounds of the type MR_n that are still stable at temperatures of about 0 °C have so far only been accessible if the β-C atom bears no hydrogen ($R = CH_3$, $CH_2C_6H_5$, $CH_2C(CH_3)_3$, $CH_2Si(CH_3)_3$, *etc.*[2]) or if formation of the π-olefin-metal hydride intermediate *(1)* is precluded by the α-C atom being a bridgehead of a bicyclic hydrocarbon (R = 1-adamantyl[3], bicyclo[2.2.1]hept-1-yl[4]).

In spite of this rule we have been able to prepare tetraisopropylchromium *(2)* by reaction of chromium(III) chloride with isopropylmagnesium bromide in diethyl ether. The

[*] Doz. Dr. J. Müller and Dipl.-Chem. W. Holzinger
Anorganisch-chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

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

pronounced increase in the yield of *(2)* on UV irradiation during the reaction suggests the intermediacy of free radicals:

$$CrCl_3 + 3\ i\text{-}C_3H_7MgBr \xrightarrow[-3\ "MgBrCl"]{} Cr(i\text{-}C_3H_7)_3$$

$$\xrightarrow{h\nu} i\text{-}C_3H_7^{\bullet} + Cr(i\text{-}C_3H_7)_2 \ (\rightarrow \text{decomp.})$$

$$i\text{-}C_3H_7^{\bullet} + Cr(i\text{-}C_3H_7)_3 \rightarrow Cr(i\text{-}C_3H_7)_4$$

(2)

Apparently the formation of *(2)* is the result of the joint action of several favorable factors (stability of the radicals, steric effects) since under identical reaction conditions no CrR_4 species could be obtained with $R=CH_3$, C_2H_5, *tert*-C_4H_9.

Compound *(2)*, which is pyrophoric in finely crystalline form, gives dark brownish red crystals (m. p. *ca.* 20 °C) which are highly soluble in pentane, benzene, ether, or tetrahydrofuran (THF). It can be chromatographed on Al_2O_3/5% H_2O, and is thus resistant to hydrolysis. Although pure *(2)* can be stored for a long time under N_2 at room temperature, rapid, and in some cases (*e.g.* on metal surfaces) spontaneous, decomposition is observed in high vacuum at 20 °C. However, it can be sublimed onto a cold finger (−78 °C) in a high vacuum at 0 °C.

The magnetic moment μ_{eff} of *(2)* is $2.81 \pm 0.1\ \mu_B$ (^{1}H-NMR chemical shift method), corresponding to two unpaired electrons (d^2 system). The IR spectrum (capillary) displaying a marked paucity of bands between 4000 and 600 cm^{-1} merely contains absorptions in the ν(C—H) (2955, 2923, 2845 cm^{-1}) and δ(C—H) regions (1454, characteristic doublet at 1370 and 1358 cm^{-1}) and isopropyl skeletal vibrations at 1155 (sh) and 1120 cm^{-1}.

The stability of *(2)* could be due on the one hand to steric reasons and on the other to the difficult formation of a π-olefin intermediate analogous to *(1)*, owing to the high oxidation state of the central metal atom. According to this concept the synthesis of further tetraisopropylmetal compounds would appear to be possible.

Procedure[5]:

A Grignard solution prepared from Mg (1.22 g, 50.2 mmol) and *i*-C_3H_7Br (4.76 ml) in ether (50 ml) is added to a stirred suspension of $CrCl_3$ (2 g, 12.6 mmol) also in ether (100 ml) at −78 °C. The reaction mixture is allowed to slowly warm up to room temperature (reaction starts above *ca.* −15 °C) and irradiated for 8 h with UV light (Hg high pressure lamp Q 81, Heraeus, Hanau). The ether is evaporated off at −20 °C, the residue extracted with pentane, and the pentane solution filtered over Al_2O_3 (4% H_2O). The pentane is evaporated off at −40 °C, the residue taken up in THF and again filtered over Al_2O_3 (4% H_2O). After concentration of the THF solution compound *(2)* crystallizes at −78 °C; it is filtered off at very low temperature and dried for 14 h at −40 °C in a high vacuum. Yield 350 mg (12% based on $CrCl_3$; 24% based on the proposed formation equation) of analytically pure product.

Received: August 4, 1975 [Z 303 IE]
German version: Angew. Chem. 87, 781 (1975)

CAS Registry numbers:
$CrCl_3$, 10025-73-7; *i*-C_3H_7Br, 75-26-3; $Cr(i\text{-}C_3H_7)_4$, 38711-69-2

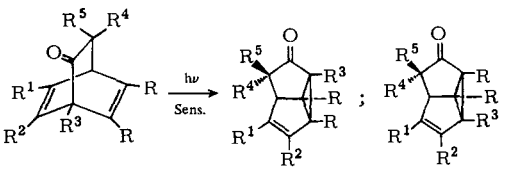
[1] *R. P. A. Sneeden* and *H. H. Zeiss*, J. Organometal. Chem. *22*, 713 (1970).
[2] *P. J. Davidson, M. F. Lappert*, and *R. Pearce*, Acc. Chem. Res. *7*, 209 (1974).
[3] *R. M. G. Roberts*, J. Organometal. Chem. *63*, 159 (1973).
[4] *B. K. Bower* and *H. G. Tennent*, J. Am. Chem. Soc. *94*, 2512 (1972).
[5] All operations performed under N_2.

Photochemical Rearrangement and Fragmentation of Bicyclo[2.2.2]octadienones

By *Hans-Dieter Becker* and *Bernd Ruge*[*]

The photosensitized rearrangement of bicyclo[2.2.2]octadienones has hitherto only been studied with benzo-annelated derivatives. In all cases the triplet reaction was found to result in a 1,2-acyl shift to give the product of an oxa-di-π-methane rearrangement[1, 2]. On the other hand, from the excited singlet state bicyclo[2.2.2]octadienones aromatize by elimination of ketene[3].

By Diels-Alder addition of dimethyl acetylenedicarboxylate to 2,4-cyclohexadienones we have synthesized the previously unknown bicyclo[2.2.2]octadienones *(1a)* to *(1g)* which, from the excited triplet state, could yield not only two conceivable isomerization products of oxa-di-π-methane rearrangements but also give four different isomerization products of structurally feasible di-π-methane rearrangements. Surprisingly, we found that the acetophenone-sensitized triplet reaction of *(1a)* to *(1g)* proceeds with a remarkable degree of regiospecificity and affords exclusively compounds *(2a)* to *(2g)* resulting from a di-π-methane rearrangement (see Table 1).



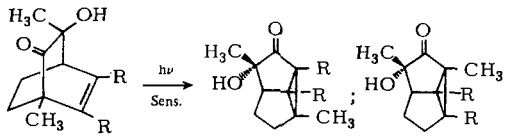
(1a)–(1g) *(2a)–(2g)* *(3)*

R = $COOCH_3$

Table 1. Substituents of the bicyclo[2.2.2]octadienones *(1)* and their photoproducts *(2)* (R = $COOCH_3$).

	R¹	R²	R³	R⁴ R⁵	yield [%] *(2)*	m. p. [°C] *(2)*
a	CH_3	H	H	—O—CH_2—	42	138—140
b	CH_3	CH_3	H	—O—CH_2—	70	123—124
c	H	H	CH_3	—O—CH_2—	46	114—116
d	H	H	CH_3	OH CH_3	57	100—102
e	CH_3	H	CH_3	—O—CH_2—	53	130—131
f	CH_3	H	CH_3	OH CH_3	40	101—103
g	t-C_4H_9	H	CH_3	—O—CH_2—	61	111—112

Structure *(2)* is unequivocally confirmed for the photoproducts from *(1a)* and *(1b)*, where $R^3=H$, by NMR spectroscopy. In all other cases, where $R^3=CH_3$, spectroscopic methods fail to distinguish between *(2)* and an oxa-di-π-methane rearrangement product of structure *(3)*. We have therefore ruled out structure *(3)* in the case of the photoproduct from *(1d)* in the following manner: Selective hydrogenation of *(1d)* gave the bicyclo[2.2.2]octenone *(4)* which was isomerized by acetophenone-sensitized oxa-di-π-methane rearrangement. The resulting compound *(5)* (m. p. 93—96 °C) was not identi-



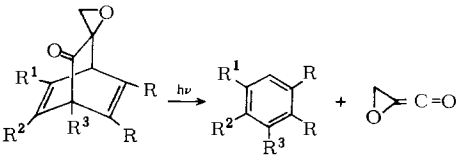
(4) *(5)* *(6)*

R = $COOCH_3$

[*] Doz. Dr. H.-D. Becker and Dr. B. Ruge
Department of Organic Chemistry
Chalmers University of Technology and University of Göteborg
S-402 20 Göteborg 5 (Sweden)

cal with the compound *(6)* (m. p. 116—118 °C) obtained from the photoproduct *(2d)* by catalytic hydrogenation.

On direct irradiation of the spirooxirane-substituted bicyclo[2.2.2]octadienones *(1)* ($\lambda > 300$ nm; 1 g/65 ml chloroform in the presence of ethanol) smooth reaction takes place to give the hitherto unknown 2-carbonyloxirane *(8)* and the dimethyl esters of phthalic acids *(7)*. Compound *(8)* was trapped with ethanol and characterized as ethyl glycidate (yield 66 %). In similar manner the bicyclooctadienones *(1d)*



(1a)-(1c)
(1e), (1g)

(7)
R = $COOCH_3$

(8)

and *(1f)* afforded the dimethyl phthalates *(7d)* and *(7f)* together with the previously unknown hydroxy(methyl)ketene CH_3—C(OH)=C=O, which gave ethyl lactate by addition of ethanol.

Dimethyl 6',7'-dimethyl-3'-oxospiro[oxirane-2,4'-tricyclo-[3.3.0.0^{2,8}]oct[6]ene]-1',8'-dicarboxylate (2b)

A solution of *(1b)* (2.0 g, 6.85 mmol) in acetophenone (175 ml) was irradiated with a 450 W Hanovia medium pressure mercury arc for 1 h under N_2 in a Pyrex apparatus. The acetophenone was then distilled off at about 5×10^{-2} torr. The residue crystallized on addition of ether and was recrystallized from propanol; yield 1.4 g of *(2b)*.

Received: August 4, 1975 [Z 307 IE]
German version: Angew. Chem. 87, 782 (1975)

CAS Registry numbers:
(1a), 57091-34-6; *(1b)*, 57091-35-7; *(1c)*, 57091-36-8; *(1d)*, 57091-37-9; *(1e)*, 57091-38-0; *(1f)*, 57091-39-1; *(1g)*, 57091-40-4; *(2a)*, 57091-41-5; *(2b)*, 57091-42-6; *(2c)*, 57091-43-7; *(2d)*, 57091-44-8; *(2e)*, 57091-45-9; *(2f)*, 57091-46-0; *(2g)*, 57091-47-1; *(4)*, 57109-88-3; *(5)*, 57091-48-2; *(6)*, 57091-49-3; *(7a)*, 20116-65-8; *(7b)*, 17649-59-1; *(7c)*, 131-11-3; *(7g)*, 57091-50-6; *(8)*, 57091-51-7

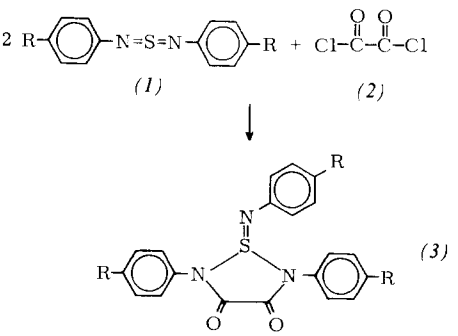
[1] For a review of the di-π-methane and oxa-di-π-methane rearrangements, see *S. S. Hixson, P. S. Mariano*, and *H. E. Zimmerman*, Chem. Rev. *73*, 531 (1973).
[2] For a survey of the photochemistry of β,γ-unsaturated ketones, see *W. G. Dauben, G. Lodder*, and *J. Ipaktschi*, Top. Curr. Chem. Fortschr. Chem. Forsch. *54*, 73 (1975).
[3] *R. K. Murray, Jr.* and *H. Hart*, Tetrahedron Lett. *1968*, 4995.

2,5-Diaryl-1-(arylimino)-1λ⁴,2,5-thiadiazolidine-3,4-diones: New Five-Membered Heterocycles[**]

By *Richard Neidlein* and *Peter Leinberger*[*]

Dedicated to Professor Klaus Schäfer on the occasion of his 65th birthday

We recently reported [1] simple syntheses of 5-oxo-1,3λ⁴,2,4-dithiadiazoles and the hitherto unknown 5-acylimino-1,3λ⁴,2,4-dithiadiazoles by cleavage of *N,N'*-disilylated sulfur diimides with bifunctional acyl chlorides. *N,N'*-Diarylated sulfur diimides *(1)*[2] react with oxalyl chloride *(2)* at room temperature to give 2,5-diaryl-1-(arylimino)-1λ⁴,2,5-thiadiazolidine-3,4-diones *(3)*.



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

	R	M. p. [°C]	Yield [%]
(3a)	H	243—244	85
(3b)	CH_3	223—224	86
(3c)	Cl	250	84
(3d)	Br	236—238	82

The cyclic diketones *(3)* are the first representatives of a new class of compounds. They form white well-crystalline needles which dissolve very readily in CH_2Cl_2, readily in methanol, and only sparingly in CCl_4 and *n*-hexane.

Compounds *(3a)* to *(3d)* were characterized by elemental analysis and mass, IR, ^{1}H-NMR, and ^{13}C-NMR spectra.

2,5-Diphenyl-1-(phenylimino)-1λ⁴,2,5-thiadiazolidine-3,4-dione (3a)

(2) (3.78 g, 30 mmol) dissolved in anhydrous CCl_4 (20 ml) is slowly added to a solution of *N,N'*-diphenyl sulfur diimide *(1a)* (6.42 g, 30 mmol) in anhydrous CCl_4 (30 ml). The temperature of the reaction mixture should not be allowed to rise above 35 °C. After stirring for another 3 h at room temperature the white precipitate is filtered off and washed with a little CCl_4; white needles from CH_2Cl_2/CCl_4.

Received: August 22, 1975 [Z 308 IE]
German version: Angew. Chem. 87, 811 (1975)

CAS Registry numbers:
(1a), 3839-89-2; *(1b)*, 3839-88-1; *(1c)*, 2648-43-3; *(1d)*, 3839-86-9; *(2)*, 79-37-8; *(3a)*, 57091-52-8; *(3b)*, 57091-53-9; *(3c)*, 57091-54-0; *(3d)*, 57139-16-9

[1] *R. Neidlein* and *P. Leinberger*, Chem.-Ztg., in press.
[2] *G. Kresze* and *W. Wucherpfennig*, Angew. Chem. 79, 109 (1967), in particular p. 124; Angew. Chem. internat. Edit. *6*, 149 (1967); *H.-H. Hörbold* and *J. Beck*, J. Prakt. Chem. *311*, 621 (1969); *T. Minami, H. Miki, H. Matsumoto, Y. Oshiro*, and *T. Agawa*, Tetrahedron Lett. *1968*, 3049; *E. S. Levchenko* and *Z. J. Shokol*, Zh. Org. Khim. *5*, 472 (1969).

[*] Prof. Dr. R. Neidlein and P. Leinberger
Pharmazeutisch-chemisches Institut der Universität
69 Heidelberg, Im Neuenheimer Feld 364 (Germany)

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

Alkylation of Tl[I] Alkoxides. A Useful Modification of the Williamson Etherification

By *Hans-Otto Kalinowski, Dieter Seebach*, and *Gerhard Crass*[*]

For our work on the use of tartaric acid derivatives as auxiliaries for asymmetric synthesis[1] we needed a simple, selective, and mild method of etherification of OH groups in alcohols *(1)* with long chain alkyl halides which is compatible with readily racemized chiral centers. Neither the combination NaH/RX nor the classical Ag_2O/RX method gave satisfactory results[2]. Looking for an alternative, we discovered that certain thallium(I) alkoxides *(2)*[3] can be alkylated to give ethers *(3)* in excellent yields[4].

To this end, we react the ROTl derivatives *(2)*, accessible from commercial $TlOC_2H_5$[5], with alkyl halides in acetonitrile

[*] Dr. H.-O. Kalinowski, Prof. Dr. D. Seebach, and G. Crass
Institut für Organische Chemie des Fachbereichs 14 der Universität
63 Giessen, Ludwigstrasse 21 (Germany)

$$R\text{–}OH \xrightarrow[C_6H_6]{TlOC_2H_5} R\text{–}OTl \xrightarrow[CH_3CN]{R'X} R\text{–}O\text{–}R'$$
(1) *(2)* *(3)*

C_nH_{2n+1}–OTl, $TlO\text{–}(CH_2)_n\text{–}OTl \ll TlO\text{–}(CH_2)_4\text{–}OTl$ ($n \geq 5$)

$\sim RO\text{–}(CH_2)_2\text{–}OTl < TlO\text{–}CH_2\text{–}CH_2\text{–}\underset{\displaystyle CH_3}{\underset{|}{CH}}\text{–}OTl$

$< TlO\text{–}CH_2\text{–}CH_2\text{–}OTl < R\text{–}\underset{\displaystyle OTl}{\underset{|}{CH}}\text{–}COOR \ll R\text{–}\underset{\displaystyle OTl}{\underset{|}{CH}}\text{–}CONRR'$

Procedure:

The number of equivalents of the hydroxy compound *(1)* as stated in Table 1 (column 3) is added with stirring to a solution of $TlOC_2H_5$ (20 mmol) in benzene (100—250 ml). In most cases, a white or yellow precipitate of the desired Tl alkoxide *(2)*[8] is formed quantitatively within 1 h at room temperature. The solvent is removed in a rotary evaporator and the residue suspended in dry acetonitril (150—200 ml). Alkyl halide (amount see Table 1, column 3) is added, and the mixture is stirred at 20–60 °C for 0.5–24 h (GC, DC, or NMR control). The Tl halide is filtered off and washed with chloroform; the filtrate is either concentrated directly or after filtration through a short column of silica gel to remove residual thallium.

Table 1. Alkylations of hydroxy compounds *(1)* using thallium(I) alkoxides *(2)* in acetonitrile (see *Procedure*).

Substrate ROH *(1)*	Alkyl halide R'X	Molar ratio *(1)*/ Tl^I/R'X	Reaction time [h]/ temp. [°C]	Product *(3)*	Yield [a] [%]	Physical data [b]
1-octanol	CH_3I	1/1/1	14/20	$n\text{-}C_8H_{17}OCH_3$	26	b. p. as [9]
ethylene glycol monomethyl ether	$C_6H_5CH_2Br$	1/1/1	24/20	$CH_3O\text{–}CH_2CH_2\text{–}OCH_2C_6H_5$	81	b. p. 54–56 °C/0.35 torr
trans-1,2-cyclohexanediol	CH_3I	1/2/2	14/20	*trans*-2-methoxycyclohexanol	85 [c]	b. p. as [9]
1,3-butanediol	$n\text{-}C_6H_{13}I$	1/2/2	14/20 then 2/70 (in DMF)	$CH_3\text{–}CH(OH)\text{–}CH_2\text{–}CH_2OC_6H_5$	62 [c]	b. p. 60 °C/0.3 torr
1,4-butanediol	CH_3I	1/2/2	14/20	$HO\text{–}(CH_2)_4\text{–}O\text{–}CH_3$	77 [c]	b. p. as [9]
triethylene glycol	CH_3I	1/2/2	14/20	triethylene glycol dimethyl ether	75	b. p. as [10]
glycerol	$C_6H_5CH_2Br$	1/2/2	72/20	$(C_6H_5CH_2OCH_2)_2CHOH$	61 [c]	b. p. 136 °C/0.01 torr
ethyl lactate	CH_3I	1/1/1	14/20	$CH_3\text{–}CH(OCH_3)\text{–}COOC_2H_5$	68	b. p. as [9]
diethyl malate	CH_3I	1/1/1	14/20	$C_2H_5OOC\text{–}CH_2\text{–}CH(OCH_3)\text{–}COOC_2H_5$	74	b. p. as [9]
diethyl (*R*,*R*)-(+)-tartrate	CH_3I	1/2/2	20/60	$C_2H_5OOC\text{–}CH(OR)\text{–}CH(OR)\text{–}COOC_2H_5$ $R = CH_3$	>90	b. p. and $[\alpha]_D$ as [9]
	$n\text{-}C_6H_{13}I$	1/2/2	20/60	$R = C_6H_{13}$	>90	non-distillable oil
(*R*,*R*)-(+)-*N*,*N*-*N*',*N*'-tetramethyltartaramide	CH_3I	1/2/2	3/45	$(CH_3)_2NCO\text{–}CH(OR)\text{–}CH(OR)\text{–}CON(CH_3)_2$ $R = CH_3$	78	$[\alpha]_D^{20} = +93°$ ($c = 3$; C_6H_6); [9]: 94.4°, 95°
	$CH_2{=}CH\text{–}CH_2Br$	1/2/2	2/20 then 3/60	$R = CH_2{=}CH\text{–}CH_2$	82	$[\alpha]_D^{20} = +94.0°$ ($c = 3.1$; C_6H_6)
	$n\text{-}C_{16}H_{33}I$	1/2/2	12/20 then 4/40	$R = C_{16}H_{33}$	95	m. p. 65–67 °C
	CH_2I_2	1/2/1	12/20 then 3/60	$\text{–}R\text{–}R\text{–}=\text{–}CH_2\text{–}$	25	$[\alpha]_D^{20} = -56.2°$ ($c = 2.9$; $CHCl_3$)
	$BrCH_2COOC_2H_5$	1/2/2	14/20	$R = CH_2COOC_2H_5$	90	$[\alpha]_D^{20} = +68.5°$ ($c = 2.0$; C_6H_6)
(*R*,*R*)-(+)-*N*,*N*'-dimethyltartaramide	CH_3I	1/2/2	15/30	$CH_3NHCO\text{–}CH(OCH_3)\text{–}CH(OCH_3)\text{–}CONHCH_3$	75	m. p. as [9]

[a] Yields of purified (distilled, recrystallized, or chromatographed) products.
[b] IR, NMR, and, in the case of new compounds, elemental analysis data are fully compatible with the structures given.
[c] No higher alkylated product can be detected besides the monoether shown.

or other polar solvents. Some results are listed in Table 1. The rate of etherification increases with increasing "donating power" (alkyl < RO < TlO < COOR < $CONR_2$) and decreasing distance of an oxygen atom present in the same molecule; the reaction is accelerated by increasing solvent polarity (C_6H_6, $CCl_4 \ll CH_3CN$ < DMF); it proceeds under the conditions tested so far only with primary alkyl halides (allyl, benzyl > methyl > *n*-alkyl halides; iodide > bromide ≫ tosylate) and primary or secondary, non-benzylic hydroxyl groups.

These pronounced reactivity differences permit selective monoalkylation of glycols. No racemizations or epimerizations were observed on alkylation of lactic, malic, and tartaric acid derivatives[6]. Acylations and silylations of OH groups can also be achieved by this method. Amino alcohols with primary, secondary, and tertiary amino groups could not be etherified[7].

Received: August 11, 1975 [Z 309a IE]
German version: Angew. Chem. 87, 812 (1975)

[1] *D. Seebach, H. Dörr, D. Bastani,* and *V. Ehrig,* Angew. Chem. *81,* 1002 (1969), Angew. Chem. internat. Edit. *8,* 982 (1969); *D. Seebach* and *H. Daum,* J. Am. Chem. Soc. *93,* 2795 (1971); *D. Seebach* and *H. A. Oei,* Angew. Chem. *87,* 627 (1975); Angew. Chem. internat. Edit. *14,* 634 (1975).
[2] Methyl ether formation using these methods: *U. E. Diner, F. Sweet,* and *R. K. Brown,* Can. J. Chem. *44,* 1591 (1966), and literature cited therein; *S. Bose* and *P. L. Soni,* Sci. Cult. *40,* 368 (1974).
[3] Surveys of Tl derivatives in organic synthesis: *E. C. Taylor* and *A. McKillop,* Acc. Chem. Res. *3,* 338 (1970); Chem. Brit. *9,* 4 (1973); *O. Saiko,* Kontakte; Merck *1973,* 33.

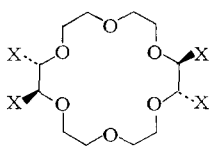
[4] In the early work published by *R. C. Menzies* (J. Chem. Soc. *1947*, 1378 and literature cited therein) there are scattered examples of etherifications with Tl alkoxides.
[5] *M. R. de Forcrand*, C. R. Acad. Sci. *176*, 20 (1923); *S. Sakai, Y. Kuroda*, and *Y. Ishii*, J. Org. Chem. *37*, 4198 (1972).
[6] The glycol cleavage by Tl^{I} as observed for benzophenone pinacols [*A. McKillop, R. H. Raphael*, and *E. C. Taylor*, J. Org. Chem. *37*, 4204 (1972)] does not occur with the tartaric acid derivatives.
[7] Heterocyclic compounds can be *N*-alkylated through their Tl derivatives: *E. C. Taylor et al.*, J. Org. Chem. *34*, 1170 (1969); *36*, 3993 (1971); J. Med. Chem. *14*, 242 (1972); J. Chem. Soc. Perkin Trans. 1 *1972*, 2292.
[8] Elemental analyses of the derivatives obtained from ethylene glycol and the tartaric acid diamide show that dithallium salts are formed.
[9] See *Beilstein:* Handbuch der Organischen Chemie.
[10] See *D'Ans-Lax:* Taschenbuch für Chemiker und Physiker.

A Polyfunctional Chiral Macrocyclic Polyether Derived from L-(+)-Tartaric Acid

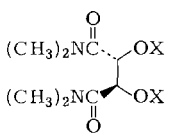
By *Jean-Marc Girodeau, Jean-Marie Lehn*, and *Jean-Pierre Sauvage*[*]

Macropolycyclic systems possess a wealth of interesting properties in various fields of chemistry[1-3]. Macrocyclic polyethers of the "crown" type *(1)* form complexes with primary ammonium salts as well as with various metal cations[3]. Chiral macropolycyclic systems have been synthesized[4, 5] and functionalized "crown" ethers containing the binaphthyl unit display efficient chiral recognition toward various ammonium salts[4].

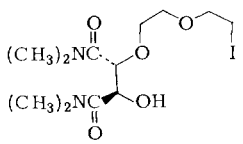
Using the "crown" entity *(1)* itself as a building block for macropolycyclic mesomolecules[2] requires the introduction of functional groups on the periphery of the macrocycle if possible with control of stereochemistry and chirality. We describe here a simple route to the chiral crown ether *N,N,N',N',N'',N'',N''',N'''*-octamethyl-1,4,7,10,13,16-hexaoxacyclooctadecane-2,3,11,12-tetracarboxamide *(2)* containing four carboxamide groups[6].



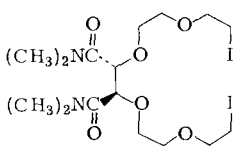
(1), X = H
(2), X = $CON(CH_3)_2$



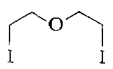
(3a), X = H
(3b), X = Tl



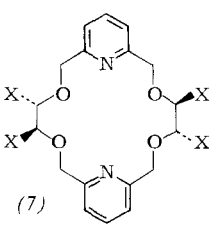
(4)



(5)



(6)



(7)

Tartaric acid with its four functional groups and very easy availability in optically active form seemed a most promising starting point if incorporation into a macrocyclic system could be achieved *via* alkylation of the hydroxyl groups. We have employed a new method[7] of preparing systems of type *(2)*, *viz.* ether formation *via* alkylation of thallium(I) alkoxides.

The starting materials are readily available reagents: the bis(*N,N*-dimethylamide) of L-(+)-tartaric acid *(3a)*[8], the diiodide *(6)*, and thallium(I) ethoxide. Several coupling schemes of starting units may be envisaged: a) $2\times(3)+2\times(6)$; b) $(3)+(5)$; c) $(4)+(4)$. Treatment of a suspension of the dithallium salt *(3b)* [from *(3a)*+TlOEt in dry DMF] with a fivefold excess of diiodide *(6)* (95 °C, under nitrogen; 3 h) gives a mixture of *(4)* and *(5)* which is easily separated by solvent distribution and filtration over alumina. The relative proportions of *(4)* and *(5)* in the product can be altered by modifying the reaction conditions.

Addition of two equivalents of TlOEt (2.9 ml) to a solution of *(3a)* (4.1 g) and *(6)* (6.55 g) in dry DMF (400 ml) heated to 90 °C with efficient stirring leads to immediate precipitation of *(3b)*, which then reacts with *(6)*. An orange precipitate of TlI forms rapidly. After 90 min the mixture is cooled, treated with 50 ml water, and evaporated under vacuum. The residue is taken up in chloroform and filtered over alumina. Crystallization from acetone/heptane gives 3 crops of *(2)* (m. p. 186 °C; 1.1 g; 20% yield). Applying a similar reaction procedure to *(4)* (1 eq.)+TlOEt (1 eq.) gives *(2)* in about 30% yield. Finally, using *(5)* (1 eq.)+*(3a)* (1 eq.)+TlOEt (2 eq.) also gives a 30% yield of *(2)*.

The analytical and spectral data (mass; ^{1}H- and ^{13}C-NMR) of *(2)* are in agreement with the proposed structure. Expectedly[3], *(2)* forms 1:1 cation complexes with KI, NaI, NH_4SCN, $C_6H_5CH_2CH_2NH_3Cl$, $CaCl_2$, $Pb(NO_3)_2$ (NMR observation). The stability constant of the K^+ complex ($K_s = 35$ in water at 25 °C) is comparable with that of related macrocycles. The optical rotation is strongly affected on complexation: $[\alpha]_D^{25} = +108°$ *(2)*, +33.5° (NaI complex), +69° (KI complex), +76° (RbI complex), +50° (NH_4I complex) ($c = 1.5$; $CHCl_3$).

Applying procedure a) to diethylene glycol ditosylate gives *(2)* in 10% yield. Similarly, with 2,6-bis(bromomethyl)pyridine the macrocycle *(7)* is obtained (15% yield; m. p. 224 °C; $[\alpha]_D^{25} = +107°$)[9]. Incorporation of other units (I-R-I; 2,5-bis(chloromethyl)furan; *etc.*) may be envisaged[10].

Received: August 20, 1975 [Z 309b IE]
German version: Angew. Chem. *87*, 813 (1975)

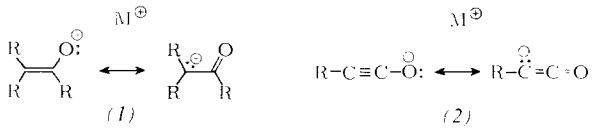
[*] J. M. Girodeau, Prof. J. M. Lehn, and Dr. J. P. Sauvage
Institut Le Bel, Université Louis Pasteur, 4 rue Blaise Pascal
67 Strasbourg (France). ERA 265 du C.N.R.S.

[1] *J. M. Lehn*, Struct. Bonding *16*, 1 (1973).
[2] *J. M. Lehn, J. Simon*, and *J. Wagner*, Angew. Chem. *85*, 621, 622 (1973); Angew. Chem. internat. Edit. *12*, 578, 579 (1973).
[3] *C. J. Pedersen* and *H. K. Frensdorff*, Angew. Chem. *84*, 16 (1972); Angew. Chem. internat. Edit. *11*, 16 (1972).
[4] *D. J. Cram* and *J. M. Cram*, Science *183*, 803 (1974).
[5] *D. Dietrich, J. M. Lehn*, and *J. Simon*, Angew. Chem. *86*, 443 (1974); Angew. Chem. internat. Edit. *13*, 406 (1974), and references cited therein.
[6] An achiral dicarboxylic acid derivative of [18]-crown-6 ether has been described recently: *J. M. Timko* and *D. J. Cram*, J. Am. Chem. Soc. *96*, 7159 (1974); see also *F. Vögtle*, Chem. Ber. *102*, 1734, 1784 (1969); *105*, 2955 (1972); *M. Newcomb* and *D. J. Cram*, J. Am. Chem. Soc. *97*, 1257 (1975).
[7] *H. O. Kalinowski, D. Seebach*, and *G. Crass*, Angew. Chem. *87*, 812 (1975); Angew. Chem. internat. Edit. *14*, 762 (1975), and references cited therein.
[8] *D. Seebach, H. Dörr, B. Bastani*, and *V. Ehrig*, Angew. Chem. *81*, 1002 (1969); Angew. Chem. internat. Edit. *8*, 982 (1969).
[9] For other macrocycles containing a pyridine unit see, *e. g. G. R. Newkome, G. L. McClure, J. B. Simpson*, and *F. Danesh-Khosboo*, J. Am. Chem. Soc. *97*, 3232 (1975), and references cited therein.
[10] The stability of the Ca^{2+} complex of *(2)* is remarkable ($K_s = 100$ in water at 26 °C) since dicyclohexyl-*(1)* complexes calcium only weakly ($K_s \approx 3$; see *R. M. Izatt, D. J. Eatough*, and *J. J. Christensen*, Struct. Bonding *16*, 161 (1973)).

Lithium Phenylethynolate and Its Reaction with Carbonyl Compounds to Give β-Lactones

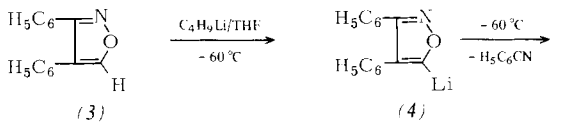
By *Ulrich Schöllkopf* and *Inga Hoppe*[*]

While enolates *(1)* have numbered among the most important reagents of organic chemistry for more than a century, ynolates *(2)* have hitherto remained unknown although their chemistry should certainly be no less interesting than that of the former class of compounds. They could react both at the oxygen and at the carbon on treatment with electrophiles.

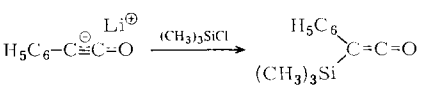


(1) *(2)*

We obtained lithium phenylethynolate *(2a)* by (one- or two-step) elimination of benzonitrile from 5-lithio-3,4-diphenylisoxazole *(4)*.



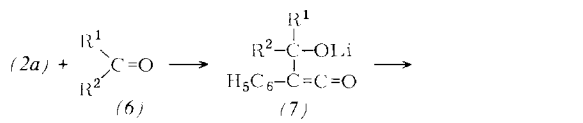
(3) *(4)*



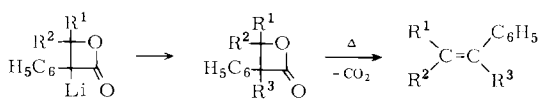
(2a) *(5)*

(2a) can be trapped in the form of phenyl(trimethylsilyl)ketene *(5)* with chlorotrimethylsilane (yield 41%, b.p. 60°C/2 torr). It is unclear whether phenyl(trimethylsilyloxy)acetylene is formed initially in a kinetically controlled reaction. The reaction provides a facile entry to metalated ketenes[1].

Reaction with aldehydes and ketones *(6)* affords (after protonation) the β-lactones *(9)* (cf. Table 1). We formulate the carbonyl adducts *(7)*, which cyclize to the metalated β-lactones



(6) *(7)*



(8) *(9)* *(10)*

Table 1. β-Lactones *(9)* and olefins *(10)* prepared.

	R^1	R^2	R^3	*(9)* yield [%]	*(10)* yield [%]
(a)	CH_3	CH_3	H	59	88
(b)	$-(CH_2)_5-$		H	51	92
(c)	$(CH_3)_3C$	H	H	65 [a]	
(d)	C_6H_5	H	C_6H_5CHOH	79 [b]	
(e)	CH_3	CH_3	$C_6H_5CH_2$	56	93
(f)	C_6H_5	H	$C_6H_5CH_2$	68	95 [c]

[a] *trans* Isomer characterized by reaction with benzylamine to give *N*-benzyl-3-hydroxy-4,4-dimethyl-2-phenylpentanamide.
[b] Mixture of diastereoisomers. Yield based on benzaldehyde.
[c] *Z* form.

[*] Prof. Dr. U. Schöllkopf and Dr. I. Hoppe
Organisch-Chemisches Institut der Universität
34 Göttingen, Tammannstrasse 2 (Germany)

(8), as intermediates of this synthesis. However, a concerted cycloaddition *(2a)* + *(6)* → *(8)* cannot be ruled out. On treatment of *(2a)* with benzaldehyde we obtained *(9d)*, the product of a second reaction between *(8)* and the aldehyde. *(8)* can be reacted *in situ* with alkylating agents to give tri- and tetrasubstituted β-lactones [cf. *(9e)* and *(9f)*]. As in other cases[2], the β-lactones *(9)* can be decarboxylated quantitatively and stereospecifically to the olefins *(10)* on heating to 140°C.

We view the reaction of alkynolates *(2)* with carbonyl compounds *(6)*, with its smooth C—C linkage and cyclization step [*(2)* + *(6)* and *(7)* → *(8)*] as providing a favorable synthesis of (highly substituted) β-lactones and their products (olefins, β-hydroxy carboxylic acids, *etc.*)[3]. Our next aim is to synthesize further alkynolates *(2)*.

3-Phenyl-β-lactones (9)

Butyllithium (15 mmol, as 1.55 N solution in hexane) and then a solution of *(6)* (15 mmol) in THF (10 ml) are added dropwise to a solution of *(3)*[4] (3.3 g, 15 mmol) in dry THF (25 ml) at −60°C under N_2. After 30 minutes' stirring at −60°C glacial acetic acid (0.9 g, 15 mmol) in THF (5 ml) is added to the reaction mixture which is then allowed to warm up to room temperature before removal of the solvent by vacuum distillation. Subsequent addition of benzene (70 ml) and standing for 2—3 h at 0°C are followed by filtration. The solvent is removed and the β-lactone *(9)* purified by chromatography on silica gel (200 g) with benzene as eluant. In the synthesis of *(9e)* and *(9f)* hexamethylphosphoric triamide (9.0 g, 50 mmol) is added at the beginning of the reaction and benzyl bromide (2.6 g, 15 mmol) is used in place of glacial acetic acid. Alkylation is complete within about 20 min.

Received: September 1, 1975 [Z 310 IE]
German version: Angew. Chem. 87, 814 (1975)

CAS Registry numbers:
(2a), 57015-19-7; *(6a)*, 67-64-1; *(6b)*, 108-94-1; *(6c)*, 630-19-3; *(6d)*, 100-52-7; *(8a)*, 57015-20-0; *(8b)*, 57015-21-1; *(8c)*, 57015-22-2; *(8d)*, 57015-23-3

[1] *S. V. Ponomarev*, Angew. Chem. 85, 673 (1973); Angew. Chem. internat. Edit. 12, 675 (1973); *Y. I. Baukov* and *I. F. Lutsenko*, Organomet. Chem. Rev. A 6, 355 (1970).
[2] *H. Kröper* in Houben-Weyl-Müller: Methoden der organischen Chemie. Thieme, Stuttgart 1963, 4th Edit., Vol. 6/2, p. 556; *W. Adam, J. Baeza*, and *Ju-Chao Liu*, J. Am. Chem. Soc. 94, 2000 (1972).
[3] Cf. *L. Paquette*: Modern Heterocyclic Chemistry. W. W. Benjamin, New York 1968, pp. 89ff.
[4] *K. Bast, M. Christl, R. Huisgen, W. Mack*, and *R. Sustmann*, Chem. Ber. 106, 3258 (1973).

Intramolecular Interaction of Cyclopropylidene with the Bicyclo[1.1.0]butane System[**]

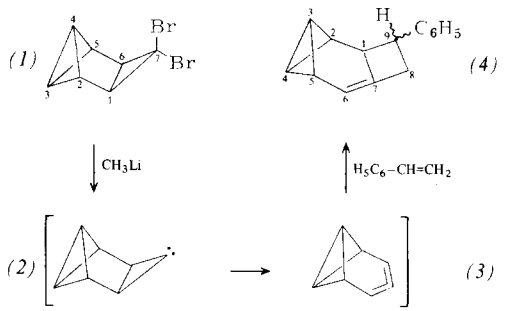
By *Manfred Christl* and *Monika Lechner*[*]

The reaction of 7,7-dibromotetracyclo[4.1.0.0^{2,4}.0^{3,5}]heptane *(1)*[1,2] and the homologous compound 8,8-dibromotetracyclo[5.1.0.0^{2,4}.0^{3,5}]octane *(6)* with methyllithium should give rise to the cyclopropylidenes *(2)* and *(7)* respectively.

Treatment of *(1)* dissolved in ether with methyllithium at −15°C affords only a viscous oil. On working in styrene, an approved reagent for 1,2-cyclohexadiene[3], it is possible to trap *(3)*. We isolated 61% of 9-phenyltetracyclo[5.2.0.0^{2,4}.0^{3,5}]non-6-ene *(4)* as a colorless oil, b.p. 80 to 90°C (bath)/0.001 torr. Apart from elemental analysis and mass spectrometry, the structure of *(4)* is established by the

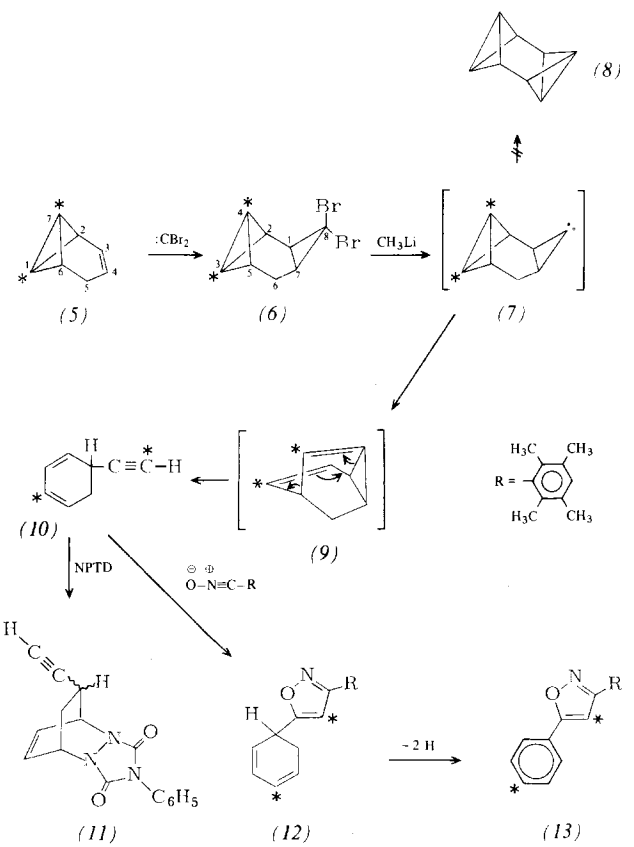
[*] Dr. M. Christl and M. Lechner
Institut für Organische Chemie der Universität
87 Würzburg, Am Hubland (Germany)

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



^{1}H-NMR spectrum, displaying a signal for only one olefinic proton (m, $\delta = 5.52$ ppm), and the ^{13}C-NMR spectrum, in particular by the characteristic high field absorption of the bicyclobutane bridgehead carbons C-3 and C-4 at $\delta = 4.2$ and 4.8 ppm.

The reaction of tricyclo[4.1.0.0^{2,7}]hept-3-ene *(5)*[2, 4] with bromoform and potassium *tert*-butoxide affords 68% of the tetracycle *(6)* as a colorless liquid, b. p. 50—60 °C (bath)/0.001 torr. Treatment of its ethereal solution with methyllithium at 0 °C should generate *(7)*. The expected insertion of the



carbene into the *syn*-C—H bond of position 6 to give *(8)* fails to take place. Instead, another C_8H_8 isomer, namely 5-ethynyl-1,3-cyclohexadiene *(10)*[5], is formed in about 40% yield as the product of a far-reaching reorganization. Its structure was verified on the basis of the adduct *(11)* formed with 4-phenyl-1,2,4-triazolinedione (NPTD), m. p. 181 to 183 °C, and the duronitrile oxide adduct *(12)* which was dehydrogenated without purification with dichlorodicyano-*p*-benzoquinone to give *(13)*, the duronitrile oxide adduct of phenylacetylene, m p. 180—181 °C.

Presumably, the carbene center in *(7)* attacks the atom C-4 to form a double bond with concomitant rupture of the bonds linking C-2 and C-3 to C-4 and introduction of a double bond between C-2 and C-3. The resulting highly strained bicyclo[2.2.2]octa-2,5-diene derivative *(9)* then suffers Diels-Alder cycloreversion to give *(10)*.

In order to test this proposal we used 1,7-dideuterated *(5)*[6] as starting material to produce *(13)* containing a D atom only in the *para* position of the phenyl ring. Apparently the acetylenic deuterium in *(10)* had been replaced by hydrogen. Moreover, we synthesized *(5)* containing practically no ^{13}C in position 1[7]. This compound gave *(13)* having the label uniformly distributed between the *para* position of the phenyl ring and the isoxazole 4-position, as shown by the halved intensity of the respective signals in the ^{13}C-NMR spectrum

On reduction of *(6)* with sodium in liquid ammonia the hydrocarbon *(14)* is formed, which was synthesized recently *via* another route[8]. At variance with the results of the gas phase pyrolysis[8] in [D_8]-toluene/tetramethylethylenediamine solution at 210 °C *(14)* is converted mainly into *trans*-tricyclo[4.2.0.0^{2,4}]oct-7-ene *(15)*, identified by its characteristic NMR spectrum[9].

Received: September 8, 1975 [Z 314 IE]
German version: Angew. Chem. 87, 815 (1975)

CAS Registry numbers:
(1), 50399-12-7; *(3)*, 57015-34-6; *(4)*, 57015-35-7; *(5)*, 35618-58-7; *(6)*, 57015-36-8; *(7)*, 57015-37-9; *(8)*, 35434-67-4; *(10)*, 57015-38-0; *(11)*, 57015-39-1; *(12)*, 57015-40-4; *(13)*, 2904-75-8

[1] *M. Christl*, Angew. Chem. *85*, 666 (1973); Angew. Chem. internat. Edit. *12*, 660 (1973).
[2] *M. Christl* and *G. Brüntrup*, Angew. Chem. *86*, 197 (1974); Angew. Chem. internat. Edit. *13*, 208 (1974).
[3] *W. R. Moore* and *W. R. Moser*, J. Org. Chem. *35*, 908 (1970).
[4] *G. W. Klumpp* and *J. J. Vrielink*, Tetrahedron Lett. *1972*, 539.
[5] Compound *(10)* is also formed from the reaction of *trans*-4,4,8,8-tetrabromotricyclo[5.1.0.0^{3,5}]octane, the 2:1 adduct of dibromocarbene to 1,4-cyclohexadiene, with methyllithium; *G. Szeimies* and *K. Mannhardt*, personal communication.
[6] *M. Christl, U. Heinemann*, and *W. Kristof*, J. Am. Chem. Soc. *97*, 2299 (1975).
[7] Prepared according to ref. [2] from ^{12}C-labeled benzvalene obtained by the method of *Katz et al.* with $^{12}CH_2Cl_2$; *T. J. Katz, E. J. Wang*, and *N. Acton*, J. Am. Chem. Soc. *93*, 3782 (1971); see also *R. D. Suenram* and *M. D. Harmony*, *ibid.* *95*, 4506 (1973).
[8] *R. T. Taylor* and *L. A. Paquette*, Angew. Chem. *87*, 488 (1975); Angew. Chem. internat. Edit. *14*, 496 (1975).
[9] *W. R. Roth* and *B. Peltzer*, Liebigs Ann. Chem. *685*, 56 (1965).

2*H*-1,3-Thiazete: A New Heterocyclic System[**]

By *Klaus Burger*, *Josef Albanbauer*, and *Manfred Eggersdorfer*[*]

While the stabilizing effect of *tert*-butyl groups (steric stabilization) on small ring systems has been known for a long time, little use has been made of the stabilizing effect of trifluoromethyl groups (electronic stabilization)[1] in the synthesis of strained ring systems. We have exploited this generally valid stabilization principle for the first recorded synthesis of 2*H*-1,3-thiazete *(2)*.

Thiocarboxamides take up two equivalents of hexafluoroacetone at −20 to 0 °C Subsequent elimination of water with $POCl_3$/pyridine proceeds *via* cyclization to give 2,2,6,6-tetra-

[*] Priv.-Doz. Dr. K. Burger, Dipl.-Chem. J. Albanbauer, and M. Eggersdorfer
Organisch-Chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

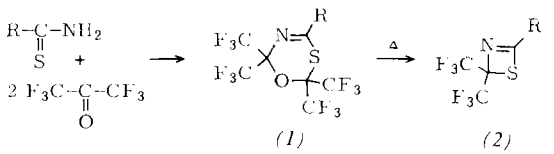
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Table 1. Data for compounds *(1)* and *(2)*. The molecular ion is observed in the 70 eV mass spectrum of all compounds.

	R	*(1)* yield [%]	*(1)* b. p. [°C/torr] m. p. [°C]	*(2)* yield [%]	*(2)* b. p. [°C/torr] m. p. [°C]	IR [cm^{-1}]	^{19}F-NMR [c]
(a)	C_6H_5	58	52/0.1 39	76	88/12	1602, 1560 [a]	−4.9
(b)	p-$CH_3C_6H_4$	54	40	78	112/12	1605, 1585, 1560 [a]	−4.8
(c)	p-$CH_3OC_6H_4$	52	53—54	65	118	1600, 1580, 1560 [b]	−5.0
(d)	p-ClC_6H_4	57	68	72	74—76	1602, 1582, 1560 [b]	−5.1

[a] Film; [b] in KBr; [c] δ values [ppm] relative to CF_3COOH as external standard, in $CHCl_3$, singlets.

kis(trifluoromethyl)-6*H*-1,3,5-oxathiazines *(1)*[2], which afford 2*H*-1,3-thiazetes *(2)* on thermolysis (140 °C/12 torr) (Table 1).



(1) *(2)*

This ring contraction is the result of a retro-Diels-Alder reaction[3] followed by an electrocyclic ring closure[4].

The constitution of compounds *(1)* and *(2)* is verified by the spectroscopic data, the fragmentation pattern in the mass spectrum, and by elemental analysis[5].

General procedure:

Two equivalents of hexafluoroacetone is passed onto a vigorously stirred solution of a thiocarboxamide (20 g) in anhydrous ether (250 ml) at −20 to 0 °C. The reaction mixture is then treated simultaneously with an equimolar amount of $POCl_3$ and a fourfold amount of pyridine and left to stand for 48 to 72 h at −30 °C. After removal of precipitated salt, the ethereal phase is washed with ice-water, dried over Na_2SO_4, and concentrated. The residue is digested several times with hexane and recrystallized from methanol after removal of hexane.—Product *(1)* obtained in this way is decomposed at 120—140 °C/12 torr in the course of 20 to 80 h. The crude product *(2)* is purified by column chromatography [silica gel; elution of any residual *(1)* with CCl_4, and of *(2)* with $CHCl_3$] and then fractionally distilled or recrystallized from hexane.

Received: September 15, 1975 [Z 315a IE]
German version: Angew. Chem. 87, 816 (1975)

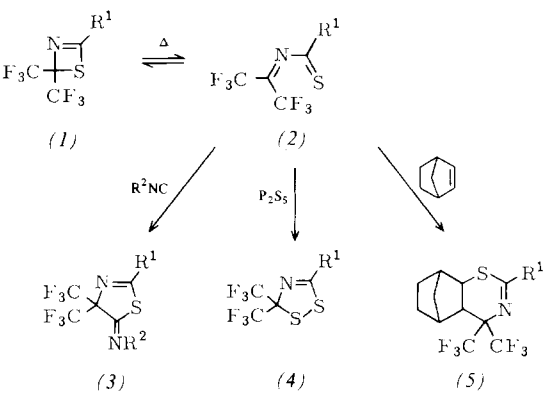
CAS Registry numbers:
(1a), 57014-91-2; *(1b)*, 57014-92-3; *(1c)*, 57014-93-4; *(1d)*, 57014-94-5; *(2a)*, 57014-95-6; *(2b)*, 57014-96-7; *(2c)*, 57014-97-8; *(2d)*, 57014-98-9; hexafluoroacetone, 684-16-2; $C_6H_5C(=S)$-NH_2, 227-79-4; p-$CH_3C_6H_4C(=S)$-NH_2, 2362-62-1; p-$CH_3OC_6H_4C(=S)$-NH_2, 2362-64-3; p-$ClC_6H_4C(=S)$—NH_2, 2521-24-6

[1] *D. M. Lemal* and *L. H. Dunlap jr.*, J. Am. Chem. Soc. *94*, 6562 (1972); *W. Adam, J.-C. Liu*, and *O. Rodriguez*, J. Org. Chem. *38*, 2269 (1973).
[2] 1,3,5-Oxathiazin-6-ones, see: *A. Schulze* and *J. Goerdeler*, Tetrahedron Lett. *1974*, 221.
[3] *H. Wollweber*: Diels-Alder-Reaktion. Thieme, Stuttgart 1972, pp. 152ff.
[4] *G. Maier*: Valenzisomerisierungen. Verlag Chemie, Weinheim 1972, pp. 89ff.
[5] *J. Albanbauer*, Dissertation, Technische Universität München, scheduled for 1975.

Detection of Valence Tautomerism between 2*H*-1,3-Thiazete and *N*-Alkylidenethiocarboxamide[**]

By *Klaus Burger*, *Josef Albanbauer*, and *Walter Foag*[*]

The 2*H*-1,3-thiazetes *(1)*[2] shown by their spectra[1] to exist exclusively in cyclic form at room temperature are in valence-tautomeric equilibrium with the open chain *N*-(perfluoroisopropylidene)thiocarboxamides *(2)* at elevated temperature. The presence of *(2)*, and thus the occurrence of thermally induced ring opening[3], is proved by trapping reactions.



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

Table 1. Data for compounds *(3)* to *(5)*. The molecular ion is observed in the 70 eV mass spectrum of all compounds.

Cpd.	R^1 R^2	Yield [%]	M. p. [°C] b. p. [°C/torr]	^{19}F-NMR [a] δ [ppm], J [Hz]
(3a)	C_6H_5 t-C_4H_9	73	81	−6.8 (s)
(3b)	C_6H_5 c-C_6H_{11}	75	56	−6.7 (s)
(3c)	p-$CH_3C_6H_4$ t-C_4H_9	79	75	−6.7 (s)
(3d)	p-$CH_3C_6H_4$ c-C_6H_{11}	78	58	−6.7 (s)
(4a)	C_6H_5	78	67—68/0.1	−4.7 (s)
(4b)	p-$CH_3C_6H_4$	81	96—98/0.2	−4.9 (s)
(5a)	C_6H_5	86	61—63	−6.9 (q, 11.0) [b] −9.7 (q, 11.0)
(5b)	p-ClC_6H_4	81	86—88	−6.9 (q, 11.0) [b] −9.7 (q, 11.0)

[a] Relative to CF_3COOH as external standard, in $CHCl_3$.
[b] Shows additional fine structure.

[*] Priv.-Doz. Dr. K. Burger, Dipl.-Chem. J. Albanbauer, and W. Foag
Organisch-Chemisches Institut der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

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

Smooth conversion of *(1)* into the 5-imino-1,3-thiazol-2-ines *(3a)* to *(3d)* is accomplished in boiling xylene in the presence of isocyanides[4]. Reaction of *(1)* with phosphorus pentasulfide without solvent at 140 °C gives good yields of 3*H*-1,2,4-dithiazoles *(4a)* and *(4b)* which are also accessible from the *N*-(perfluoroisopropylidene)carboxamides[5] and phosphorus pentasulfide[6]; finally the trapping reaction with norbornene affords the annelated 5,6-dihydro-4*H*-1,3-thiazines *(5a)* and *(5b)*.

If *(1)* is heated to 140 °C without a trapping reagent it turns yellowish brown but immediately regains its original pale yellow color on cooling.—The reactions mentioned can readily be described in terms of a thermally mobile equilibrium $(1) \rightleftharpoons (2)$.

5-Imino-4,4-bis(trifluoromethyl)-1,3-thiazol-2-ines (3)

Equimolar amounts of *(1)*[2] and isocyanide are refluxed for 12 to 36 h in anhydrous xylene. The residue left on distillation of the solvent crystallizes on rubbing; it is recrystallized from hexane.—The procedure can be applied directly for the preparation of compounds *(5)*.

3,3-Bis(trifluoromethyl)-3H-1,2,4-dithiazoles (4)

Equimolar amounts of *(1)* and phosphorus pentasulfide are stirred for 24 h at 140 °C. Workup is by column chromatography on silica gel (elution with CCl_4) and subsequent fractional distillation.

Received: September 15, 1975 [Z 315b IE]
German version: Angew. Chem. 87, 816 (1975)

CAS Registry numbers:
(1), $R^1 = C_6H_5$, 57014-95-6; *(1)* $R^1 = p\text{-}CH_3C_6H_4$, 57014-96-7; *(1)*, $R^1 = p\text{-}ClC_6H_4$, 57014-98-9; *(2)*, $R^1 = C_6H_5$, 57015-05-1; *(2)*, $R^1 = p\text{-}CH_3C_6H_4$, 57015-06-2; *(2)*, $R^1 = p\text{-}ClC_6H_4$, 57015-07-3; $t\text{-}C_4H_9NC$, 7188-38-7; $c\text{-}C_6H_{11}NC$, 931-53-3; *(3a)*, 57014-99-0; *(3b)*, 57015-00-6; *(3c)*, 57015-01-7; *(3d)*, 57015-02-8; *(4a)*, 55015-72-0; *(4b)*, 55015-74-2; *(5a)*, 57015-03-9; *(5b)*, 57015-04-0

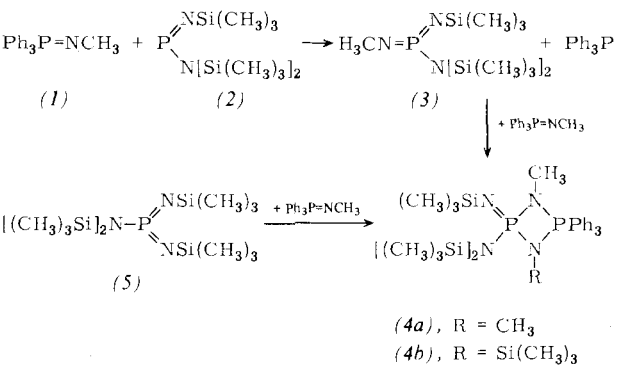
[1] The ^{19}F-NMR spectra of *(1)* and *(4)* contain the signals of the two magnetically equivalent CF_3 groups at $\delta = -4.7$ to -5.1 ppm, whereas for *(2)* a chemical shift resembling that of *N*-(perfluoroisopropylidene)carboxamides ($\delta = -9$ to -10 ppm) should be expected.
[2] *K. Burger, J. Albanbauer*, and *M. Eggersdorfer*, Angew. Chem. *87*, 816 (1975); Angew. Chem. internat. Edit. *14*, 766 (1975).
[3] Electrocyclic reactions, see *G. Maier*: Valenzisomerisierungen. Verlag Chemie. Weinheim 1972, pp. 89ff., and references cited therein.
[4] *N. P. Gambaryan, E. M. Rokhlin, Yu. V. Zeifman, L. A. Simonyan*, and *I. L. Knunyants*, Dokl. Akad. Nauk SSSR *166*, 864 (1966); Chem. Abstr. *64*, 15861 (1966).
[5] *W. Steglich, K. Burger, M. Dürr*, and *E. Burgis*, Chem. Ber. *107*, 1488 (1974).
[6] *K. Burger, J. Albanbauer*, and *W. Strych*, Synthesis *1975*, 57.

Diazadiphosphetidines by Reaction of Aminoiminophosphanes with Iminophosphoranes[1]

By *Rolf Appel* and *Mechthild Halstenberg*[*]

The use of iminophosphoranes as donors of imino groups has previously only been known for those reactions, which—as *e.g.* the reactions with carbonyl compounds[2] or epoxides[3]—lead to the corresponding oxophosphoranes *via* O/NR exchange. We have now found that direct transference of the methylimino group and liberation of the tertiary phosphane takes place when triphenyl(methylimino)phosphorane *(1)* is allowed to react with bis(trimethylsilyl)aminotrimethylsilyliminophosphorane *(2)*[4, 5]. Thus, we have possible means of access to the novel aminobis(imino)phosphoranes[5, 6] without having to resort to reactions involving azides.

Bis(trimethylsilyl)aminomethyliminotrimethylsilyliminophosphorane *(3)* occurs only as intermediate product in the reaction of *(2)* with *(1)*, as can be observed by the appearance and disappearance of the ^{31}P-NMR signal at -46.7 ppm during the course of the reaction. On addition of a second molecule of *(1)* to the ylidic $P{=}NCH_3$ bond a compound is finally obtained which melts at 171 °C, is readily soluble in most organic solvents, and to which we assign the structure of a 1,3-dimethyl-2-bis(trimethylsilyl)amino-2-trimethylsilylimino-4,4,4-triphenyl-1,3,2λ^5,4λ^5-diazadiphosphetidine *(4a)* on the basis of elemental analysis, molecular weight determination, and NMR spectra[7].



Evidence for this reaction is also afforded by the fact that compound *(5)*, obtainable from *(2)* and trimethylsilyl azide, reacts smoothly with *(1)* to give *(4b)*[7].

Experimental:

A neat mixture of *(1)* (1.46 g, 5 mmol) and *(2)* (0.70 g, 2.5 mmol) is heated for 2 h at 140 °C. The triphenylphosphane that is formed is removed by sublimation (*ca.* 5 h at 100 °C/0.4 torr; 0.53 g, 81 %). The residue is recrystallized twice from acetonitrile (2 × 5 ml); 0.81 g (54 %) of analytically pure *(4a)* is obtained. In the analogous reaction in dichloromethane a transitory sharp signal is observed at -46.7 ppm in the ^{31}P-NMR spectrum.

A solution of *(1)* (0.58 g, 2 mmol) and *(5)* (0.73 g, 2 mmol) in dichloromethane (2 ml) is stirred for 24 h at room temperature. On addition of acetonitrile a precipitate is formed, which after filtration and multiple recrystallization from dichloromethane/acetonitrile affords pure *(4b)* [0.17 g, 15 % yield, m.p. 116 °C].

Received: August 11, 1975 [Z 306a IE]
German version: Angew. Chem. 87, 810 (1975)

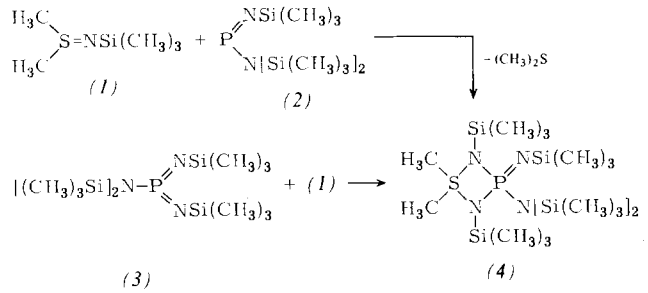
[*] Prof. Dr. R. Appel and Dipl.-Chem. M. Halstenberg
Anorganisch-chemisches Institut der Universität
53 Bonn, Max-Planck-Strasse 1 (Germany)

[1] Part 66 of Non-metallic Imine Compounds.—Part 65: *R. Appel* and *M. Halstenberg*, Chem. Ber., in press.
[2] *H. Staudinger* and *E. Hauser*, Helv. Chim. Acta *4*, 861 (1921); *R. Appel* and *A. Hauss*, Chem. Ber. *93*, 405 (1960).
[3] *R. Appel* and *M. Halstenberg*, Chem. Ber., in press.
[4] *E. Niecke* and *W. Flick*, Angew. Chem. *85*, 586 (1973); Angew. Chem. internat. Edit. *12*, 585 (1973).
[5] *O. J. Scherer* and *N. Kuhn*, Chem. Ber. *107*, 2123 (1974).
[6] *E. Niecke* and *W. Flick*, Angew. Chem. *86*, 128 (1974); Angew. Chem. internat. Edit. *13*, 134 (1974).
[7] *(4a)*: ^{31}P-NMR (in $CHCl_2$): AB type: $\delta = -6.0$ (d), -4.9 (d) ppm; $^2J_{PP} = 32$ Hz. ^1H-NMR (in $CDCl_3$): $\delta = -0.05$ (s) silylamino-H, $+0.08$ (s) silylamino-H, -2.20 (d) CH_3, -7.18 to -7.97 (m) ppm C_6H_5; $^3J_{PNCH} = 13.5$ Hz.
(4b): ^{31}P-NMR (in $CHCl_2$): AB type: $\delta = -0.6$ (d), $+3.3$ (d) ppm; $^2J_{PP} = 34$ Hz. ^1H-NMR (in $CDCl_2$): $\delta = 0.6$ to -0.25 (m) silyl-H, -2.44 (d) CH_3, -7.35 to -8.18 (m) ppm C_6H_5; $^3J_{PNCH} = 15$ Hz.

$1\lambda^4,2,4,3\lambda^5$-Thiadiazaphosphetidine, A Sulfur-Nitrogen-Phosphorus Four-Membered Ring Compound[1]

By *Rolf Appel* and *Mechthild Halstenberg*[*]

When *N*-silylated imino-λ^4-sulfones, such as *e.g.* *(1)* are heated in the presence of phosphanes reaction takes place with transference of NR to give iminophosphoranes and thioethers[2]. We have now found that the aminoiminophosphane *(2)*[3] behaves similarly towards *(1)*[4]; but the reaction is distinctly exothermic on account of the higher reactivity of *(2)* compared to that of the tertiary phosphanes. Dimethylsulfane is formed along with, not the phosphorane *(3)*, but a colorless product melting at 143 °C, which, from elemental analysis data, molecular weight determination, and mass and NMR spectra[5] was identified as 1,1-dimethyl-2,4-bis(trimethylsilyl)-3-bis(trimethylsilyl)amino-3-trimethylsilylimino-$1\lambda^4,2,4,3\lambda^5$-thiadiazaphosphetidine *(4)*.



Previously, the aminobis(imino)phosphorane *(3)* assumed to be formed as intermediate in this reaction could not be detected directly; it can be shown however that *(1)* and compound *(3)*, which was prepared *via* an alternative route from *(2)* and trimethylsilyl azide[6], undergo smooth cycloaddition to give *(4)*. A similar cycloaddition occurs between aminoiminothiophosphoranes and sulfur diimides[7].

Experimental:

(1)[4] (0.6 g, 4 mmol) and *(2)* (0.56 g, 2 mmol) are mixed with stirring. The mixture becomes warm and after a few minutes the greater part is solid. The dimethylsulfane that is formed is removed by evaporation under oil-pump vacuum and collected in a cold trap (0.11 g = 85 %). The residue is dissolved in *n*-pentane (7 ml). On cooling to −78 °C colorless crystals of *(4)* separate out. Further recrystallization from pentane affords 0.65 g (63 % yield) of pure *(4)*.

A mixture of *(3)* (0.73 g, 2 mmol) and *(1)* (0.3 g, 2 mmol) in dichloromethane (2 ml) is stirred for 3 h. On addition of a little acetonitrile colorless crystals of *(4)* are formed which can be purified by recrystallization from CH_2Cl_2/CH_3CN; yield 0.69 g (67 %).

Received: August 11, 1975 [Z 306b IE]
German version: Angew. Chem. 87, 810 (1975)

[*] Prof. Dr. R. Appel and Dipl.-Chem. M. Halstenberg
Anorganisch-chemisches Institut der Universität
53 Bonn, Max-Planck-Strasse 1 (Germany)

[1] Part 67 of Non-metallic Imine Compounds.—Part 66: *R. Appel* and *M. Halstenberg*, Angew. Chem. *87*, 810 (1975); Angew. Chem. internat. Edit. *14*, 768 (1975).
[2] *I. Ruppert*, *V. Bastian*, and *R. Appel*, Chem. Ber. *108*, 2329 (1975).
[3] *E. Niecke* and *W. Flick*, Angew. Chem. *85*, 586 (1973); Angew. Chem. internat. Edit. *12*, 585 (1973); *O. J. Scherer* and *N. Kuhn*, Chem. Ber. *107*, 2123 (1974).
[4] Prepared as follows:

R. Appel and *P. Weinreis*, unpublished.
[5] *(4)*: ^{31}P-NMR (in CH_2Cl_2): $\delta = -6.75$ ppm. ^{1}H-NMR ($CDCl_2$): $\delta = -0.28$ silyl-H, -2.56 ppm CH_3. MS: $m/e = 514$ (M^+, 3 %).
[6] *E. Niecke* and *W. Flick*, Angew. Chem. *86*, 128 (1974); Angew. Chem. internat. Edit. *13*, 134 (1974).
[7] *N. T. Kulbach* and *O. J. Scherer*, Tetrahedron Lett. *1975*, 2297.

ABSTRACTS

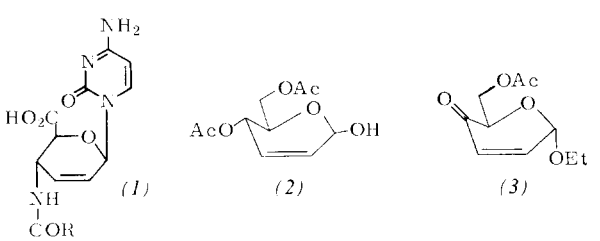
Reviews

Abstracts of selected progress reports and review articles

The rate-determining step of enzyme-catalyzed reactions has been considered by *W. W. Cleland*. The rate is usually limited by conformational changes of the enzyme protein and liberation of the product; the chemical reaction *per se* seldom plays a rate-determining role. [What Limits the Rate of an Enzyme-Catalyzed Reaction? Acc. Chem. Res. *8*, 145—151 (1975); 43 references]

[Rd 800 IE—L]

2,3-Unsaturated sugars and their derivatives are considered by *B. Fraser-Reid*. Some representatives occur in Nature; *e.g.* blasticidin S *(1)* in a *Streptomyces* species. From among the numerous compounds synthesized, mention is made of *(2)* and *(3)*. These 2,3-unsaturated sugars are suitable not

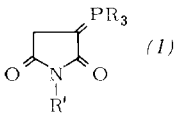


(1) *(2)* *(3)*

only as precursors of branched-chain sugars but also for a whole variety of "organic" reactions and investigations. [Some Progeny of 2,3-Unsaturated Sugars—They Little Resemble Grandfather Glucose. Acc. Chem. Res. *8*, 192—201 (1975); 72 references]

[Rd 805 IE—L]

The preparative aspects of Ag^+-catalyzed rearrangements of polycyclic systems are reviewed by *L. A. Paquette*. An example of a bicyclo[1.1.0]butane rearrangement is the quantitative and rapid transformation of *(1)* into 1,3-cycloheptadiene in the presence of Ag^+. The less strained bicyclo[2.1.0]pentane



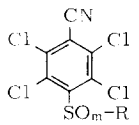
(1)

R = an alkyl (C_1—C_{18}) or phenyl group; R' = H or an alkyl (C_1—C_4) or phenyl group

cularly suitable for the preparation of precatalyzed epoxide resins requiring increased times of reaction. [DOS 2403407; The Dow Chemical Co., Midland, Mich. (USA)]

[PR 293—D IE]

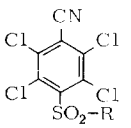
Tetrachloro-4-cyanophenyl sulfoxides and sulfones of formula *(1)* are new compounds active against bacteria and fungi. They are obtained by treatment of pentachlorobenzonitrile with thiols and subsequent oxidation. Especially cited is the



(1)

m = 1,2

R = Alkyl, Aryl, Aralkyl



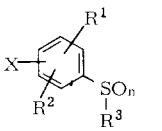
(2)

R = CH_3, C_2H_5, CH_2–CH_2Cl, C_4H_9

efficiency of the compounds against, *e.g.* Phytophthora, Alternaria, Helminthosporium, and Uromyces as well as against Staphylococci, Streptococci, and Salmonella. [DOS 2458657; Diamond Shamrock Corp., Cleveland, Ohio (USA)]

[PR 294—S IE]

A new group of herbicides, excellent in preventing growth from seeds of grass-like plants (*e.g.* types of millet, wild oats, *etc.*), are provided by sulfides, sulfoxides, and sulfones of type *(1)*. The compounds *(2)* are selected as especially effective.



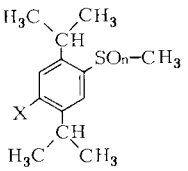
(1)

R^1, R^2 = Alkyl (C_2–C_7)

R^3 = Alkyl (C_1–C_3)

n = 0, 1, 2

X = F, Cl, Br, I, CN



(2)

X = Br, Cl, CN

n = 0, 2

[DOS 2442684; E. I. du Pont de Nemours and Co., Wilmington, Del. (USA)]

[PR 295—S IE]

BOOK REVIEWS

Practical Inorganic Chemistry (Preparations, Reactions and Instrumental Methods). By *G. Pass* and *H. Sutcliffe*. Chapman and Hall, London 1974. 2nd Edit., XVI, 239 pp., 36 figs., bound, £ 2.50.

This book, now published in its second edition, is intended to fill a gap between mainly theoretically and mainly preparatively slanted monographs in the field of inorganic chemistry. It can be said straight away that this aim has been substantially achieved. The student will find here, compressed into a relatively small space, information about work in an inorganic laboratory that elsewhere he could obtain only by reading several books.

In each of the chapters presenting examples of *e.g.* oxygen acids, double salts, clathrates, and inorganic polymers theoretical explanations are attached. The principles of some experimental methods (high-temperature reactions, electrochemical oxidation and reduction, homogeneous catalysis, work in nonaqueous solvents and under an inert gas) are also given. The chapters on classical analytical methods (conductivity measurements and potentiometric titration) would have been better treated together, and the same is true of the treatment of physical measurements (spectroscopy, polarimetry, and magnetic measurements) important for structure determinations. A short outline of ESR, NMR, and CD spectroscopy (in the chapter on polarimetry) would perhaps have been useful.

The book can be recommended for chemistry students in their first term, particularly in view of its low price.

Achim Müller [NB 275 IE]

Electroanalytical Chemistry. Vol. 10. Advances in Analytical Chemistry and Instrumentation. Edited by *H. W. Nürnberg*. John Wiley & Sons Ltd., New York—London 1974. 1st Edit. XI, 609 pp., numerous figs. and tables, bound, £ 18.50.

In seven sections this book contains reviews of selected areas of electrochemical analysis prepared by competent specialist authors. Specifically, the following themes are covered: Advances in Instrumentation for DC Polarography and Coulometry *(D. J. Fisher)*; Applications of Polarography and Coulometry in Actinide Analysis *(G. W. C. Milner* and *G. Phillips)*; Voltammetry in Organic Analysis *(P. J. Elving)*; Polarographic Analysis in Pharmacy *(H. Hoffmann* and *J. Volke)*; Analytical Aspects of Voltammetry in Non-Aqueous Solvents and Melts *(J. Badoz-Lambling* and *G. Cauquis)*; Joint Application of Electrochemical and ESR Techniques *(B. Kastening)*; pH-Measurements and their Applications *(K. Schwabe)*.

In several of the presentations a larger number of practical examples and tables would have been welcome, such as are provided by *Badoz-Lambling* and *Cauquis* in their clear and extensive first-ever collection for work in many different solvents and melts with various electrodes.

These review articles, all written clearly and provided with a rich set of references, constitute a valuable addition to the literature, for which thanks are due to the editor.

Rolf Neeb [NB 276 IE]

Schutz gegen atmosphärische Korrosion (Atmospheric Corrosion Protection). By *Karel Barton*. Verlag Chemie, GmbH, Weinheim 1973, 1st Edit., X, 209 pp., 62 figs., 19 tables, cloth, DM 75.—.

This monograph is the first of its kind concerned with the field so important for the whole environment and in particular for industry. The author sets out to build a bridge between theory and practice and in this he has been very successful. As the director, for many years, of a national institute for materials he is protection versed in these problems and he has worked the essential practical experience and the latest research results into a modern presentation in which he has not failed to include, for example, the problems of accelerated tests, a discussion of corrosion mechanisms from the latest points of view, and the most important aspects

of corrosion-resistant construction. The inclusion of the East European literature, particularly Russian—elsewhere so difficult to find—is noteworthy. The book contains the following as main chapters:

1. Introduction; 2. The Atmosphere as a Corrosive Environment; 3. Mechanisms and Kinetics of Atmospheric Corrosion; 4. Uneven and Structural Phenomena of Corrosion; 5. Fundamentals of Protection against Atmospheric Corrosion; 6. Fundamentals of Methods for Studying the Effects of Atmospheric Corrosion; 7. Synopsis of Industrial and Economic Considerations concerning Protection against Atmospheric Corrosion.

The monograph can be fully recommended to all engaged in practice, techniques of application, or research.

Ewald Heitz [NB 278 IE]

Bonded Stationary Phases in Chromatography. By *E. Grushka.* Ann Arbor Science Publ., Inc., Ann Arbor, Mich./USA 1974. 1st Edit., IX, 237 pp., numerous figs., bound, £ 9.20.

Eli Grushka, Professor of Chemistry at the State University of New York, Buffalo, has collaborated with other authors from Universities and Industry in a book that reviews a rather narrowly limited but very topical sector of chromatography.

The authors are undoubtedly highly proficient in their field, and out of their own experience have provided useful facts on the use, choice, and comparative value of bonded stationary phases. The ten chapters are devoted to the following topics: Chemically Bonded Packings *(M. Lynn* and *A. M. Filbert)*; Modification of Silicagels *(W. A. Aue* and *S. Kapila)*; Chemically Bonded Stationary Phases for Reserved-Phase Partition Chromatography *(R. C. Williams)*; Permanently Bonded Stationary Phases in Gas and Liquid Chromatography *(J. N. Little, D. F. Horgan Jr., R. L. Cotter,* and *R. V. Vivilecchia)*; Pellicular Ion Exchangers *(C. Horvath)*; Support Materials for Immobilized Enzymes and Affinity Chromatography *(G. P. Royer* and *W. E. Meyers)*; Polyamide Chromatography *(F. M. Rabel)*; Bonded Phases on Small Porous Particles *(R. E. Majors)*; Use of Novel Silanes for the Solid-Phase Peptide Synthesis and the Preparation of Polar Chemically Bonded Phases for Liquid Chromatography *(W. Parr* and *N. Novotny)*; Chromatography on Silylated Surfaces *(M. Novotny)*.

The chapters differ in size, presentation, and value to the user. The reviewer would like to commend the two bonded phases by *Majors* and *Novotny* because of their general presentation and provision of information, as also *Horvath*'s comprehensive and systematic article on pellicular ion-exchangers. The chapters on polyamide chromatography and affinity chromatography are somewhat outside the theme laid down, but offer interesting stimulation.

Although all the chapters are assigned to the special theme of 'Bonded Stationary Phases in Chromatography' the authors' individuality has made it difficult to maintain clear systematics; for example, in the discussion of carrier materials the user expects a clear differentiation between porous layer beads and porous supports and between chemically bonded and physically treated surfaces without being muddled by use of the various commercial names.

Unfortunately, the index also does not make for clarity. The reviewer would have liked a book that did more than offer a series of papers with similar themes and was not restricted to American authors and literature. Close study of the individual chapters will provide the chemist and the biochemist with a valuable stimulus toward modern chromatographic methods of separation.

Friedhelm Eisenbeiss [NB 280 IE]

Biochemie der Pflanzen (Biochemistry of Plants). By *H. Kindl* and *G. Wöber.* Springer-Verlag, Berlin—Heidelberg—New York 1975. 1st Edit., IX, 364 pp., 271 figs., bound, DM 78.—.

"General biochemistry" covers the profound differences between the different kingdoms of organisms with generalizations that are not always reliable and often misleading. Bound by their roots to the soil and robbed by their organization of any possibility of freedom from the shackles by which their metabolism ties them to the surrounding world, plants have developed a number of biochemical peculiarities which in a general consideration may retreat into the background as exceptions although they are every bit as impressive in extent as in biochemical ingenuity.

A biochemistry of plants is thus a book that one picks up with special curiosity. In view of the prescribed space and the objective of complementing plant physiology with plant biochemistry for students of biology, one must naturally accept limitations, but the selection of the material shows skill of presentation and treatment. The resulting balance is that, in spite of its long history, biochemistry of plants cannot describe and interpret much out of its own knowledge and independently of the much more thoroughly studied biochemistry of bacteria and animals. Thus it is that the first 100 or so pages of this book have no specific application to plants but describe the elementary processes and central dogmas so to speak second-hand. Starting from generally recognized principles, it is indeed unlikely that plants should follow different rules; yet one may be glad to learn that this is indeed so, and to have it demonstrated by examples from their biochemistry. In later sections several plant specialities come into view, *e. g.* the glyoxylate cycle, α-oxidation of fatty acids, mobilization of fats and proteins in germinating seeds, formation of special sugars and cyclitols, of acetogenins and isoprenoids, of phenylpropane derivatives, flavones, and alkaloids, and especially of course of chlorophyll; finally, there is photosynthesis, photophosphorylation, and CO_2 fixation. All this is bedded in a very useful and clear presentation of—even so!—a "general biochemistry", which makes this work a good textbook for the above subject, with but a slight botanical accent (an amiable one, of course). Didactic help is provided by important summarizing prologs to chapters and by the graphic emphasis of important stages and relations. Additional chapters on stereochemical problems in biochemistry and on inhibitors complete the book, which can certainly be recommended to science students and to chemists who chose biochemistry as their main subject. No striking errors came to light.

Lothar Jaenicke [NB 283 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Analytical Chemistry of Platinum Metals. By *S. I. Ginzburg, N. A. Ezerskaya, I. V. Prokof'eva, N. V. Fedorenko, V. I. Shlenskaya,* and *N. K. Bel'skii.* From the series "Analytical Chemistry of the Elements". Edited by *A. P. Vinogradov.* John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1975. XII, 673 pp., bound, £ 24.50.

Topics in Current Chemistry—Fortschritte der chemischen Forschung. Edited by *F. L. Boschke*. Vol. 57: Cyclic Compounds. By *T. Eicher, J. L. Weber, M. V. Sargent*, and *T. M. Cresp*. Springer-Verlag, Berlin 1975. IV, 143 pp., bound, DM 59.—

Mössbauer Spectroscopy. Edited by *U. Gonser*. Vol. 5 of the series "Topics in Applied Physics". Founded by *K. V. Lotsch*. Springer-Verlag, Berlin 1975. XII, 241 pp., bound, DM 70.—.

Organoborane Chemistry. By *Th. Onak*. From the series "Organometallic Chemistry". Edited by *P. M. Maitlis, F. G. A. Stone*, and *R. West*. Academic Press, New York 1975. X, 360 pp., bound, $ 38.00.

Catalysis in Micellar and Macromolecular Systems. By *J. H. Fendler* and *E. J. Fendler*. Academic Press, New York 1975. XII, 545 pp., bound, $ 44.00.

Structure and Bonding, Vol. 21: Recent Impact of Physics on Inorganic Chemistry. Edited by *J. D. Dunitz et al.* Springer-Verlag, Berlin 1975. IV, 144 pp., bound, DM 58.—.

Structure and Bonding, Vol. 23: Biochemistry. Edited by *J.-D. Dunitz et al.* Springer-Verlag, Berlin 1975. IV, 193 pp., bound, DM 74.—.

A Handbook of Organic Analysis. Qualitative and Quantitative. By *H. T. Clarke*, revised by *B. Haynes*. Edward Arnold, London 1975. 5th Edit., X, 291 pp., bound, $ 12.00.

The Alkaloids. Chemistry and Physiology. Vol. 15. Edited by *R. H. F. Manske*. Academic Press, New York 1975. XV, 315 pp., bound, $ 39.50.

Advances in Free-Radical Chemistry, Vol. 5. Edited by *G. H. Williams*. Elek Science, London 1975. VII, 394 pp., bound, £ 15.00.

Nuclear Magnetic Resonance, Vol. 4. Senior Reporter: *R. K. Harris*. The Chemical Society, London 1975. XIX, 340 pp., bound, £ 15.50.—A volume of the series "Specialist Periodical Reports".

Analytical Chemistry of Radium. By *V. M. Vdovenko* and *Yu. V. Dubasov*. From the series "Analytical Chemistry of the Elements". Edited by *A. P. Vinogradov*. John Wiley & Sons, New York/Israel Program for Scientific Translations, Jerusalem 1975. VIII, 198 pp., bound, £ 12.25.

Mathematik für Naturwissenschaftler. By *H.-D. Försterling*. Band 6 of the series "Studienbücher Naturwissenschaft und Technik". Vieweg, Braunschweig 1975. 289 pp., stitched, DM 38.—.

Tantalum Thin Films. By *W. D. Westwood, N. Waterhouse*, and *P. S. Wilcox*. Academic Press, London 1975. XIII, 436 pp., bound, £ 15.00.

Aromatic and Heteroaromatic Chemistry, Vol. 3. Senior Reporters: *C. W. Bird* and *G. W. H. Cheeseman*. The Chemical Society, London 1975. XV, 503 pp., bound, £ 20.00.—A volume of the series "Specialist Periodical Reports".

Edible Starches and Starch-Derived Syrups. By *N. B. Petersen*. Food Technology Review No. 24. Noyes Data Corporation, Park Ridge 1975. XII, 427 pp., bound, $ 36.00.

Models for Flow Systems and Chemical Reactors. By *C. Y. Wen* and *L. T. Fan*. Vol. 3 of the series "Chemical Processing and Engineering". Edited by *L. F. Albright, R. N. Maddox*, and *J. J. McKetta*. Marcel Dekker, New York 1975. IX, 570 pp., bound, $ 29.75.

Analyse der Metalle. Band 3: Probenahme. Issued by the Chemistry Committee of the GDMB-Gesellschaft Deutscher Metallhütten- und Bergleute e. V. Springer-Verlag, Berlin/Verlag Stahleisen, Düsseldorf 1975. 2nd revised edition. XII, 535 pp., bound, DM 162.—.

Alicyclic Chemistry, Vol. 3. Senior Reporter: *W. Parker*. The Chemical Society, London 1975. VIII, 581 pp., bound, £ 24.00.—A volume of the series "Specialist Periodical Reports".

Photochemistry, Vol. 6. Senior Reporter: *D. Bryce-Smith*. The Chemical Society, London 1975. XXIII, 796 pp., bound, £ 27.50.—A volume of the series "Specialist Periodical Reports".

Chemical Information Systems. By *J. E. Ash* and *E. Hyde*. Ellis Horwood, Chichester/John Wiley & Sons, New York 1975. X, 309 pp., bound, £ 12.00.

Gmelins Handbuch der Anorganischen Chemie. Supplementary Vol. 20: Transurane/Transuranium Elements, Part D, 1. Springer-Verlag, Berlin 1975. 8th Edition, VI, VII, 176 pp., bound, DM 239.—.

Gmelins Handbuch der Anorganischen Chemie. Supplementary Vol. 21: Transurane/Transuranium Elements, Part D, 2: Chemie in Lösung. Springer-Verlag, Berlin 1975. 8th Edit., VI, VII, 278 pp., bound, DM 448.—.

Gmelins Handbuch der Anorganischen Chemie. Main work, System-Nr. 56: Mangan/Manganese. Part C: Die Verbindungen, 2: Mangaatverbindungen mit Metallen (von Li bis U). Springer-Verlag, Berlin 1975. 8th Edit., VI, X, 302 pp., bound, DM 487.—.

Inorganic Series Two, Vol. 4: Organometallic Derivatives of the Main Group Elements. Edited by *B. J. Aylett*. From the series "International Review of Science". Butterworths, London/University Park Press, Baltimore 1975. 417 pp., bound, £ 14.35.

The Exciplex. Edited by *M. Gordon* and *W. R. Ware*. Academic Press, New York 1975. ix, 372 pp., bound, $ 17.50.

Allgemeine und spezielle Pharmakologie und Toxikologie. For medical pharmacy, chemistry, and biology students, doctors, and pharmacists. Edited by *W. Forth, D. Henschler*, and *W. Rummel*. B.I.-Wissenschaftsverlag des Bibliographischen Instituts, Mannheim 1975. 606 pp., bound, DM 78.—.

Advances in Chromatographie, Vol. 13. Edited by *J. C. Giddings, E. Grushka, R. A. Keller*, and *J. Cazes*. Marcel Dekker, New York 1975. xiv, 324 pp., bound, $ 28.50.

Advances in Heterocyclic Chemistry, Vol. 18. Edited by *A. R. Katritzky* and *A. J. Boulton*. Academic Press, New York 1975. ix, 486 pp., bound, $ 48.50.

Advances in Carbohydrate Chemistry and Biochemistry, Vol. 31. Edited by *R. S. Tipson* and *D. Horton*. Academic Press, New York 1975. ix, 415 pp., bound, $ 38.50.

Protein Nutritional Quality of Foods and Feeds. Part 1: Assay Methods—Biological, Biochemical, and Chemical. Edited by *M. Friedman*. Vol. 1 of the series "Nutrition and Clinical Nutrition". Edited by *R. E. Olson*. Marcel Dekker, New York 1975. xx, 626 pp., bound, $ 49.50.

Comprehensive Chemical Kinetics. Edited by *C. H. Bamford* and *C. F. H. Tipper*. Vol. 14: Degradation of Polymers. Elsevier Scientific Publishing Company, Amsterdam 1975. xvi, 560 pp., bound, Dfl. 200.00.

Fortschritte der Chemie organischer Naturstoffe, Vol. 32. Founded by *L. Zechmeister*. Edited by *W. Herz, H. Grisebach*, and *G. W. Kirby*. Springer-Verlag, Berlin 1975. viii, 560 pp., bound, DM 220.00.

Electron Densities in Molecules and Molecular Orbitals. By *J. R. Van Wazer* and *I. Absar*. Vol. 35 of the series "Physical Chemistry". Edited by *E. M. Loebl*. Academic Press, New York 1975. x, 101 pp., bound, $ 14.50.

Experimentelle Einführung in die Potentiometrie. By *S. Ebel* and *W. Parzefall*. From the series "reprotext". Verlag Chemie GmbH, Weinheim 1975. 190 pp., stitched, DM 38.00.

Auswertung und Analyse kinetischer Messungen. By *E. S. Swinbourne*. Vol. 37 of the series "taschentext". Verlag Chemie GmbH, Weinheim 1975. x, 166 pp., stitched, DM 17.80.

Lehrprogramm Chemie I und II. Teacher's copy. By *J. Nentwig, M. Kreuder*, and *K. Morgenstern*. Verlag Chemie GmbH, Weinheim 1975. 3rd Edit., 174 pp., stitched, DM 12.00.

Ullmanns Encyklopädie der technischen Chemie. Vol. 9: Butadien bis Cytostatica. Verlag Chemie GmbH, Weinheim 1975. Fourth new and completely revised edition, xv, 714 pp. bound, DM 385.00.

Organophosphorus Stereochemistry, Part I: Origins and P(III) and P(IV) Compounds. Edited by *W. E. McEwen* and *K. D. Berlin*. From the series "Benchmark Papers in Organic Chemistry". Dowden, Hutchinson & Ross, Stroudsburg 1975. xviii, 387 pp., bound, $ 30.00.

Biochemistry and Chemistry of Plant Growth Regulators. Proceedings of the International Symposium held in Cottbus, September 24—26, 1974. Edited by *K. Schreiber, H. R. Schütte*, and *G. Sembdner*. Institute of Plant Biochemistry, Academy of Sciences of the German Democratic Republic 1975. VIII, 432 pp., stitched, DM 40.—.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 14036, Telex 465516 vchwh d.

Editor: *H. Grünewald* **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and 24/28 Oval Road, London NW1, England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim, Pappelallee 3, P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 14 · Number 12
December 1975
Pages 775–830

Reactions of Vinyl Azides[**]

Gerrit L'abbé[*]

This review is designed to demonstrate the versatility of vinyl azides in organic reactions. The reactive azide function is susceptible to thermolysis, photolysis, cycloadditions, and attack by nucleophiles and electrophiles. The neighboring double bond accentuates the reactivity of the azide function and provides additional intramolecular pathways for reaction. Last but not least, the presence of an appreciable electron density at the β-vinyl carbon makes this class of compounds comparable with enamines in their reactions with electrophiles and 1,3-dipoles.

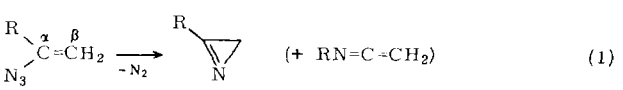
1. Introduction

Since the discovery of several methods for the synthesis of vinyl azides[1], their reactions have been extensively developed and a large amount of information is now available. In this review I shall discuss the existing state of our knowledge on vinyl azide reactions, excluding material related to azidoquinones which has been reviewed by *Moore*[2].

2. Thermal and Photochemical Decomposition

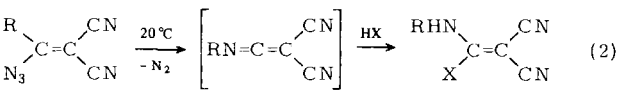
2.1. Internal Vinyl Azides

Smolinsky[3] first investigated the pyrolysis of internal (*i.e.* α-substituted) vinyl azides and found that 1-azirines are formed in addition to small amounts of ketenimines [eq. (1)].



(1)

Further work by several investigators established the generality of the azirine synthesis by thermolysis and photolysis of vinyl azides[4]. Although photolysis appears to be more selective than thermolysis in many cases[5], the formation of ketenimines in the latter process can be inhibited by the presence of tertiary amines[6]. Vinyl azides containing two β-cyano substituents produce ketenimines exclusively [eq. (2)][7]. The ketenimines were too unstable to be isolated, but their presence was inferred from trapping experiments.



(2)

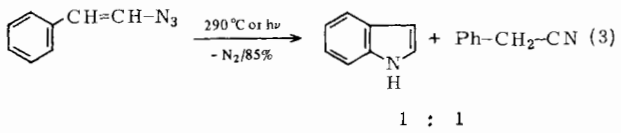
R = H, CH_3, C_6H_5

2.2. Terminal Vinyl Azides

In contrast to internal vinyl azides, terminal (*i.e.* α-unsubstituted) vinyl azides do not give stable azirines but instead decompose to different kinds of products depending on the constitution of the molecule[8]. In many cases nitriles or polymeric materials are obtained. When a phenyl group is located at the β-position of the vinyl azide, indoles are formed together with nitriles [eq. (3)][9].

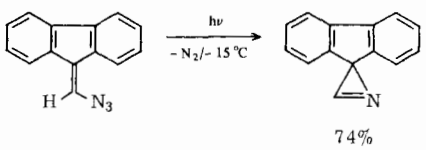
[*] Prof. Dr. G. L'abbé
Department of Chemistry, University of Leuven
Celestijnenlaan 200 F, 3030 Heverlee (Belgium)

[**] The follow abbreviations are used in the chemical formulas: Et = C_2H_5, Ph = C_6H_5, Ts = *p*-H_3C—C_6H_4—SO_2.



1 : 1

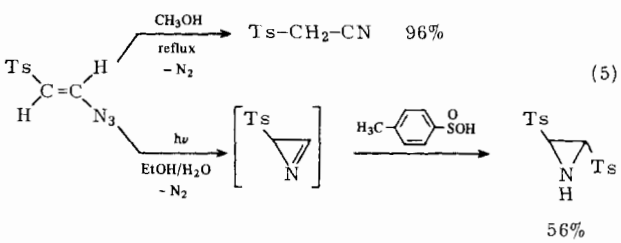
The decomposition mechanism of terminal vinyl azides has been debated for a long time, but it is now clear that azirines are intermediates. Photo-induced, in contrast to thermally induced decomposition of these azides, frequently allows the isolation of azirines. *Bauer* and *Hafner*[10], for instance, were able to prepare the spiroazirine from azidomethylenefluorene by photolysis at −15 °C [eq. (4)]. Thermally, the azirine readily lost hydrogen cyanide to give a carbene.



(4)

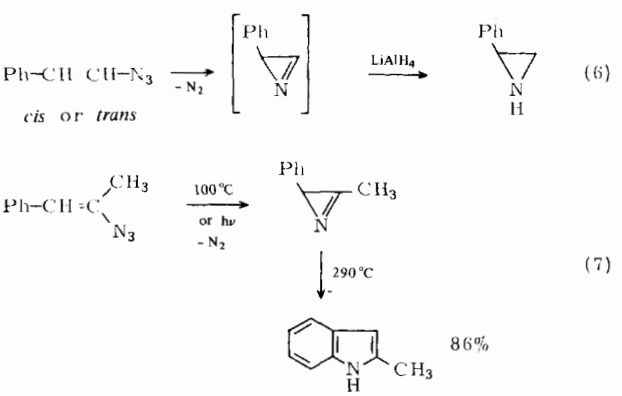
74%

Meek and *Fowler*[11] reported that β-azidovinyl *p*-tolyl sulfone decomposes thermally to give the nitrile, whereas irradiation produces 2,3-di-*p*-toluenesulfonylaziridine [eq. (5)]. The latter was shown to arise from the azirine by addition of *p*-toluenesulfinic acid generated during photolysis.



(5)

Isomura et al.[9] observed by spectroscopic methods that an azirine is formed after thermolysis or photolysis of β-styryl azide. The unstable azirine was reduced by lithium tetrahydridoaluminate to give 2-phenylaziridine [eq. (6)]. The azirine derived from β-azido-β-methylstyrene, a nonterminal vinyl azide, can be pyrolyzed to 2-methylindole at higher temperature [eq. (7)][9].

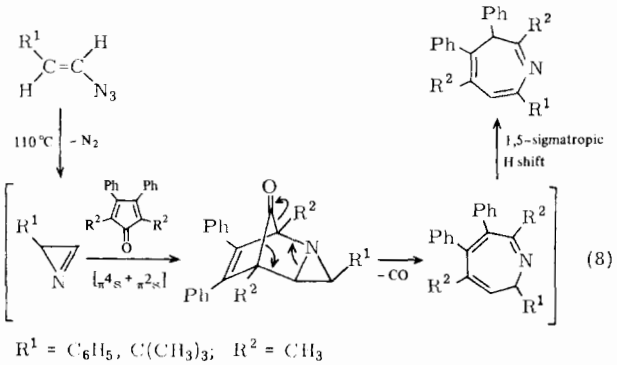


(6)

(7)

86%

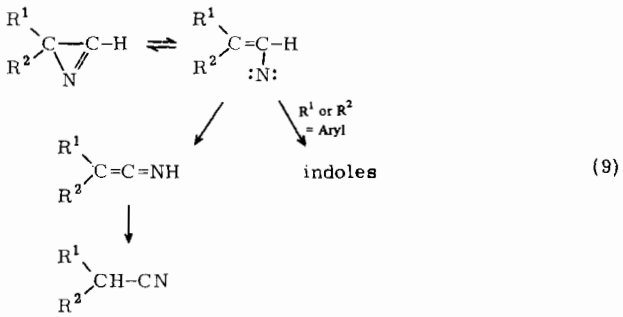
Finally, *Hassner* and *Anderson*[12] intercepted several azirines of fleeting existence in a Diels-Alder fashion with cyclopentadienones [eq. (8)]. Previous work by the same authors and by *Nair*[13] has indeed shown that stable azirines react with these dienes to give 3*H*-azepines.



(8)

R^1 = C_6H_5, $C(CH_3)_3$; R^2 = CH_3

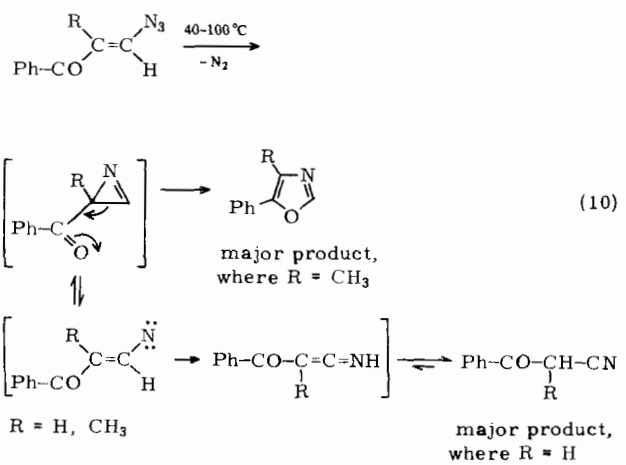
From these results it is apparent that 2-unsubstituted azirines are much less stable than the substituted ones. In fact, azirines bearing a hydrogen atom at the 2-position are too unstable to survive most pyrolytic conditions. Ring opening of the azirines produces vinyl nitrenes which can either rearrange to ketenimines and nitriles or undergo insertion into the C—H bond of a phenyl substituent to give indoles [eq. (9)].



(9)

2.3. β-Azidovinyl Ketones and Esters

The nature of the decomposition products is significantly different for *cis*- and *trans*-β-azidovinyl ketones[*]. Pyrolysis of the *trans* isomers gives a mixture of oxazole and nitrile, presumably formed *via* the corresponding azirine [eq. (10)][14].



(10)

major product, where R = CH_3

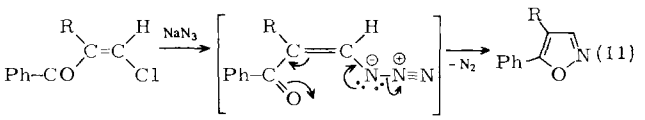
major product, where R = H

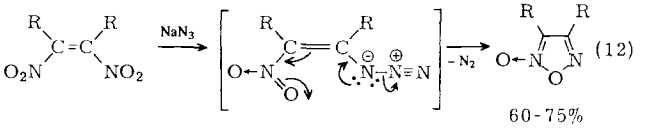
R = H, CH_3

cis-β-Azidovinyl ketones, however, are unstable at room temperature and decompose to isoxazoles [eq. (11)][14, 15], presumably *via* a concerted mechanism as shown in eq. (11).

[*] *cis* and *trans* refer to the positions of the acyl and azide group.

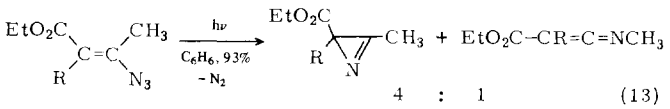
This assumption is based on results obtained for *ortho*-substituted phenyl azides, where a CO or NO_2 substituent has been shown to provide anchimeric assistance during decomposition[16]. In line with these findings are the results of *Emmons et al.*[17] that β-nitrovinyl azides cannot be isolated. All attempts to prepare them have only led to the formation of furoxans [eq. (12)].

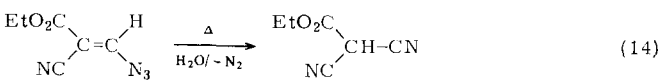

(11)

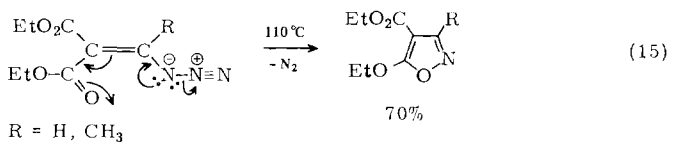

(12)

60-75%

Several β-azidovinyl esters have been subjected to thermal and photochemical decomposition, and it was found that the nature of the reaction products largely depends on the constitution of the molecule. Internal vinyl azides furnish azirines and/or ketenimines [eq. (13)][18, 19], terminal vinyl azides yield nitriles [eq. (14)][19], and *cis*-β-azidovinyl esters decompose smoothly to isoxazoles, probably by a concerted mechanism [eq. (15)][19].


(13)

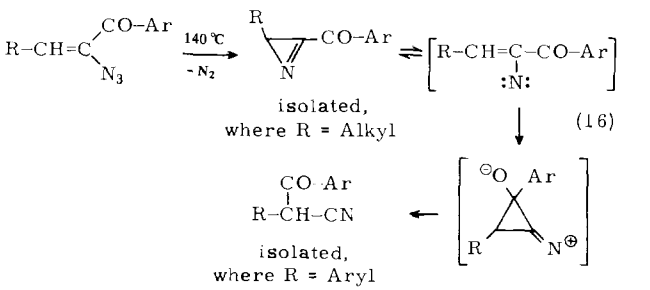

(14)


(15)

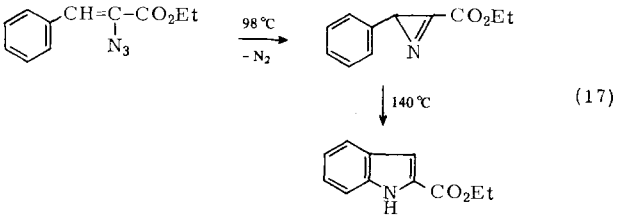
R = H, CH_3

2.4. α-Azidovinyl Ketones and Esters

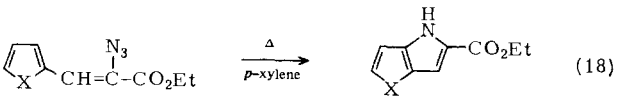
Whereas β-alkyl α-azidovinyl ketones decompose to azirines[20], those with a β-aryl substituent furnish rearranged nitriles[21]. A mechanistic rationalization of this unusual reaction is outlined in eq. (16). The detection and isolation of azirines in some particular cases substantiates their occurrence as intermediates.


(16)

Thermolysis of α-azidocinnamates produces indole-2-carboxylic esters *via* the intermediacy of azirines [eq. (17)][22]. α-Azidovinyl esters bearing heteroaromatic ring systems attached to the β-carbon atom give similar results, as illustrated in eq. (18)[23].


(17)

90-98%


(18)

X = O, 90%; X = S, 97%; X = N–CH_3, 85%

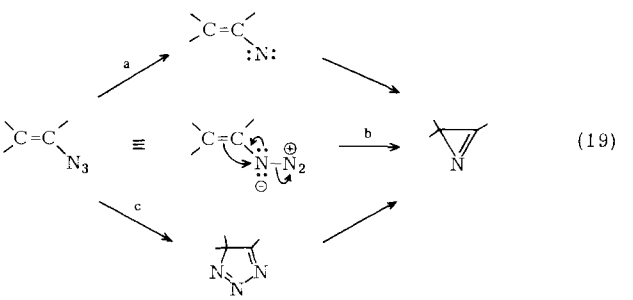
2.5. Mechanism of Azirine Formation

It is clear from the above discussion that apart from isoxazole and furoxan formation [eqs. (11) and (12)], vinyl azides give azirines at least in the primary stage of their decomposition. According to *Smolinsky*[3], three mechanistic pathways are plausible [eq. (19)]:

i) intervention of a vinyl nitrene (path a),

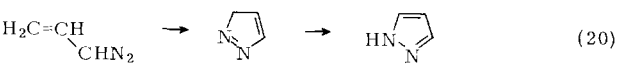
ii) a concerted process involving ring closure simultaneous with loss of nitrogen (path b), and

iii) the intermediate formation of an unstable 1,2,3-4*H*-triazole (path c).


(19)

A nitrene mechanism (path a) is easily excluded on the basis of recent kinetic results which revealed that vinyl azides exhibit moderate energies of activation (26 to 30 kcal/mol) and rather low entropies of activation (−3 to +5 e.u.)[24]. Indeed, these values are in sharp contrast with those found for aryl azides which decompose to nitrenes (*e.g.* $E_a = 39.0$ kcal/mol and $\Delta S^* = 18.7$ e.u. for phenyl azide)[25] but, instead, are comparable with those reported for the Curtius rearrangement[26] and for some *ortho*-substituted aryl azides manifesting neighboring group participation[16].

Although path b is consistent with the kinetic results and is most likely in the author's opinion, path c cannot be excluded at this time since it is also expected to occur with a rather low entropy of activation. This conclusion was reached by studying the kinetics of decomposition of vinyldiazomethane, ΔS^* being −3.6 e.u.[24]. This compound decomposes by a mechanism analogous to path c, giving 1*H*-pyrazole *via* the 3*H*-pyrazole [eq. (20)].


(20)

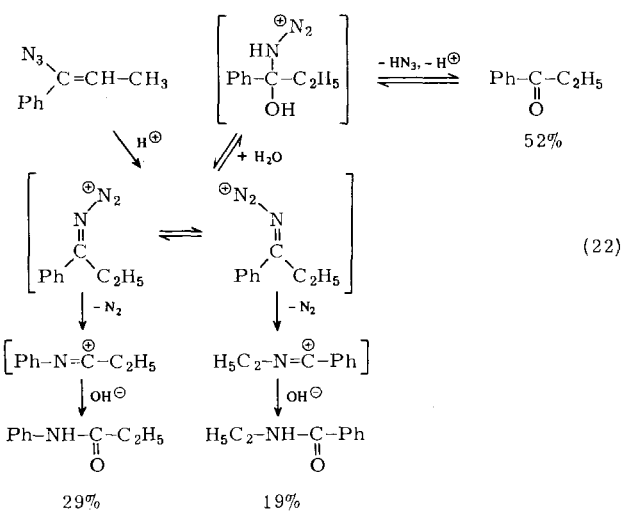
In addition, path c is in keeping with the findings that vinyl azides possessing an acidic β-H atom undergo a facile base-promoted cyclization to triazoles [eq. (21)][27].

(21)

In conclusion, the decomposition of vinyl azides is best rationalized by a process involving anchimeric assistance (paths b or c), thus explaining their low decomposition temperatures (below 100 °C) compared with the 140—170 °C decomposition range of ordinary aryl azides.

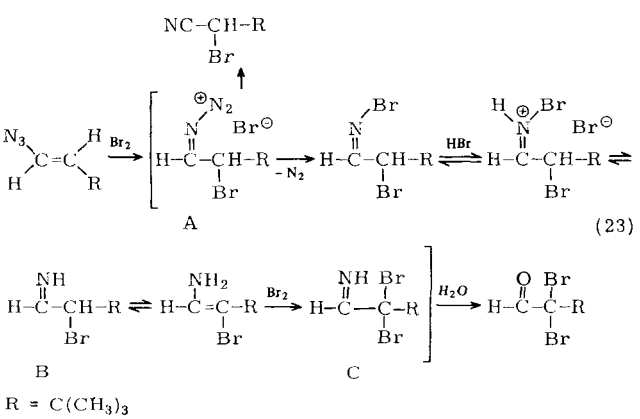
3. Attack by Electrophilic Reagents

The attachment of an azide function to an olefinic double bond increases the electron density at the β-carbon atom through resonance[28]. Hence, electrophilic attack can occur at this β-vinyl carbon as a possible alternative to the well known attack at the α-nitrogen atom of the azide. *Hassner et al.*[29], for instance, have found that acid hydrolysis of simple vinyl azides yields the same proportion of amides as obtained in the Schmidt reaction[30] of the corresponding ketones under identical conditions [eq. (22)]. This suggests that the same intermediates are involved in the two reactions. These intermediates are the *cis*- and *trans*-iminodiazonium ions (in rapid equilibrium) which are supposed to rearrange in an *anti*-fashion[31] analogous to the well known Beckmann rearrangement.



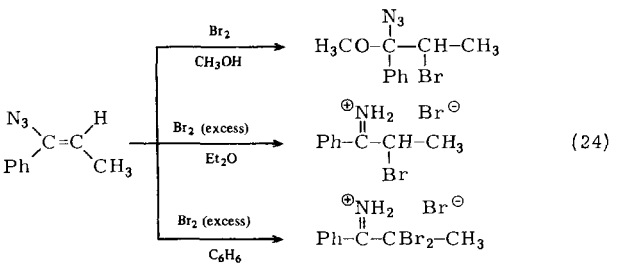
(22)

In contrast to protonation, bromination of vinyl azides does not result in alkyl or phenyl migration to nitrogen, but instead furnishes different kinds of products depending on the nature of the substituents and the solvent[32]. For instance, treatment of 1-azido-3,3-dimethyl-1-butene with an excess of bromine in ether, followed by water workup, yields an α-bromonitrile (major product) and an α,α-dibromoaldehyde (minor product) [eq. (23)].



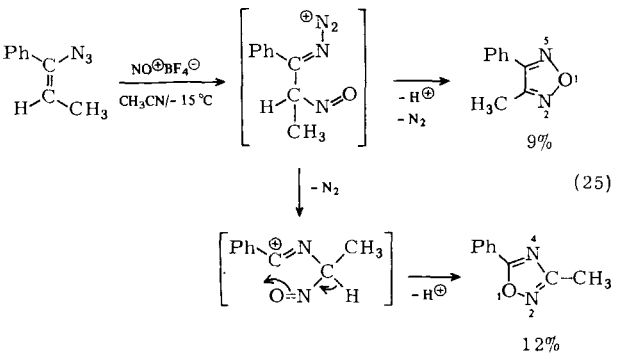
(23)

Strong evidence for the proposed mechanism is provided by the bromination of (*E*)-1-azido-1-phenyl-1-propene in three different solvents (methanol, ether, and benzene), leading respectively to three reaction products [eq. (24)]. They result from interception of intermediates of type A, B, and C in eq. (23).



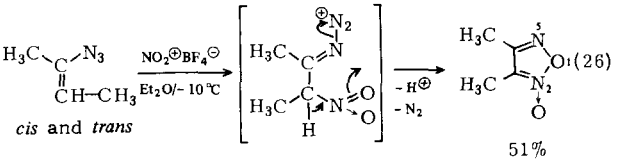
(24)

Initial attack at the β-vinyl carbon is also observed in the reactions of simple vinyl azides containing a β-H atom with nitrosyl tetrafluoroborate, giving 1,2,5-oxadiazoles along with 1,2,4-oxadiazoles in some cases [eq. (25)][33].



(25)

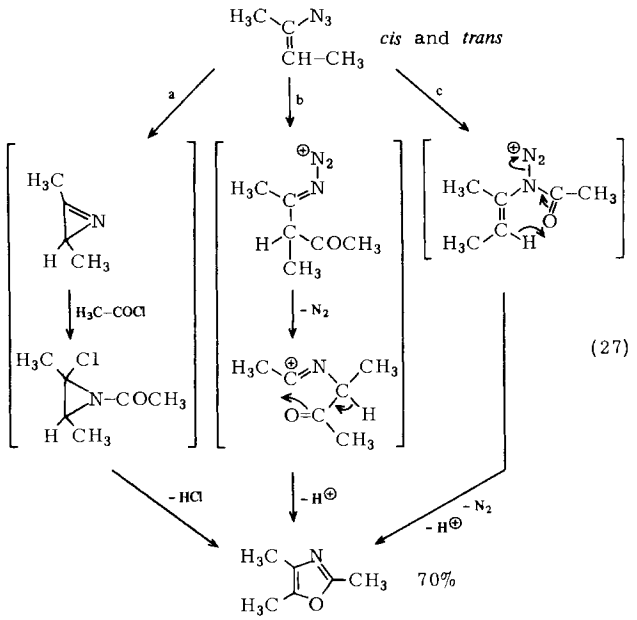
Similarly, the reaction of 1,2-dialkyl substituted vinyl azides with nitryl tetrafluoroborate produces furoxans [eq. (26)][33].



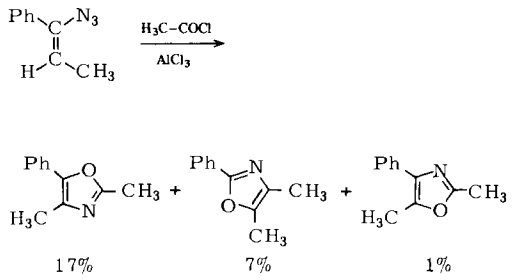
(26)

Acetyl chloride can also be used as electrophilic reagent to react with vinyl azides in the presence of aluminum chloride[33]. Starting with *cis*- or *trans*-2-azido-2-butene, 2,4,5-trimethyloxazole is obtained in 70% yield [eq. (27)]. Three mechanisms can account for the formation of this product. In path a, the vinyl azide decomposes to the azirine under the influence of aluminum chloride. Further reaction of the azirine with acetyl chloride to give the oxazole *via* the intermediacy of 1-acetyl-2-chloroaziridine is well known[34]. Path b is analogous to that of eq. (25), and path c involves initial attack of the acyl cation at the α-nitrogen atom of the azide, followed by loss of nitrogen and ring formation.

The three pathways in eq. (27) would lead to three isomeric oxazoles when a methyl substituent in the starting vinyl azide is substituted for a phenyl group. This was indeed observed, as shown in eq. (28)[33].

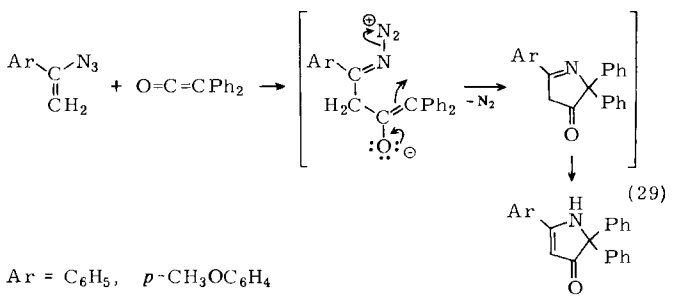


(27)



(28)

Hassner et al.[35] reported the reactions of simple vinyl azides with diphenylketene. α-Azidostyrene, or its *p*-methoxy derivative, reacts slowly with diphenylketene at room temperature to give a 2-pyrrolin-4-one with loss of nitrogen [eq. (29)]. The reaction appears to involve nucleophilic attack of the β-vinyl carbon upon the ketene, followed by ring closure and loss of nitrogen.

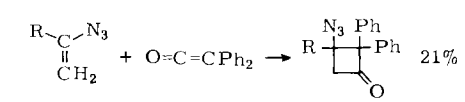


(29)

Ar = C_6H_5, p-$CH_3OC_6H_4$

45-50%

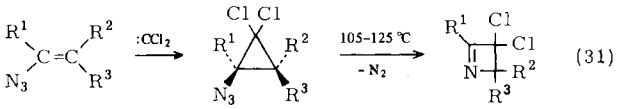
Reaction of 2-azido-1-hexene with diphenylketene proceeds in a different manner, leading to an azidocyclobutanone [eq. (30)][35]. Whether the formation of this product occurs by a concerted $[\pi 2_s + \pi 2_a]$cycloaddition or by a stepwise process remains to be established.



(30)

R = $(CH_2)_3$-CH_3

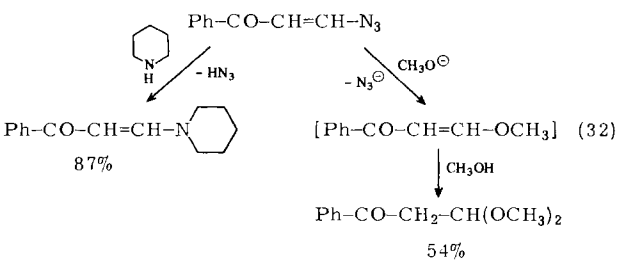
Generation of dichlorocarbene in the presence of simple vinyl azides results in formation of azidodichlorocyclopropanes [eq. (31)][36]. These compounds can be thermolyzed to 1-azetines in a highly regiospecific reaction[36, 37]. Indeed, migration of the electron-rich CR^2R^3 rather than the CCl_2 ring moiety to the electron-deficient nitrogen atom is observed.



(31)

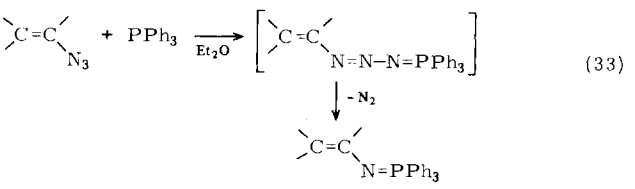
4. Attack by Nucleophilic Reagents

Vinyl azides possessing a strong electron-withdrawing substituent at the β-vinyl carbon can undergo displacement reactions with some nucleophiles. Thus, β-azidovinyl phenyl ketone reacts with piperidine and methoxide ion to give a piperidinovinyl ketone and a dimethyl acetal, respectively [eq. (32)][38]. The reactions parallel those of acyl azides, azidoformates, and carbamoyl azides where nucleophilic attack occurs at the carbonyl function with elimination of the azide ion[39].



(32)

Apart from the specific examples mentioned above, nucleophilic attack on vinyl azides is believed to occur at the terminal nitrogen atom to give triazenes in the first stage of the reaction[39]. The triazenes may then decompose or cyclize if appropriate functions are present on the molecule, leading to open-chain or heterocyclic nitrogen-containing compounds. An illustration of the former reaction is the synthesis of vinyliminophosphoranes in high yields from the interaction of vinyl azides with tertiary phosphanes [eq. (33)][18a, 40]. This Staudinger reaction[41] is general for azides and proceeds *via* a phosphoranylidenetriazene as intermediate[39].

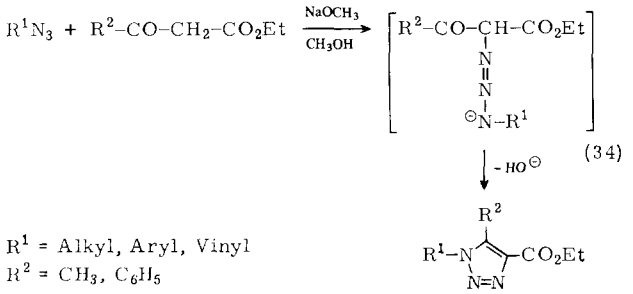


(33)

> 90%

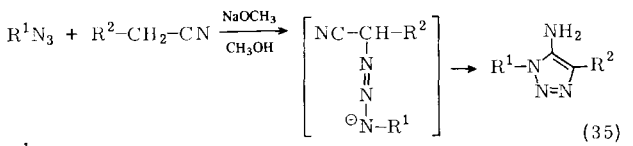
It is well known that active methylene compounds react with alkyl azides and aryl azides in the presence of alkoxides to give substituted triazoles [eqs. (34) and (35)][42], a reaction called the Dimroth reaction after its discoverer[43]. This synthetically important reaction has been shown to proceed as a stepwise cycloaddition *via* a triazene intermediate[44].

The reaction has been extended to simple vinyl azides, giving vinyl-substituted triazoles[45]. Even β-azidovinyl ketones undergo the Dimroth reaction in slightly modified conditions [$(C_2H_5)_3N$/DMF], as illustrated in eq. (36)[46].



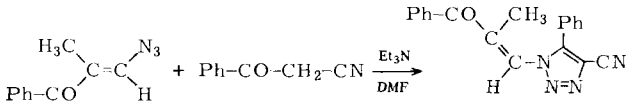
(34)

R^1 = Alkyl, Aryl, Vinyl
R^2 = CH_3, C_6H_5



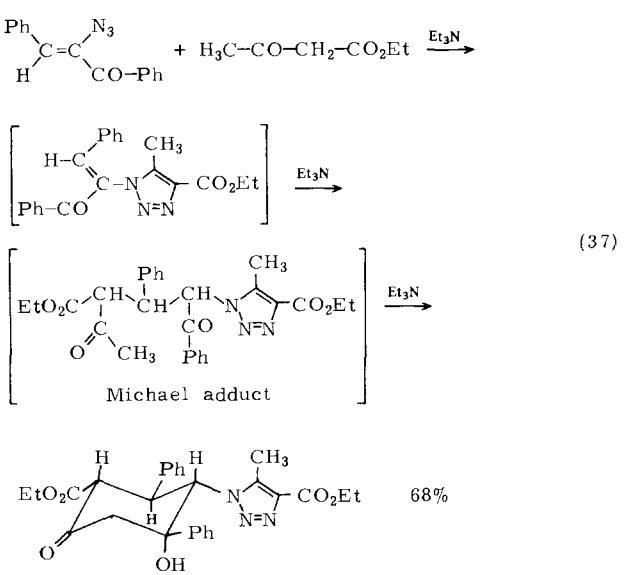
(35)

R^1 = Alkyl, Aryl, Vinyl
R^2 = C_6H_5, CO_2CH_3, $CONH_2$



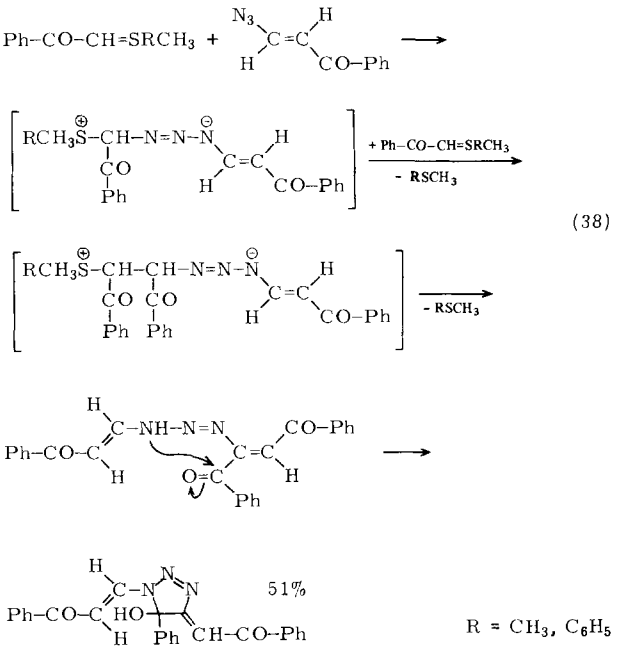
86% (36)

On reaction of α-azidovinyl ketones with compounds having an activated methylene group no vinyltriazoles but products of further addition are isolated[47]. For instance, triethylamine-catalyzed reaction of ethyl acetocetate with α-azidochalcone, or its nitro-substituted derivative, furnishes a 4-triazolylcyclohexanone [eq. (37)]. It is apparent that the initially formed "Dimroth product" undergoes a Michael-type addition with the active methylene compound in the presence of triethylamine. This reaction is expected to occur readily since the electron density of the olefinic double bond is decreased by the presence of two strongly electron-withdrawing substituents (namely the acyl and triazole substituents). Under the basic reaction conditions, the Michael adduct then undergoes an intramolecular aldolization, resulting in the formation of the cyclohexanone[47a].



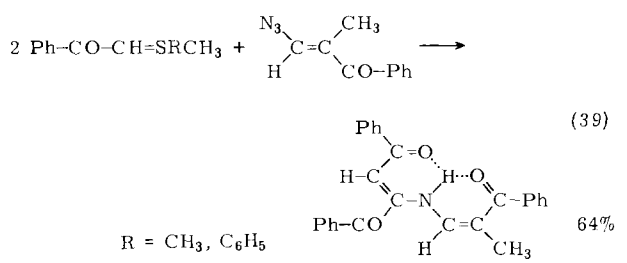
(37)

Sulfur ylides have received increasing interest since *Johnson*'s book on ylide chemistry was published in 1966[48]. Several azides have been reacted with non-stabilized[49] and carbonyl-stabilized sulfonium ylides[50] and a variety of reaction products were obtained including enamines, vinyltriazenes, cyclopropyltriazenes and 2-triazolines. The reaction of β-azidovinyl phenyl ketone (or its methyl-substituted derivative) with a phenacylidenesulfurane at room temperature produces a vinyltriazoline [eq. (38)][51]. Mechanistically, two triazene anionic intermediates are postulated which result from the azide by successive addition of two molecules of ylide. Elimination of the sulfide moiety and proton shift then furnishes a vinyltriazene which exists in the cyclic triazoline form, at least in solution.



(38)

α-Azidochalcones also furnish vinyltriazolines, whereas (*E*)-β-azido-α-methylvinyl phenyl ketone yields a vinylenamine with loss of nitrogen [eq. (39)][51].

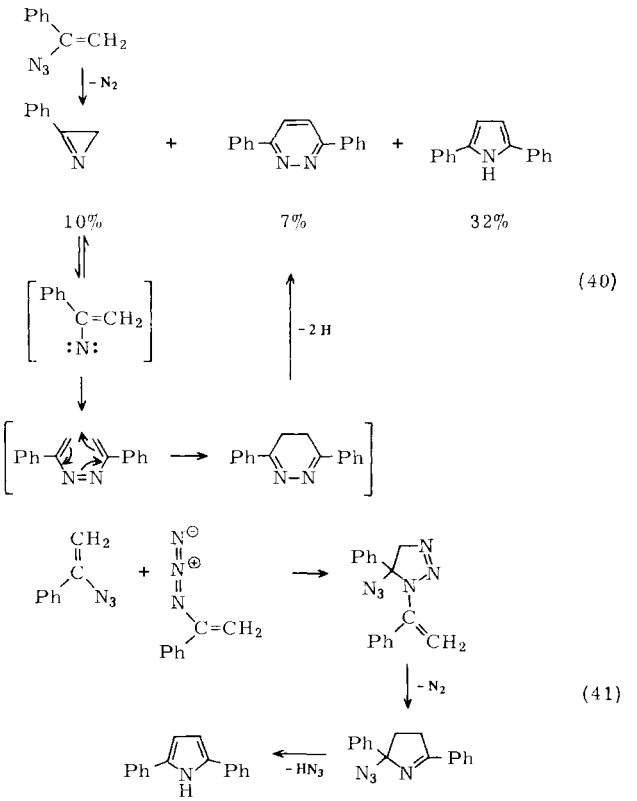


(39)

5. 1,3-Dipolar Cycloadditions

The presence of an azide function together with a C=C bond in the molecule would allow self-addition of vinyl azides to occur, but this has never been reported explicitly. However, one example exists in the literature where this process might have occurred. Thus, *Boyer et al.*[52] reported that α-azidostyrene decomposes slowly at room temperature (one month) to give a mixture of 2-phenylazirine, 3,6-diphenylpyridazine, and 2,5-diphenylpyrrole in respectively 10%, 7%, and 32% yield based on 40% recovered starting material [eq. (40)]. 3,6-Diphenylpyridazine is presumably formed by dimerization of α-styrylnitrene, followed by valence isomerization and aromatization [see eq. (40)]. The formation of 2,5-diphenylpyrrole, on the other hand, can be interpreted in terms of 1,3-dipolar cycloaddition of the azide onto the electron-rich double bond of a second molecule to give a 2-triazoline which decomposes

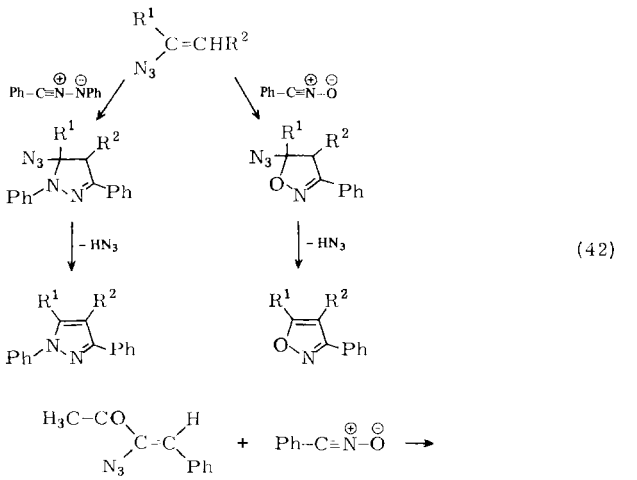
by loss of N_2 and elimination of HN_3 [eq. (41)]. Other less plausible mechanisms were formulated by the authors[52].



(40)

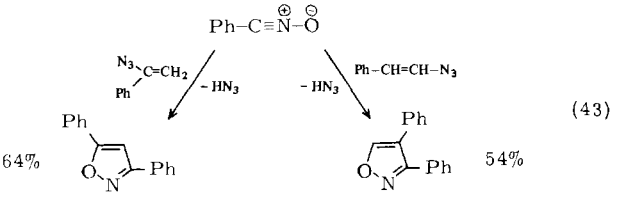
(41)

Nitrile imines[53] and nitrile oxides[54] have been added onto the C=C bond of diversely substituted vinyl azides. In all cases studied, the azide function completely controlled the regiochemistry of the addition process, analogous to the well established directional effect of the amine function in enamines[26, 55]. This is schematized in eq. (42). Although the initially formed 5-azidopyrazolines and 5-azidoisoxazolines can be detected or isolated in many cases, they readily loose HN_3 with formation of the aromatic pyrazoles and isoxazoles respectively.



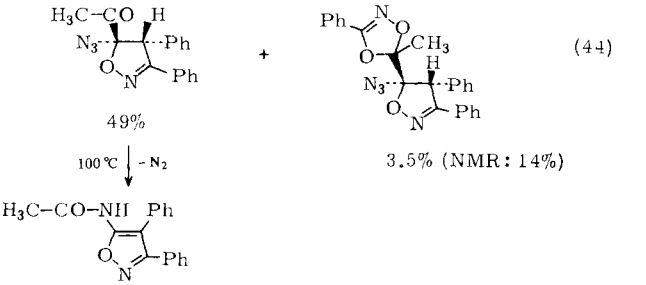
(42)

An interesting aspect of the observed regiospecificity is that 3,5- and 3,4-diphenylisoxazole can be prepared in separate reactions from α- and β-azidostyrene as shown in eq. (43)[54].



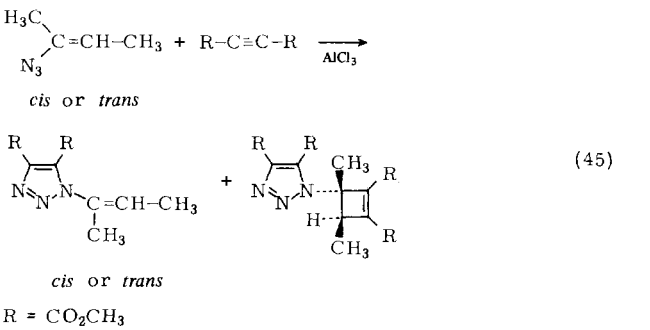
(43)

α-Azidovinyl ketones exhibit unusual behavior towards benzonitrile oxide since addition not only occurs onto the C=C bond but also onto the C=O bond[54, 56]. For instance, α-azidostyryl methyl ketone interacts with benzonitrile oxide to give both a monoadduct (C=C addition) and a bisadduct (C=O and C=C addition) [eq. (44)]. Interestingly, the monoadduct rearranges thermally at *ca.* 100 °C with acyl migration from carbon to nitrogen (cf. ref.[57]).



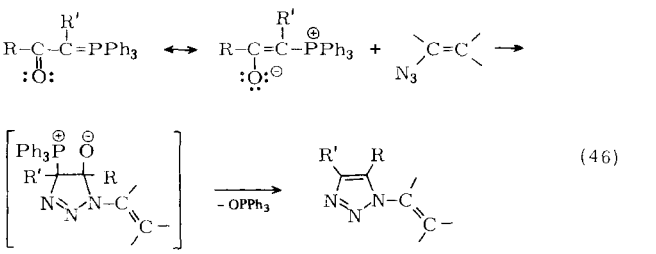
(44)

Only a few reactions of vinyl azides with dipolarophiles have been reported. Dimethyl acetylenedicarboxylate reacts with simple vinyl azides to yield 1-vinyl substituted 1,2,3-triazoles, but in the presence of aluminum chloride a considerable amount of a bisadduct is also obtained [eq. (45)][33]. According to the authors, both *cis*- and *trans*-2-azido-2-butene give the same bisadduct [see eq. (45)]. Furthermore, the monoadduct 1-vinyltriazole cannot be induced to react further with dimethyl acetylenedicarboxylate in the presence of aluminum chloride and, hence, is not a precursor of the bisadduct.



(45)

Monosubstituted alkynes such as methyl propiolate and phenylacetylene react with simple vinyl azides in a non-regiospecific manner[58]. This disadvantage of producing two regioisomeric triazoles can be avoided by using 2-oxoalkylidenephosphoranes [eq. (46)][59]. Indeed, these ylides are known to exist essentially in the enolate structure (C=O at *ca.* 1530 cm^{-1}) and manifest a pronounced dipolarophilic activity



(46)

towards azides[60]. The reaction proceeds *via* a concerted cycloaddition of the azide onto the C=C bond of the ylide to give an unstable betaine intermediate which immediately loses triphenylphosphane oxide in a Wittig-type reaction.

Received: February 3, 1975 [A 89 IE]
German version: Angew. Chem. *87*, 831 (1975)

[1] *G. L'abbé* and *A. Hassner*, Angew. Chem. *83*, 103 (1971); Angew. Chem. internat. Edit. *10*, 98 (1971).

[2] *H. W. Moore*, Chem. Soc. Rev. *2*, 415 (1973).

[3] *G. Smolinsky*, J. Am. Chem. Soc. *83*, 4483 (1961); J. Org. Chem. *27*, 3557 (1962).

[4] a) *F. W. Fowler*, Adv. Heterocycl. Chem. *13*, 45 (1971); *G. Smolinsky* and *C. A. Pryde* in *S. Patai:* The Chemistry of the Azido Group. Interscience, New York 1971, Chapter 10; b) see also *C. S. Cleaver* and *C. G. Krespan*, J. Am. Chem. Soc. *87*, 3716 (1965); *R. E. Banks* and *G. J. Moore*, J. Chem. Soc. *C 1966*, 2304; *C. G. Krespan*, J. Org. Chem. *34*, 1278 (1969); *R. E. Banks* and *M. J. McGlinchey*, J. Chem. Soc. *C 1970*, 2172; *M. Rens* and *L. Ghosez*, Tetrahedron Lett. *1970*, 3765; *A. G. Hortmann, D. A. Robertson*, and *B. K. Gillard*, J. Org. Chem. *37*, 322 (1972).

[5] *A. Hassner* and *F. W. Fowler*, Tetrahedron Lett. *1967*, 1545; J. Am. Chem. Soc. *90*, 2869 (1968).

[6] *M. Komatsu, S. Ichijima, Y. Ohshiro*, and *T. Agawa*, J. Org. Chem. *38*, 4341 (1973).

[7] *K. Friedrich*, Angew. Chem. *79*, 980 (1967); Angew. Chem. internat. Edit. *6*, 957 (1967).

[8] *G. Smolinsky* and *C. A. Pryde*, J. Org. Chem. *33*, 2411 (1968).

[9] *K. Isomura, S. Kobayashi*, and *H. Taniguchi*, Tetrahedron Lett. *1968*, 3499; *K. Isomura, M. Okada*, and *H. Taniguchi, ibid. 1969*, 4073.

[10] *W. Bauer* and *K. Hafner*, Angew. Chem. *81*, 787 (1969); Angew. Chem. internat. Edit. *8*, 772 (1969).

[11] *J. S. Meek* and *J. S. Fowler*, J. Org. Chem. *33*, 3418 (1968).

[12] *D. J. Anderson* and *A. Hassner*, J. Org. Chem. *38*, 2565 (1973).

[13] *D. J. Anderson* and *A. Hassner*, J. Am. Chem. Soc. *93*, 4339 (1971); *94*, 8255 (1972); J. Org. Chem. *39*, 3070 (1974); *V. Nair, ibid. 37*, 802 (1972).

[14] *M. I. Rybinskaya, A. N. Nesmeyanov*, and *N. K. Kochetkov*, Russ. Chem. Rev. *38*, 961 (1969).

[15] *U. Türck* and *H. Behringer*, Chem. Ber. *98*, 3020 (1965); *A. Hassner, G. L'abbé*, and *M. J. Miller*, J. Am. Chem. Soc. *93*, 981 (1971).

[16] *L. K. Dyall* and *J. E. Kemp*, J. Chem. Soc. *B 1968*, 976, and references cited therein.

[17] *W. D. Emmons* and *J. P. Freeman*, J. Org. Chem. *22*, 456 (1957); *T. E. Stevens* and *W. D. Emmons*, J. Am. Chem. Soc. *80*, 338 (1958).

[18] a) *R. Harvey* and *K. W. Ratts*, J. Org. Chem. *31*, 3907 (1966); b) *A. Hassner* and *F. W. Fowler, ibid. 33*, 2686 (1968).

[19] *K. Friedrich* and *H. K. Thieme*, Chem. Ber. *103*, 1982 (1970).

[20] *H. Hemetsberger* and *D. Knittel*, Monatsh. Chem. *103*, 205 (1972).

[21] *D. Knittel, H. Hemetsberger, R. Leipert*, and *H. Weidmann*, Tetrahedron Lett. *1970*, 1459.

[22] *H. Hemetsberger, D. Knittel*, and *H. Weidmann*, Monatsh. Chem. *101*, 161 (1970).

[23] *H. Hemetsberger* and *D. Knittel*, Monatsh. Chem. *103*, 194 (1972).

[24] *G. L'abbé* and *G. Mathys*, J. Org. Chem. *39*, 1778 (1974).

[25] *R. A. Abramovitch* and *E. P. Kyba* in *S. Patai:* The Chemistry of the Azido Group. Interscience, New York 1971, p. 221.

[26] *G. L'abbé*, Chem. Rev. *68*, 345 (1968).

[27] *J. S. Meek* and *J. S. Fowler*, J. Am. Chem. Soc. *89*, 1967 (1967); J. Org. Chem. *33*, 985 (1968); see also *F. P. Woerner* and *H. Reimlinger*, Chem. Ber. *103*, 1908 (1970); *G. Beck* and *D. Günther, ibid. 106*, 2758 (1973).

[28] *K. Isomura, M. Okada*, and *H. Taniguchi*, Nippon Kagaku Zasshi *91*, 746 (1970); *G. L'abbé*, Chem. Ind. (London) *1971*, 278.

[29] *A. Hassner, E. S. Ferdinandi*, and *R. J. Isbister*, J. Am. Chem. Soc. *92*, 1672 (1970).

[30] For a recent review, see *D. V. Banthorpe* in *S. Patai:* The Chemistry of the Azido Group. Interscience, New York 1971, Chapter 7.

[31] The terms *cis* and *trans* are used for configurational assignments, and *syn* and *anti* for describing transformations during chemical processes.

[32] *A. Hassner* and *A. B. Levy*, J. Am. Chem. Soc. *93*, 5469 (1971).

[33] *A. N. Thakore, J. Buchshriber*, and *A. C. Oehlschlager*, Can. J. Chem. *51*, 2406 (1973).

[34] *S. Sato, H. Kato*, and *M. Ohta*, Bull. Chem. Soc. Jap. *40*, 1014 (1967); *F. W. Fowler* and *A. Hassner*, J. Am. Chem. Soc. *90*, 2875 (1968).

[35] *A. Hassner, A. S. Miller*, and *M. J. Haddadin*, J. Org. Chem. *37*, 2682 (1972).

[36] *A. B. Levy* and *A. Hassner*, J. Am. Chem. Soc. *93*, 2051 (1971).

[37] For other thermolysis and photolysis reactions of cyclopropyl azides, see *D. S. Wulfman* and *T. R. Steinheimer*, Tetrahedron Lett. *1972*, 3933; *G. Szeimies, U. Siefken*, and *R. Rinck*, Angew. Chem. *85*, 173 (1973); Angew. Chem. internat. Edit. *12*, 161 (1973); *S. Szeimies* and *J. Harnisch*, J. C. S. Chem. Commun. *1973*, 739; *A. Hassner, A. B. Levy, E. E. McEntire*, and *J. E. Galle*, J. Org. Chem. *39*, 585 (1974).

[38] *A. N. Nesmeyanov* and *M. I. Rybinskaya*, Bull. Acad. Sci. USSR, Div. Chem. Sci. *1962*, 761.

[39] *G. L'abbé*, Ind. Chim. Belge *34*, 519 (1969).

[40] *G. L'abbé* and *A. Hassner*, J. Org. Chem. *36*, 258 (1971); *E. Ciganek, ibid. 35*, 3631 (1970).

[41] *H. Staudinger* and *J. Meyer*, Helv. Chim. Acta *2*, 635 (1919); *H. Staudinger* and *E. Hauser, ibid. 4*, 861 (1921).

[42] *G. L'abbé*, Ind. Chim. Belge *36*, 3 (1971).

[43] *O. Dimroth*, Ber. Dtsch. Chem. Ges. *35*, 1029, 4041 (1902).

[44] *C. E. Olsen* and *C. Pedersen*, Tetrahedron Lett. *1968*, 3805; *R. L. Tolman, C. W. Smith*, and *R. K. Robins*, J. Am. Chem. Soc. *94*, 2530 (1972).

[45] *G. L'abbé* and *A. Hassner*, J. Heterocycl. Chem. *7*, 361 (1970).

[46] *S. Maiorana*, Ann. Chim. (Rome) *56*, 1531 (1966).

[47] *G. L'abbé, G. Mathys*, and *S. Toppet*, J. Org. Chem. *40*, 1549 (1975).

[47a] Triazolylcyclohexanones were also obtained by reaction of α-azidovinyl ketones with 2,4-pentanedione: *J.-P. Dekerk*, Thesis, Leuven 1975.

[48] *A. W. Johnson* in *A. T. Blomquist:* Ylid Chemistry. Academic Press, New York 1966.

[49] *G. Gaudiano, C. Ticozzi, A. Umani-Ronchi*, and *P. Bravo*, Gazz. Chim. Ital. *97*, 1411 (1967).

[50] *E. Van Loock, G. L'abbé*, and *G. Smets*, J. Org. Chem. *36*, 2520 (1971); Tetrahedron *28*, 3061 (1972).

[51] *G. L'abbé, G. Mathys*, and *S. Toppet*, Chem. Ind. (London) *1975*, 278.

[52] *J. H. Boyer, W. E. Krueger*, and *R. Modler*, Tetrahedron Lett. *1968*, 5979.

[53] *G. L'abbé* and *G. Mathys*, J. Heterocycl. Chem. *11*, 613 (1974).

[54] *G. L'abbé* and *G. Mathys*, J. Org. Chem. *39*, 1221 (1974).

[55] *R. Huisgen, R. Sustmann*, and *G. Wallbillich*, Chem. Ber. *100*, 1786 (1967); *K. Bast, M. Christl, R. Huisgen, W. Mack*, and *R. Sustmann, ibid. 106*, 3258 (1973); *C. Grundmann* and *P. Grünanger:* The Nitrile Oxides. Springer, Berlin 1971, p. 109.

[56] For additions of nitrile oxides onto C=O bonds, see *R. Huisgen* and *W. Mack*, Tetrahedron Lett. *1961*, 583; Chem. Ber. *105*, 2805 (1972).

[57] *G. L'abbé, G. Mathys*, and *S. Toppet*, J. Org. Chem. *39*, 3449 (1974).

[58] *G. L'abbé, J. E. Galle*, and *A. Hassner*, Tetrahedron Lett. *1970*, 303; *G. L'abbé* and *A. Hassner*, Bull. Soc. Chim. Belg. *80*, 209 (1971).

[59] *P. Ykman, G. Mathys, G. L'abbé*, and *G. Smets*, J. Org. Chem. *37*, 3213 (1972).

[60] *G. R. Harvey*, J. Org. Chem. *31*, 1587 (1966); *P. Ykman, G. L'abbé*, and *G. Smets*, Tetrahedron Lett. *1970*, 5225; Tetrahedron *27*, 845, 5623 (1971); J. Indian Chem. Soc. *49*, 1245 (1972).

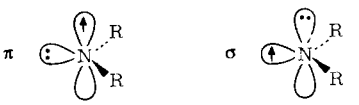
Aminyl Free Radicals

By Wayne C. Danen and Franz A. Neugebauer[*]

Recent interest in aminyl free radicals, especially in their electronic structure, has led to many investigations in this area. This report reviews the main features of the generation of aminyls, their reactivity, and electronic properties.

1. Introduction

Reactions of aminyl free radicals are gaining increasing significance in the chemistry of amines, in biological processes, and especially in the photolysis or γ-irradiation of nitrogen-containing compounds. In aminyl free radicals the central nitrogen must accommodate both an unpaired electron and a lone pair of electrons, with the result that either a π *(1)* or a σ *(2)* electronic ground state for this type of radical is possible.



(1) *(2)*

The question of the true electronic configuration in aminyls has led to many investigations in this area during recent years, and after some time of controversy, partly due to some erroneous experimental results (often caused by the corresponding nitroxides R_2NO), an interrelated picture of the physical and chemical properties of aminyl free radicals can now be at least partially outlined.

2. Generation

The first aminyl free radical was identified in 1911 by *H. Wieland*[1], who discovered that tetraphenylhydrazine *(3)* thermally dissociates at about 100 °C to form green diphenylaminyl radicals *(4)*, which can also be obtained by irradiation of the hydrazine with UV light[2, 3]. Difluoroaminyl *(6)* is likewise generated, and the thermal equilibrium with its dimer *(5)* was studied extensively[4].

$$(C_6H_5)_2N{-}N(C_6H_5)_2 \underset{}{\overset{\Delta \text{ or } h\nu}{\rightleftharpoons}} 2\ \dot{N}(C_6H_5)_2$$

(3) *(4)*

$$F_2N{-}NF_2 \overset{\Delta}{\rightleftharpoons} 2\ \dot{N}F_2$$

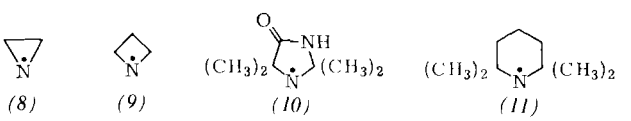
(5) *(6)*

A convenient source of many alkyl or aryl substituted aminyls is the thermal or photolytic decomposition of 2-tetrazenes *(7)*[5–7]. Dialkylaminyls are also obtained by photolyzing di-*tert*-butyl peroxide in the presence of dialkylaminophosphanes[8].

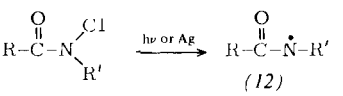
$$R_2N{-}N{=}N{-}NR_2 \xrightarrow{\Delta \text{ or } h\nu} 2\ NR_2 + N_2$$

(7)

The primary aminyl species $\dot{N}H_2$ was observed during photolysis of ammonia in an argon matrix[9]. Phenylaminyl generated by γ-irradiation of aniline was studied in an adamantane matrix[10]. This and other aryl substituted aminyls, *e.g.* the relatively stable 2,4,6-tri-*tert*-butylphenylaminyl[11] could also be observed in the flash photolysis of the parent amines[12]. N—H hydrogen abstraction of the parent amines by hydroxyl[13, 14] or *tert*-butoxyl radicals at reduced temperatures yielded a variety of interesting aminyls, *e.g.* the strained cyclic compounds 1-aziridinyl *(8)* and 1-azetidinyl *(9)*[15]. The sterically shielded aminyls *(10)* and *(11)*[16], acylaminyls *(12)*, and others were generated by photolysis of the parent *N*-chloramines[17–19] or by reacting these compounds with Ag or Ag^+[20].

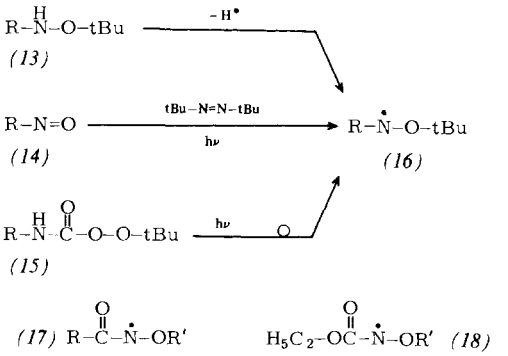


(8) *(9)* *(10)* *(11)*



(12)

A variety of *N*-alkoxyaminyls of type *(16)* were produced by photolyzing *O*-alkylhydroxylamines *(13)*[21], by abstraction of hydrogen from N—H of *(13)* with methyl or *tert*-butoxyl radicals[21] or with lead tetraacetate[22], or by trapping *tert*-butyl radicals with nitroso compounds *(14)*[23]. In addition, the same type of aminyls were observed by photolytic decomposition of *tert*-butyl *N*-alkylperoxycarbamates *(15)*[21] or by reaction of arylamines with *tert*-butoxyl radicals[21]. Similarly, *N*-alkoxyacylaminyls *(17)*[20] and *N*-alkoxyethoxycarbonylaminyls *(18)*[21] were obtained by hydrogen abstraction from the parent compounds.



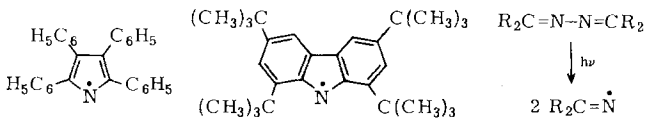
(13) *(14)* *(16)* *(15)*

(17) *(18)*

Stable aminyls are generally prepared by dehydrogenation of the parent amines with Ag_2O[24, 25] or PbO_2[26, 27], *e.g.* tetraphenyl-1-pyrrolyl *(19)*, or by electron transfer from the

[*] Prof. Dr. W. C. Danen
Department of Chemistry
Kansas State University
Manhattan, Kansas 66506 (USA)
Doz. Dr. F. A. Neugebauer
Max-Planck-Institut für Medizinische Forschung,
Abt. Organische Chemie
69 Heidelberg, Jahnstr. 29 (Germany)

amine anion with $K_3Fe(CN)_6$[28, 29], Br_2[30] or I_2[31]. An example is *(20)*[31].

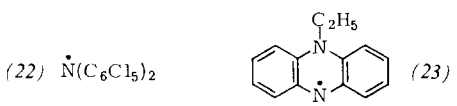


(19) *(20)* *(21)*

Iminyl radicals *(21)* are readily accessible by photolysis of azines[32] or solutions of ketimines in di-*tert*-butyl peroxide[33]. They are also observed during the thermal rearrangement of compounds such as *O*-phenylmethyleneamino-*N*,*N*-dimethylthiocarbamate[34], and appear frequently, when amines are subjected to high-energy irradiation[35-38].

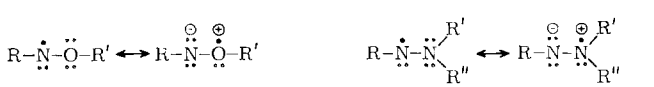
3. Reactivity

Most of the known aminyl free radicals are rather shortlived and are often observed by ESR only at reduced temperatures. Extremely shortlived aminyls, *e.g.* diacylaminyls, were only identified by trapping them with 2-methyl-2-nitrosopropane[19, 20, 39]. Steric shielding of the aminyl nitrogen is an important factor contributing to the stability of aminyl free radicals. The monomeric radicals *(20)* and *(22)* are typical examples for such a stabilization; bis(pentachlorophenyl)-aminyl *(22)* is stable almost indefinitely[40].



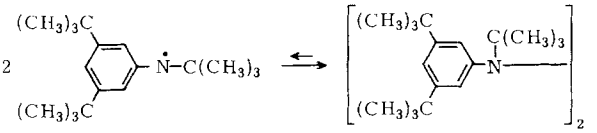
(22) *(23)*

The lifetime of aminyls is also significantly influenced by mesomeric stabilization of the radical. An example for an extensive delocalization of the unpaired electron is the deep red 10-ethyl-5-phenazinyl *(23)*[26]. The increased stability of R—Ṅ—OR′ aminyls as compared to the corresponding carbon derivatives R—Ṅ—R′ is obviously based on the contributing resonance form *(24b)*. This resonance is similar to the delocalization of the unpaired electron in hydrazyl radicals *(25)*, which can be considered as a special type of aminyl radical. In addition, the combination of electron donor and electron acceptor substituents within the same molecule, in the so-called "push-pull aminyls"[22, 25], seems to contribute to the stability of these radical species.



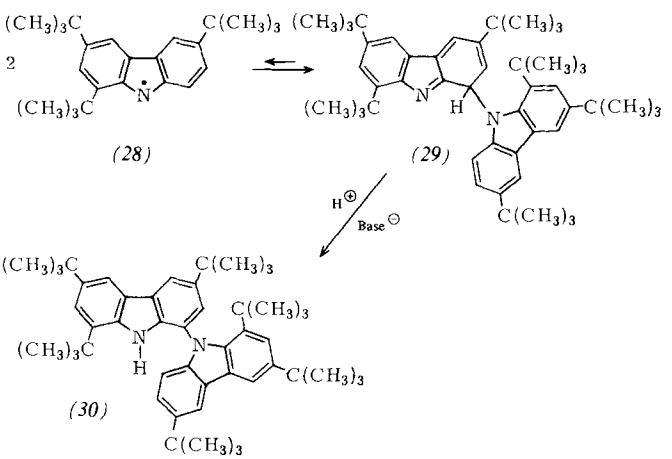
(24a) *(24b)* *(25a)* *(25b)*

If dimerization is not sterically prohibited aminyls generally couple to form hydrazines, which, in most cases, do not readily dissociate thermally. In the thermal dissociation of aryl substituted hydrazines not all substituents which afford increased delocalization of the unpaired electron increase the dissociation. The observed order of the effect of the *p*-substituents on tetraphenylhydrazine: $N(CH_3)_2 > OCH_3 > CH_3 > H > COOC_2H_5 > CN > NO_2$, indicates that the dissociation of aryl substituted hydrazines is predominantly determined by the hydrazine ground state, namely by the interaction of the nitrogen lone pair electrons with the *p*-substituents, and much less by the delocalization of the unpaired electron in the arylaminyl[3, 7, 41]. The rate of dissociation of tetraphenylhydrazine was measured by several different methods; however, the values obtained scatter considerably (E_a: 24.6—30.6 kcal/mol)[42-44]. Investigation of the equilibrium *(26)*⇌*(27)* gave $\Delta H^0 = 31.2$ kcal/mol and $\Delta S^0 = 73.6$ e. u. for the dissociation[45].



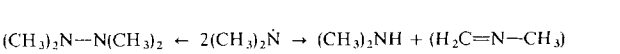
(26) *(27)*

Considerable steric shielding of the aminyl nitrogen can lead, as in *(29)*, to a C—N dimerization[31]. Traces of acids or bases isomerize *(29)* immediately and irreversibly to *(30)*. C—N structures analogous to *(29)* were also proposed for the dimers of 1-pyrrolyl and imidazolyl radicals[46]; it would seem that the formation of the disproportionation products in the thermal decomposition of tetraarylhydrazines probably occurs through shortlived kinetically preferred C—N dimers[47-50]. In special cases extensive delocalization of the unpaired electron in the aminyl can lead to formation of C—C dimers[28].

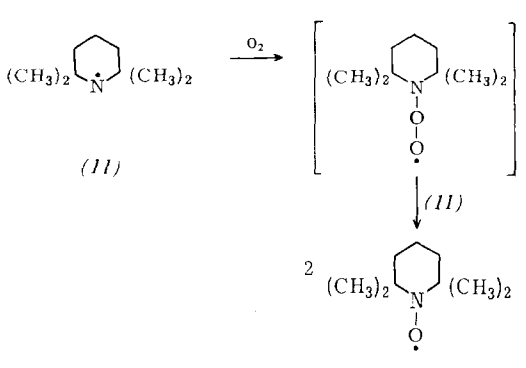


(28) *(29)* *(30)*

The other important self-reaction of aminyls is their disproportionation in which generally a β-hydrogen atom is transferred. In the absence of any other reactant, dimethylaminyl *(32)* yields not only the tetramethylhydrazine *(31)* but also dimethylamine *(33)* and the imine *(34)*[51-53]. *(34)* reacts further to give the trimer and polymers.



(31) *(32)* *(33)* *(34)*

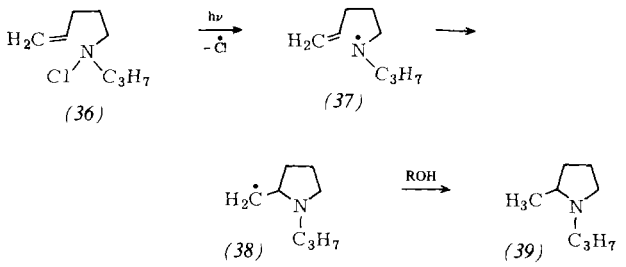


(11) *(35)*

Aminyl radicals combine with NO and also with carbon centered radicals[11]. When trapped with nitroso compounds stable nitroxides are formed which can easily be identified by ESR[19, 20, 39]. In poorly degassed aminyl samples nitroxides are frequently observed[7, 53]. Recent experiments[53] demonstrate that 2,2,6,6-tetramethyl-1-piperidyl *(11)* reacts rapidly and quantitatively with oxygen to yield the corresponding nitroxide *(35)*. This reaction may also occur with other aminyls. Stable aryl substituted aminyls, *e.g. (20)*, however, do not react with atmospheric oxygen.

Aminyl radicals are classified as feeble dehydrogenating agents, since they seem to abstract only activated hydrogens, *e.g.* from benzyl or allyl groups[54–56], and from thiols[57], *etc.* Aminyls (*e.g. (11)*), however, in which the self-reactions have been made more difficult by suitable substitution, readily abstract hydrogen from various solvents[53, 58].

Although aminyl radicals generally do not add to simple alkenes[54, 55, 59], dimethylaminyl radicals appear to react with ethylene[60]. Photolysis of the *N*-chloramine *(36)* in a neutral medium (methanol, isopropanol) yields the cyclic amine *(39)* as main product[61]. In a similar manner acylaminyls add intramolecularly to aromatic rings[62].



Aminyl radicals can also apparently effect S_H2 reactions at metal centers. When a solution of $(C_2H_5)_3Sb$ and 1,1,4,4-tetramethyl-2-tetrazene in toluene was irradiated at −81 °C the ethyl radical was observed by ESR spectroscopy[63]. *Ingold* and *Roberts* have tabulated other possible reactions of aminyls with *e.g.* Grignard reagents, with organomercury, and with organoaluminum compounds[64].

4. Electronic Properties and ESR Results

4.1. Alkylaminyl Radicals

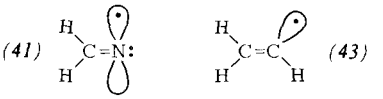
As mentioned in the introduction, aminyl free radicals are unique in that the central nitrogen atom possesses both an unpaired electron and a lone pair of electrons; they are therefore capable of existing in either a π or σ ground electronic state. For our purposes, a π radical is one in which the unpaired electron resides primarily in a nitrogen 2p orbital; a σ radical has the electron located predominantly in a hybrid orbital with a finite s component. Many aminyl radicals have been investigated by ESR and the available evidence is overwhelmingly in support of a π electronic ground state *(1)* for a variety of dialkylaminyl and related aminyl radicals. The data in Table 1 demonstrate that a^N and g are reasonably constant for rather diverse types of aminyl radicals. The a^N coupling constant should be sensitive to the nature of the orbital in which the unpaired electron resides and should become quite large for a hybrid orbital with any appreciable s character such as *(2)*, since the contribution from an electron in a nitrogen 2s orbital is ≈550 G[65]. However, recent results on bridgehead aminium radicals indicate that a^N may not be nearly so sensitive to electronic configuration as is a^{13C}[66].

Table 1. a^N Coupling Constants and g Values for Selected Nitrogen-Centered Aminyl Radicals.

		a^N [G]	g Value
(40) [9, 79]	$H_2\dot{N}$:	10.3–18.0 [a]	2.0048
(32) [6, 68]	$(CH_3)_2\dot{N}$:	14.78	2.0044
(6) [80]	$F_2\dot{N}$:	16	2.009
(8) [15]		12.52	2.0043
(41) [37, 81]	$H_2C{=}\dot{N}$:	9.5–15 [a]	2.0031
(42) [21]	$H_3C\dot{N}OCH_3$	14.30	2.0048

[a] a^N dependent on medium or matrix; lower values observed in more inert environment while higher values reflect amminium radical cation character resulting from hydrogen bonding to solvent or matrix.

The experimental values given in Table 1 are completely consistent with the unpaired electron residing in a p orbital on nitrogen, *i.e.* with a π-electron configuration, even though many structurally analogous carbon-centered radicals are known to be σ radicals. The small increase in a^N in going from *(40)* to *(32)* can be explained by an increase in bond angle (103.3° for $H_2\dot{N}$[67] as against ≈117° for $(CH_3)_2\dot{N}$[68]) and more effective π→σ spin polarization for a N—C bond as compared to a N—H bond[69]. A similar effect is noted in $\dot{C}H_3$ (a^{13C}=38.34 G[70]) versus $(CH_3)_3\dot{C}$ (a^{13C}=46.2 G[70]) although it is argued that the larger value for *tert*-butyl radical results from a non-planar geometry[71, 72]. Carbon-centered radicals, however, can readily place the unpaired electron in a hybrid orbital if electronically compelled. *Pauling*[73] has noted that the difference in electronegativity between the atoms M and X in a free radical of the form $\dot{M}X_3$ is the major factor in determining its geometry and the hybrid character of the orbital of the unpaired electron. An electronegative substituent which demands an enhanced p character in its bond to M forces s character into the orbital of the unpaired electron[74]. The large a^{13C} values observed for $\dot{C}HF_2$ (148.8 G[75]) and $\dot{C}F_3$ (271.6 G[75]) demonstrate the effect notably; yet a^N for $\dot{N}F_2$ *(6)* is insignificantly larger than a^N for $\dot{N}H_2$. Likewise, the cyclopropyl radical is known to be pyramidal about the central carbon[76] yet the related nitrogen-centered aziridinyl radical *(8)* exhibits an a^N value consistent with the unpaired electron residing in a pure 2p orbital on nitrogen.



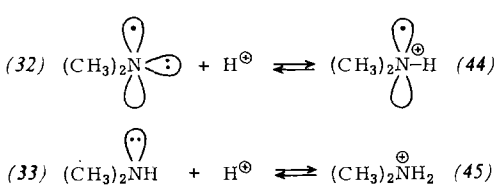
The vinyl radical *(43)* is known to be non-linear with respect to the C=C—H grouping (estimated HCC angle of 151°, a^{13C}=107.57 G[70], $a^{H_{trans}}$=68.5 G; $a^{H_{cis}}$=34.3 G[77]) yet the structurally related methaneiminyl radical *(41)* has its unpaired electron in a 2p orbital on nitrogen with both β hydrogens equivalent (a^H≈89 G[37]). Finally, a number of oxygen-substituted alkyl radicals have been shown to be pyramidal radicals[78], but attachment of an alkoxy group to an aminyl radical nitrogen, as in methoxy(methyl)aminyl *(42)* does not significantly perturb a^N.

Molecular orbital calculations in the INDO approximation for *(40)*[69], *(32)*[6], *(8)*[15], *(41)*[35], and *(42)*[21], are in complete accord with the conclusions drawn from the ESR a^N parameters, *i.e.* these aminyl radicals are π species with the unpaired electron density on nitrogen localized primarily in the 2p orbital.

The apparent differences between alkyl and aminyl radicals can be easily explained. When substituents on a trigonal carbon-centered radical require heavily p-weighted bonds to carbon, the residual s character on carbon is forced into the orbital possessing the unpaired electron. In aminyl radicals, however, the lone pair orbital acts as a ready sink for any such s character. It is, of course, energetically much more favorable to utilize the s character in such a two-electron orbital rather than in a singly occupied orbital.

In a detailed analysis of $\pi \rightarrow \sigma$ spin polarization in aminyl radicals, energy localized orbitals from INDO wave functions were scrutinized[69]. Analyses of localized lone-pair and bond-pair orbital polarizations revealed the bond pairs to be the major source of positive nitrogen atom (total s and p) spin density. Surprisingly, however, the nitrogen s orbital spin density gets its main contribution (positive) from the lone pair while the bond pairs give negative contributions.

The chemical behavior of dialkylaminyl radicals is consistent with a π electronic ground state. The pK_a of the conjugate acid *(44)* of the dimethylaminyl radical was determined as 7.0 ± 0.5[82], which may be compared with a value of 10.7 for the dimethylammonium ion *(45)*. The greater acidity of *(44)* is a result of the greater amount of s character in the lone pair orbital of the aminyl radical (approximately sp^2 hybridized) as compared to the more basic (approximately sp^3 hybridized) lone pair orbital of the amine. Simple dialkylamine radical cations, including *(44)*, have also been shown to posses π ground electronic configurations[68].



The electronegative nitrogen atom should make dialkylaminyl radicals electrophilic and evidence to this effect was obtained from a study of the relative rates of hydrogen abstraction at 136 °C from substituted toluenes by the dimethylaminyl radical which yielded $\rho = -1.08$ *versus* σ^+ constants[54]. No abstraction from toluene or cumene occurred at room temperature. The low reactivity of dialkylaminyl radicals in hydrogen abstractions is somewhat surprising since D (N—H) in dimethylamine has been determined as 95 kcal/mol[83]. The lone pair of electrons on alkylaminyl radicals is apparently quite effective in suppressing addition to simple olefins and aromatic systems[54, 84]. *Ab initio* calculations have demonstrated that there is a repulsive interaction between the nitrogen nonbonding electrons and the olefinic center which results in a calculated $E_a \approx 35$—40 kcal/mol for the addition of NH_2 to ethylene[85].

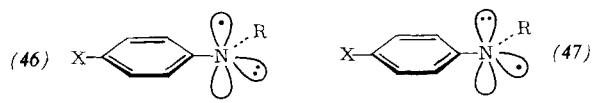
Lone pair-lone pair repulsions are apparently not significant for self-reactions of such radicals since dimethylaminyl and diethylaminyl radicals react at the diffusion-controlled limit, $(2 \pm 1) \times 10^9 \text{ mol}^{-1} \text{s}^{-1}$, to give combination and disproportionation products[53]. The bulkier diisopropylaminyl radical reacts with itself much more slowly, $(1.0 \pm 0.5) \cdot 10^7 \text{ mol}^{-1} \text{s}^{-1}$, as a result of an unfavorable entropy since $E_a \approx 0$[53].

4.2. Arylaminyl Radicals

Whereas alkylaminyl radicals possess π electronic ground states, the situation is more complex when an unsaturated substituent capable of resonance delocalization is attached to the central nitrogen atom. The arylaminyl radicals constitute such a system and two limiting cases can be envisioned for the effect of substituents on the aryl groups of such radicals:

1. The first case would be described by both electron-donor and electron-acceptor substituents delocalizing the unpaired electron. In terms of *Walter*'s criteria[86] for radical behavior, this case would exhibit class S ("same") behavior with both types of substituents causing a decrease in spin density at nitrogen.

2. The second case would be described by unpaired electron delocalization to donor substituents (—NR_2, —OR, —R, *etc.*) and nonbonding electron pair delocalization to acceptor substituents (—NO_2, —CN, —C(O)R, *etc.*). This would be a case of class O ("opposite") behavior since spin density at nitrogen would be decreased by spin delocalization onto donor substituents [*(46)*] and increased by spin localization at nitrogen due to delocalization of the nonbonding pair of



electrons onto acceptor substituents [*(47)*]. Paired electron delocalization from a p orbital *(47)* would result only if the difference in delocalization energy of two electrons *versus* one electron would be greater than the promotional energy of an electron from a nonbonding hybrid orbital to the spin bearing p orbital. This is illustrated graphically in Figure 1 which shows the crossover from the case in which the π orbital interacts only weakly with the attached aryl system to the situation in which strong resonance interaction lowers the energy of the π system to a level beneath σ.

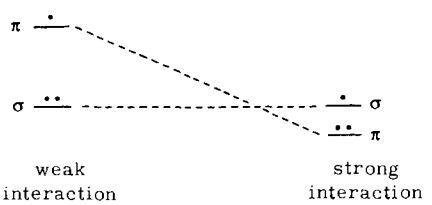


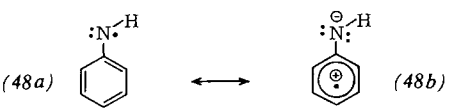
Fig. 1. Three nonbonding electrons on nitrogen interacting with an attached π system.

ESR spectroscopy should be easily capable of distinguishing between these two limiting cases. Two groups of workers have reported that substituted phenylaminyl radicals belong to Class S[7, 21]. *Nelsen et al.*[7], investigated substituted *N-tert*-butylphenylaminyl radicals and observed that all substituents decreased a^N although the effect was not pronounced as a^N varied only from 9.70G to 8.49G for the *N-tert*-butylphenylaminyl and *N-tert*-butyl-4-methoxyphenylaminyl radicals, respectively. Similar results were obtained for a series of substituted *N-tert*-butoxyphenylaminyl radicals and it was possible in addition to dissect a^N into spin delocalization and polar

contributions[21]. The a^N for the corresponding nitroxides were shown to correlate well with Hammett substituent constants indicative of Class O behavior which is commonly observed in this and other classes of radicals[87].

The phenylaminyl radical, itself, *(48)*, has been observed in an adamantane matrix[10, 88a]. The nitrogen coupling constant of 7.8 G is significantly smaller than those observed for the *N*-substituted phenylaminyl radicals discussed above and is even smaller than that observed for diphenylaminyl (8.80 G)[3]. This suggests that the Q(N) values relating the spin density on nitrogen to a^N for substituted aminyl radicals differ significantly and probably decrease in the order $Ar_2\dot{N}$ > $Ar\dot{N}H$ > $R_2\dot{N}$ > $R\dot{N}H$ > $H_2\dot{N}$. A Q(N) = 28.6 G was suggested for diphenylaminyl[3, 89] while Q(N) = 10.4 G must hold for $H_2\dot{N}$. The above ordering of Q(N) values is reasonable on the basis of decreasing group electronegativities resulting in less effective $\pi\rightarrow\sigma$ spin polarization but other effects also certainly influence the interplay between a^N and the spin density at nitrogen[69]. The futility of searching for a general Q(N) value applicable to all types of nitrogen-containing radicals hopefully has been realized and attempts have now been abandoned[90].

The phenylaminyl radical *(48)* and its monofluorinated derivatives have been compared to the isoelectronic benzyl ($C_6H_5\dot{C}H_2$) and phenoxyl ($C_6H_5\dot{O}$) radicals[88a, 88b]. The trends in the ESR parameters show that the overall spin density in the ring increases in going from benzyl to phenoxyl due to the increasing importance of an ionic resonance form which places an electron pair on the *exo* C, N, or O atom and an unpaired electron in the positively charged ring *(48b)*. INDO results showed that the aromatic ring becomes more nearly a regular hexagon in going from benzyl to phenylaminyl to phenoxyl.



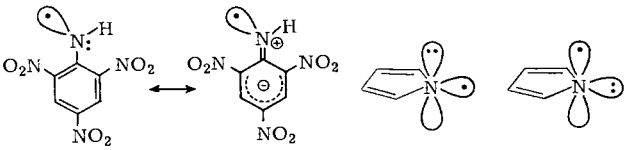
(48a) *(48b)*

Diphenylaminyl, *(4)*, and substituted diphenylaminyl radicals as well as the related 9-carbazolyl system *(49)* have been studied by ESR[3, 31]. The respective a^N values for these radicals, 8.80 and 6.9 G, reflect extensive delocalization of the unpaired electron into the aromatic rings; ρ_N was estimated as only 0.31 and 0.24, respectively, assuming $a^H = (-27\ \text{G})\rho_C$ which leads to a Q(N) ≈ 28.6 G[89]. The lower a^N and ρ_N values for *(49)* indicate more effective delocalization presumably as a result of its planar geometry.

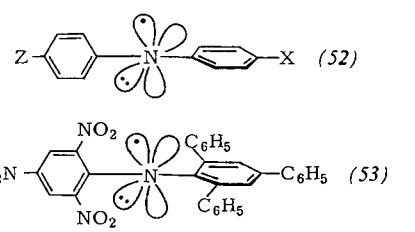
(4) *(49)*

The delocalized nature of the π arylaminyl radicals is reflected in their chemistry as evidenced by C—N and C—C dimerization as discussed in Section 3.

In summary, the evidence suggests that all arylaminyl radicals reported to date are π radicals but this may only reflect the systems investigated. Unlike alkylaminyl radicals, which by their nature must exist in a π electronic ground state, an arylaminyl radical could possess a σ ground state if a sufficiently electronegative group is attached to nitrogen to preferentially delocalize the lone pair of electrons. The picryl group *(50)* might be such a candidate. The pyrrolyl radical would retain an aromatic $(4n+2)$ sextet by adopting the σ structure *(51a)* but the observed a^N of 2.91 G strongly suggests a π ground electronic state *(51b)* for pyrrolyl and the related imidazolyl radical[91, 103].

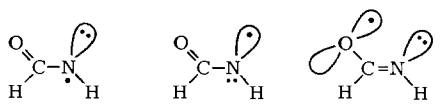

(50a) *(50b)* *(51a)* *(51b)*

In addition, redistribution of nitrogen s and p character in arylaminyl radicals as a function of substituents could also involve the bond orbitals and the interactions depicted in Fig. 1 and the above discussion has ignored this possibility. For example a rehybridization from a bent, approximately sp^2 geometry, to a linear sp configuration is a possibility for an unsymmetrically substituted diarylaminyl radical such as *(52)* if one ring possesses substituents (Z) capable of effectively delocalizing a pair of electrons and the other ring has groups (X) to stabilize a lone electron. Such a rehybridization apparently does not occur in simple arylaminyl radicals, however. The phenylaminyl radical, *(48)*, has an INDO calculated HNC angle of 111.5°[88a] and the symmetrical distribution of unpaired electron density in diphenylaminyl, *(4)*, precludes a geometry similar to *(52)*. An example, however, might be the aminyl *(53)*[29], and related species[25], in which the linear arrangement could be additionally favored by steric factors.


(52) *(53)*

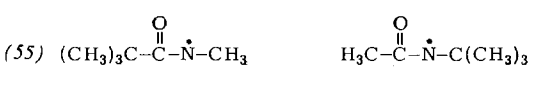
4.3. Acylaminyl Radicals

Attachment of a strongly resonance electron-withdrawing acyl group to nitrogen of an aminyl radical increases the likelihood for crossover to a σ ground electronic state (Fig. 1). In fact, the literature is confusing, with evidence purported for both structures in addition to rather frequent misassignments of ESR spectra. Theoretical calculations have not been definitive; a simple orbital perturbation method utilizing Hückel parameters suggests either a σ[92] or π[18] structure while the more rigorous although still approximate INDO method applied to formylaminyl yields a π structure for a CNH angle ≈120° *(54a)* but a σ_N structure *(54b)* for a CNH angle ≈ <180°[18]. (For a CNH angle = 180° the unpaired electron would be in a 2p orbital on nitrogen and could be considered a π radical even though the orbital is orthogonal to the molecular π system.) An unique σ_O configuration *(54c)* is also calculated to be only slightly less stable than the π state for a CNH angle of 114° although the calculated difference increases considerably upon replacing the hydrogen on nitrogen with a methyl group[18]. The geometries were only partially minimized with respect to energy in these calculations and, coupled with the inherent approximations in the INDO method, these results must be viewed with some caution.

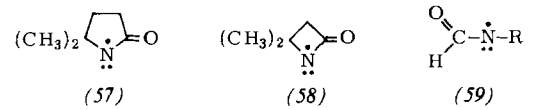


(54a), π *(54b), σ_N* *(54c), σ_O*

The first unequivocal ESR spectra of acylaminyl radicals were reported for *N*-methylpivaloylaminyl *(55)* and *N*-*tert*-butylacetylaminyl *(56)*[17]. The parameters $a^N = 15.0$ G, $a^{H_{CH_3}} = 29.3$ G observed for *(55)* can be compared with $(CH_3)_2\dot{N}$ ($a^N = 14.78$ G, $a^{H_{CH_3}} = 27.36$ G)[6] and $(CH_3)_2\dot{N}^{\oplus}H$ ($a^N = 19.28$ G, $a^{H_{CH_3}} = 34.27$ G)[68]. The ESR data appear best interpreted in terms of a π configuration with little delocalization of the unpaired electron onto the carbonyl group (similar to 2-oxoalkyl radicals)[93] although it is not possible to confidently exclude a σ_N configuration with a CNC angle $\approx < 180°$. Comparisons of the observed ESR parameters with INDO calculations are not definitive[18, 94].

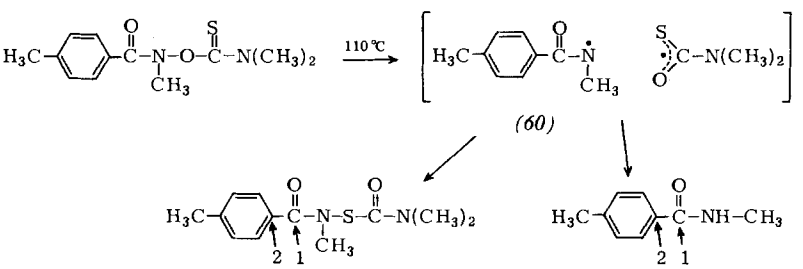


(55) *(56)*



(57) *(58)* *(59)*

The different CNC angular dependencies calculated for π and σ_N configurations make cyclic acylaminyls such as *(57)* and *(58)* attractive for ESR study but little success has greeted attempts to generate such species[18, 94]. Likewise the ESR spectrum of a formylaminyl *(59)* would be very informative by virtue of the large coupling constant a^H anticipated for a σ_N configuration ($a^H \approx 89$ G for RHC=N)[37] but attempts to generate *(59)* (R = *tert*-butyl) either in solution or in adamantane matrix[88] have not been fruitful[94]. However, a related ^{13}C-CIDNP study by *Brown* and *Lawson*[95] clearly favors a π description for the acylaminyl *(60)*. Strong polarization of C-1 is observed in both products, whereas no polarization of C-2 is found. A σ_N configuration would lead to polarization of both carbon positions.



(60)

Indirect evidence for a π ground state for *N*-alkylpivaloylaminyl radicals is available from a comparison of the β hydrogen hyperfine coupling constants of related nitrogen-centered radicals (Table 2)[94]. It has been demonstrated that the aminyls, $R_2\dot{N}$, and amine radical cations, $R_2\dot{N}^{\oplus}H$, are π radicals and geometry-optimized INDO calculations suggest CNC angles of 117° and 126°, respectively[68]. The dependence of a^{H_β} on alignment of the β hydrogen with the p orbital of the radical center is well documented[96] and the similarity in trends for the three types of radicals in Table 2 may be taken as evidence of a similar CNC angle and π ground state for the pivaloylaminyl radicals.

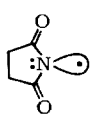
Table 2. Comparison of β Hydrogen Hyperfine Coupling Constants [G] of Related Nitrogen-Centered Radicals.

R	$R_2\dot{N}$ [6]	$R_2\dot{N}^{\oplus}H$ [66]	$(CH_3)_3C-\overset{O}{\overset{\|}{C}}-\dot{N}-R$ [94]
CH_3	27.36 *(32)*	34.27 *(44)*	29.30 *(55)*
C_2H_5	36.90	37.19	37.8
$(CH_3)_2CH$	14.31	21.7	22.10

Several *N*-alkoxyacylaminyl *(17)*[18] and *N*-alkoxy-*N*-ethoxycarbonylaminyl *(18)*[21] radicals have been identified by ESR. The a^N value of *ca.* 10.5—11.0 G, the *g* factor of 2.0056–2.0057 [for *(18)*], and interaction of the unpaired electron with the R and R′ groups indicate appreciable delocalization of spin and there is agreement that such radicals exist in a π ground state[18, 21].

The chemical behavior of simple acylaminyls does not definitely distinguish between a π and σ ground state. All reactions appear to occur at nitrogen[97] and the electron-withdrawing effect of the acyl substituent places acylaminyl radicals intermediate between neutral aminyl radicals and charged amminium radical cations in terms of electrophilicity. Simple acylaminyls undergo Hofmann-Löffler type intramolecular rearrangement and abstract allylic hydrogens but do not add readily to double bonds[84] unless electronegative α-substituents are present[98]. Acylaminyls derived from *N*-halourethanes (ROC(O)NR), and sulfonylaminyls (RSO_2NR) are apparently sufficiently electrophilic to undergo facile addition to unsaturated hydrocarbons[84].

The succinimidyl radical, a diacylaminyl radical, would appear a likely candidate for a σ ground electronic configuration *(61)*[92], although INDO calculations suggest a π or σ_O ground state[104]. Unfortunately, the ESR spectrum has not yet been reported but several spin-adducts to the nitrogen center in *(61)* have been observed[19, 105]. At one time *(61)* was thought to be the chain-carrying species in *N*-bromosuccinimide brominations. It was later shown that Br• played this role in most instances[99–101], but very recent work attributes the chain-carrying role to *(61)* under certain conditions[102]. The lowered selectivity of *(61)* as compared to Br• is consistent with a σ configuration, but a π or σ_O ground state cannot be ruled out.



(61)

To summarize, we have considered evidence for the various electronic configurations of aminyl radicals. All dialkylaminyl radicals have been shown to be π species. Diacylaminyl radicals may possess a σ ground state, although the experimental

evidence on this type of species is very meager. Arylaminyl and acylaminyl radicals are of an intermediate nature but evidence to date suggests a π configuration for both types of radicals; however appropriate substituents could presumably result in a σ electronic configuration.

We would like to acknowledge our able coworkers: Terry T. Kensler, Charles T. West, Roland W. Gellert (W.C.D.), Stephan Bamberger, and Hans Fischer (F.A.N.). Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, (W.C.D.) and to the Deutsche Forschungsgemeinschaft (F.A.N.) for partial support of this work.

Received: March 20, 1975 [A 87 IE]
German version: Angew. Chem. *87*, 823 (1975)

[1] *H. Wieland*, Liebigs Ann. Chem. *381*, 200 (1911).
[2] *G. N. Lewis* and *D. Lipkin*, J. Am. Chem. Soc. *64*, 2801 (1942).
[3] *F. A. Neugebauer* and *S. Bamberger*, Chem. Ber. *107*, 2362 (1974).
[4] *C. B. Colburn*, Chem. Br. *2*, 336 (1966).
[5] *H. Wieland* and *H. Fressel*, Liebigs Ann. Chem. *392*, 135 (1912).
[6] *W. C. Danen* and *T. T. Kensler*, J. Am. Chem. Soc. *92*, 5235 (1970).
[7] *S. F. Nelsen*, *R. T. Landis*, *L. H. Kiehle*, and *T. H. Leung*, J. Am. Chem. Soc. *94*, 1610 (1972).
[8] *R. W. Dennies* and *B. P. Roberts*, J. Organometal. Chem. *43*, C2 (1972).
[9] *S. N. Foner*, *E. L. Cochran*, *V. A. Bowers*, and *C. K. Jen*, Phys. Rev. Lett. *1*, 91 (1958).
[10] *R. V. Lloyd* and *D. E. Wood*, Mol. Phys. *20*, 735 (1971).
[11] *N. M. Atherton*, *E. J. Land*, and *G. Porter*, Trans. Faraday Soc. *59*, 818 (1963).
[12] *E. J. Land* and *G. Porter*, Trans. Faraday Soc. *59*, 2027 (1963).
[13] *P. Neta* and *R. W. Fessenden*, J. Phys. Chem. *75*, 738 (1971).
[14] *P. Wardman* and *D. R. Smith*, Can. J. Chem. *49*, 1869 (1971).
[15] *W. C. Danen* and *T. T. Kensler*, Tetrahedron Lett. *1971*, 2247.
[16] *T. Toda*, *E. Mori*, *H. Horiuchi*, and *K. Muruyama*, Bull. Chem. Soc. Jap. *45*, 1802 (1972).
[17] *W. C. Danen* and *R. W. Gellert*, J. Am. Chem. Soc. *94*, 6853 (1972).
[18] *T. Koenig*, *J. A. Hoobler*, *C. F. Klopfenstein*, *G. Hedden*, *F. Sunderman*, and *B. R. Russell*, J. Am. Chem. Soc. *96*, 4573 (1974).
[19] *C. Lagercrantz* and *S. Forshult*, Acta Chem. Scand. *23*, 708 (1969).
[20] *O. E. Edwards*, *D. H. Paskovich*, and *A. H. Reddoch*, Canad. J. Chem. *51*, 978 (1973).
[21] *W. C. Danen*, *C. T. West*, and *T. T. Kensler*, J. Am. Chem. Soc. *95*, 5716 (1973).
[22] *N. Negoita*, *R. Baican*, and *A. T. Balaban*, Tetrahedron Lett. *1973*, 1877.
[23] *W. Ahrens*, *K. Wieser*, and *A. Berndt*, Tetrahedron Lett. *1973*, 3141.
[24] *H. Wieland*, Ber. Dtsch. Chem. Ges. *48*, 1088 (1915).
[25] *A. T. Balaban*, *A. T. Frangopol*, *P. T. Frangopol*, and *N. Negoita*, Tetrahedron *23*, 4661 (1967).
[26] *H. J. McIlwain*, J. Chem. Soc. *1937*, 1704.
[27] *R. Kuhn* and *H. Kainer*, Biochim. Biophys. Acta *12*, 325 (1953).
[28] *R. Kuhn* and *F. A. Neugebauer*, Monatsh. Chem. *94*, 1 (1963).
[29] *L. Dulong* and *G. Baum*, Chem. Ber. *102*, 1626 (1969).
[30] *H. Zimmermann* and *H. Baumgärtel*, Z. Naturforsch. *18b*, 406 (1963); *K. Schilffahrt* and *H. Zimmermann*, Chem. Ber. *98*, 3124 (1965).
[31] *F. A. Neugebauer*, *H. Fischer*, *S. Bamberger*, and *H. O. Smith*, Chem. Ber. *105*, 2694 (1972).
[32] *M. Kamachi*, *K. Kuwata*, and *S. Murahashi*, J. Phys. Chem. *75*, 164 (1971).
[33] *D. Griller*, *G. D. Mendenhall*, *W. van Hoof*, and *K. U. Ingold*, J. Am. Chem. Soc. *96*, 6068 (1974).
[34] *R. F. Hudson*, *A. J. Lawson*, and *K. F. Record*, J. C. S. Chem. Commun. *1974*, 488.
[35] *D. E. Wood*, *R. V. Lloyd*, and *D. W. Pratt*, J. Am. Chem. Soc. *92*, 4115 (1970).
[36] *T. Richerzhagen* and *D. H. Volman*, J. Am. Chem. Soc. *93*, 2062 (1971).
[37] *M. C. R. Symons*, Tetrahedron *29*, 615 (1973).
[38] *W. C. Danen* and *C. T. West*, J. Am. Chem. Soc. *96*, 2447 (1974).
[39] *S. Terabe* and *R. Konaka*, J. Am. Chem. Soc. *91*, 5655 (1969).
[40] *M. Ballester*, *J. Castaner*, and *S. Olivella*, Tetrahedron Lett. *1974*, 615.
[41] *H. Wieland*, Ber. Dtsch. Chem. Ges. *48*, 1078 (1915).
[42] *C. K. Cain* and *F. Y. Wiselogle*, J. Am. Chem. Soc. *62*, 1163 (1940).
[43] *V. Franzen*, Liebigs Ann. Chem. *604*, 251 (1957).
[44] *B. S. Tanaseichuk*, *L. A. Zhivechkova*, and *A. Y. Ermishov*, Zh. Org. Khim. *8*, 758 (1972); *L. A. Zhivechkova*, *B. S. Tanaseichuk*, and *A. Y. Ermishov*, *ibid.* *7*, 2379 (1971); Chem. Abstr. *77*, 33785c (1972); *76*, 58605m (1972).
[45] *S. F. Nelsen* and *R. T. Landis*, J. Am. Chem. Soc. *95*, 8707 (1973).
[46] *D. M. White* and *J. Sonnberg*, J. Am. Chem. Soc. *88*, 3825 (1966).
[47] *P. Welzel*, Chem. Ber. *103*, 1318 (1970).
[48] *P. Welzel*, *L. Günther*, and *G. Eckhardt*, Chem. Ber. *107*, 3624 (1974).
[49] *R. F. Bridger*, J. Org. Chem. *35*, 1746 (1970).
[50] *F. A. Neugebauer* and *H. Fischer*, Chem. Ber. *104*, 886 (1971).
[51] *J. S. Watson*, J. Chem. Soc. *1956*, 3677.
[52] *F. O. Rice* and *C. J. Grelecki*, J. Am. Chem. Soc. *79*, 2679 (1957).
[53] *J. R. Roberts* and *K. U. Ingold*, J. Am. Chem. Soc. *95*, 3228 (1973).
[54] *C. J. Michejda* and *W. P. Hoss*, J. Am. Chem. Soc. *92*, 6298 (1970).
[55] *B. R. Cowley* and *W. A. Waters*, J. Chem. Soc. *1961*, 1228.
[56] *K. M. Johnston*, *G. H. Williams*, and *H. J. Williams*, J. Chem. Soc. *B 1966*, 1114.
[57] *T. J. Wallace*, *J. J. Mahon*, and *J. M. Kelliher*, Nature *206*, 709 (1965).
[58] *F. A. Neugebauer* and *S. Bamberger*, Chem. Ber. *105*, 2058 (1972).
[59] *R. S. Neale*, *N. L. Marcus*, and *R. G. Schepers*, J. Am. Chem. Soc. *88*, 3051 (1968).
[60] *A. Good* and *J. C. J. Thynne*, J. Chem. Soc. *B 1967*, 684.
[61] *J.-M. Surzur*, *L. Stella*, and *P. Tordo*, Tetrahedron Lett. *1970*, 3107.
[62] *S. A. Glover* and *A. Goosen*, J. C. S. Perkin I, *1974*, 2353.
[63] *A. G. Davies*, *S. C. W. Hook*, and *B. P. Roberts*, J. Organometal. Chem. *22*, C37 (1970).
[64] *K. U. Ingold* and *B. P. Roberts*: Free-Radical Substitution Reactions. Wiley-Interscience, New York 1971, pp. 20, 45, 67, 145.
[65] *J. E. Wertz* and *J. R. Bolton*: Electron Spin Resonance. McGraw-Hill, New York 1972, Table C (inside back cover).
[66] *W. C. Danen* and *R. C. Rickard*, J. Am. Chem. Soc. *97*, 2303 (1975).
[67] *K. Dressler* and *D. A. Ramsay*, Phil. Trans. Roy. Soc. (London) *A 251*, 553 (1959).
[68] *W. C. Danen* and *R. C. Rickard*, J. Am. Chem. Soc. *94*, 3254 (1972).
[69] *K. F. Purcell* and *W. C. Danen*, J. Am. Chem. Soc. *94*, 7613 (1972).
[70] *R. W. Fessenden*, J. Phys. Chem. *71*, 74 (1967).
[71] *D. E. Wood*, *L. F. Williams*, *R. F. Sprecher*, and *W. A. Lathan*, J. Am. Chem. Soc. *94*, 6241 (1972).
[72] *M. C. R. Symons*, Tetrahedron Lett. *1973*, 207.
[73] *L. Pauling*, J. Chem. Phys. *51*, 2767 (1969).
[74] *H. Bent*, Chem. Rev. *61*, 275 (1961).
[75] *R. W. Fessenden* and *R. H. Schuler*, J. Chem. Phys. *43*, 2704 (1965).
[76] *R. W. Fessenden* and *R. H. Schuler*, J. Chem. Phys. *39*, 2147 (1963).
[77] *E. L. Cochran*, *F. J. Adrian*, and *A. A. Bowers*, J. Chem. Phys. *40*, 213 (1963).
[78] *A. Hudson* and *K. D. J. Root*, Tetrahedron *25*, 5311 (1969).
[79] *K. V. S. Rao* and *M. C. R. Symons*, J. Chem. Soc. *A 1971*, 2163.
[80] *C. B. Colburn*, *R. Ettinger*, and *F. A. Johnson*, Inorg. Chem. *3*, 455 (1964).
[81] *K. V. S. Rao* and *M. C. R. Symons*, J. Chem. Soc. *A 1969*, 1942.
[82] *R. W. Fessenden* and *P. Neta*, J. Phys. Chem. *76*, 2857 (1972).
[83] *D. M. Golden*, *R. K. Solly*, *N. A. Gac*, and *S. W. Benson*, J. Am. Chem. Soc. *94*, 363 (1972).
[84] *R. S. Neale*, Synthesis *1971*, 1.
[85] *S. Shih*, *R. J. Buenker*, *S. D. Peyerimhoff*, and *C. J. Michejda*, J. Am. Chem. Soc. *94*, 7620 (1972).
[86] *R. I. Walter*, J. Am. Chem. Soc. *88*, 1923 (1966).
[87] *E. G. Janzen*, Acc. Chem. Res. *2*, 279 (1969).
[88a] *R. V. Lloyd* and *D. E. Wood*, J. Am. Chem. Soc. *96*, 659 (1974).
[88b] *P. Neta* and *R. W. Fessenden*, J. Phys. Chem. *78*, 523 (1974).
[89] *E. W. Stone* and *A. H. Maki*, J. Chem. Phys. *39*, 1635 (1963).
[90] *J. Q. Adams*, *S. W. Nicksic*, and *J. R. Thomas*, J. Chem. Phys. *45*, 654 (1964).
[91] *E. M. Evleth*, *P. M. Horowitz*, and *T. S. Lee*, J. Amer. Chem. Soc. *95*, 7948 (1973) calculate by INDO a π configuration for *(51)*; these results are unreliable, however [18].
[92] *E. Hedaya*, *R. L. Hinman*, *V. Schomaker*, *S. Theodoropulos*, and *L. M. Kyle*, J. Am. Chem. Soc. *89*, 4875 (1967).
[93] *D. M. Camaioni*, *H. F. Walter*, and *D. W. Pratt*, J. Am. Chem. Soc. *95*, 4057 (1973).
[94] *W. C. Danen* and *R. W. Gellert*, unpublished.
[95] *C. Brown* and *A. J. Lawson*, Tetrahedron Lett. *1975*, 191.
[96] Vgl. [65], S. 169, 170.
[97] *Y. L. Chow* and *T. C. Joseph*, Chem. Commun. *1969*, 490.
[98] *D. Tochard* and *J. Lessard*, Tetrahedron Lett. *1971*, 4425.
[99] *R. E. Pearson* and *J. C. Martin*, J. Am. Chem. Soc. *85*, 364 (1963).
[100] *G. A. Russell*, *C. DeBoer*, and *K. Desmond*, J. Am. Chem. Soc. *85*, 365 (1963).
[101] *C. Walling*, *A. L. Rieger*, and *D. D. Tanner*, J. Am. Chem. Soc. *85*, 3129 (1963).
[102] *J. G. Traynham* and *Y.-S. Lee*, J. Am. Chem. Soc. *96*, 3590 (1974); *J. C. Day*, *M. J. Lindstrom*, and *P. S. Skell*, *ibid.* *96*, 5616 (1974).
[103] *A. Samuni* and *P. Neta*, J. Phys. Chem. *77*, 1629 (1973).
[104] *T. Koenig* and *R. A. Wielesek*, Tetrahedron Lett. *1975*, 2007.
[105] *G. R. Chalfont*, *M. J. Perkins*, and *A. Horsfield*, J. Chem. Soc. *B 1970*, 401.

En Route to Multisurface Chemistry[**]

By Gerhard Quinkert[*]

Dedicated to Professor Werner Schultheis

This article considers what happens when the energy required for a compound to react is supplied by an irradiation lamp instead of by a Bunsen burner. For this purpose real examples are selected from three typical groups of cases. The respective answers obtained should indicate significant moves in organic photochemistry which may be expected to affect the further development of chemistry as a whole in the near future. During this *tour d'horizon* particular attention is paid to photochemical processes in solids or solvent matrices, light-induced reactions are especially emphasized as key reactions in (natural product) syntheses, and a strong case is made for interpreting the reactions of electronically excited molecules in terms of Salem correlation diagrams.

1. Trends in Organic Photochemistry

1.1. It all Began with *Ciamician*[2]

No-one has yet spoken so lucidly about the photochemistry of the future as *Ciamician*[3]. Even more impressive than his pioneering experimental discoveries are his visions of the practical exploitation of sunlight. Adopting the language of the prophet describing the land flowing with milk and honey, *Ciamician* sought to instigate the long treck through the wildernis of the chemistry of electronically excited molecules:

> In ordinary organic chemistry the reactions often take place in some definite way: but the photochemical reactions often furnish surprises and proceed along quite different lines[3].

And:

> Reactions caused by light are so many that it should not be difficult to find some which are of practical value. I do not believe that the industries should wait any longer before taking advantage of the chemical effects produced by light[3].

The advance through the first half of this century must have led to valuable findings if one can say:

> Preparative photochemistry has a place in general synthesis. We are at the beginning of a photochemical renaissance[4].

Nevertheless, a crucial component of the original hopes seems to have remained unfulfilled:

> The synthesis of industrial chemicals is an area in which the impact of photochemistry might have been expected to be large. In fact, the triumphs are few[5].

One reason is surely to be found in the slow development of suitable radiation sources, and a more important one in the difficulties attending the mechanistic interpretation of photochemical reactions.

What are the future prospects of organic photochemistry?

1.2. Future Areas of Development

No publicity campaigns are necessary to encourage development of photochemical reactions to a stage where they are synthetically valuable in the laboratory or acquire economic significance in industry (cf. Fig. 1). This may be left to the growing pressure exerted by well-trained photochemists and the maturing realization that the immense energy source sunlight will have to be harvested to meet the global energy deficit[6].

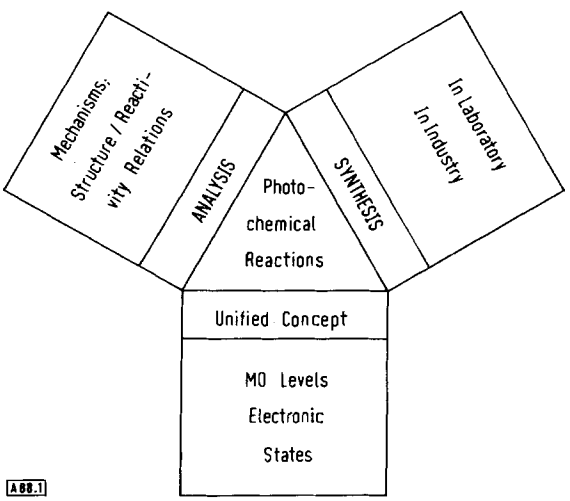


Fig. 1. Work on photochemical reactions will benefit three areas in the near future: Intensive and extensive analysis of reaction mechanisms will lead to structure/reactivity relations which can account for the hitherto neglected distinctions between compounds in their diverse electronic states. The number of synthetically utilizable reactions will increase in both preparative and industrial photochemistry. Finally, further development of unified concepts pertaining to the dynamics of reacting molecules may be expected which will embrace structural changes occurring on various energy surfaces reaching out from the platform of the molecular orbitals or especially that of the electronic states.

Directed utilization of photochemical reactions requires a thorough knowledge of fundamental mechanisms. Analysis of such processes (Fig. 1) considers the product that can

[*] Prof. Dr. G. Quinkert
Institut für Organische Chemie der Universität
Laboratorium Niederrad
6 Frankfurt am Main, Theodor-Stern-Kai (Germany)

[**] 8th Essay on Light-Induced Reactions; based on an address delivered to the GDCh Specialist Group "Photochemie" at Constance (Germany) on November 22, 1974. Ref. [1] is to be regarded as the 7th Essay.

be isolated in a specific case; the intermediary compounds, the kinetic stability of which is often so low that they defy observation, let alone isolation, under normal conditions; and electronically excited compounds occurring during the photochemical primary process. In keeping with the tradition of chemical dynamics, correlations between the structure of the electronically excited states and their respective reactivity constitute a principal aim of such analysis.

Apropos reactivity! Although this concept is unequivocally tied to the rate of a particular elementary reaction, it often happens that the photochemical efficiency, *i.e.* the quantum yield, or sometimes even the chemical yield is erroneously employed as a measure of reactivity[7]:

> While there is a tendency in photochemistry, at its present stage of development, to utilize quantum yields as a measure of reactivity, quantum yields really afford only the tendency of the excited state to form product relative to all other competing processes. Ideally one should have the absolute rate[8].

Photochemical literature not only contains an above-average proportion of undigested facts—as may of course be considered much more likely for an area of overlap between several sub-disciplines than for the traditional fields of chemistry—but suffers from a proliferation of too rapidly published material[9]:

> Photochemistry often seems a speculative science when mechanistic details come to be discussed. Ideally mechanistic schemes should be based on kinetic and quantum yield measurements and experimental variables should be altered one at a time while the others are held constant; however, this can take many months and when photochemists discover something new many of them find it difficult to control their impatience to communicate the discovery as soon as possible. As a result some suggested 'mechanisms' are based on very inadequate evidence[10].

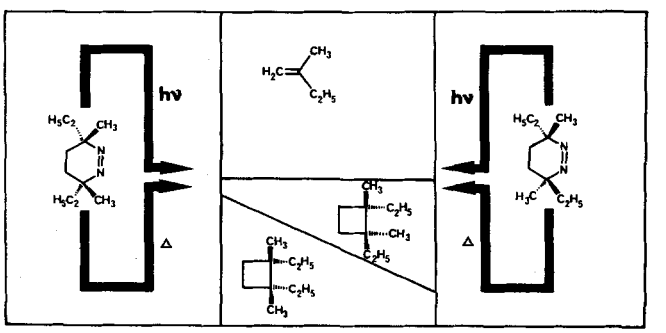
Mechanistic analysis of photochemical reactions has noticeably narrowed the formerly gaping deficit in our knowledge during the past 15 years, and the problem of the availability of inexpensive radiation sources no longer plays a serious role nowadays. Thus the prospects for industrial photochemistry have significantly improved.

Nevertheless, the most important contribution photochemistry will have made tomorrow to the development of organic chemistry as a whole probably lies in the third field of development (cf. Fig. 1): in the evolution of a unified theory of the chemical reaction in which the reactant and primary product may occur in the electronic ground state or both, or just one of them, in an electronically excited state.

Just as stereochemistry acquired a new dimension through the appearance of conformational analysis and dynamic stereochemistry took its place alongside static stereochemistry, *unisurface chemistry* is expanding into *multisurface chemistry*. This statement requires some explanation. However, we shall first employ three exemplary cases to raise and answer a number of questions which take account of the fact that an irradiation lamp can be used in place of a Bunsen burner to initiate a chemical reaction.

2. Case I: Thermoproducts and Photoproducts of a Reactant Are Identical

The first case is characterized by the appearance of the same reaction products, regardless of whether heat or light has been used to energize the respective reactants. The example of denitrogenation of stereoisomeric azo compounds (cf. Fig. 2) comes from *Bartlett*'s laboratory[11]. The quantitative composition of the complex hydrocarbon product, which can be seen in the central portion of Figure 2, depends solely upon the configuration of the reactant and not upon the kind of energy used for nitrogen extrusion. Both procedures—the thermo- and photo-chemical ones—apparently lead in the primary reaction step to the same difunctional intermediate, the secondary reactions of which—fragmentation or coupling—furnish the olefin and the cyclobutane derivative.



A88.2

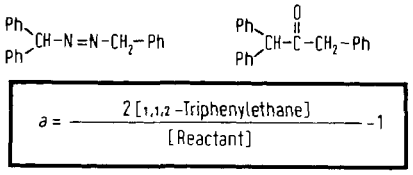
Fig. 2. Thermal and photochemical denitrogenation of the stereoisomeric 1,2-diaza-3,6-dimethyl-3,6-diethylcyclohexenes [11].

Since the internal mobility of the difunctional intermediate is affected by the viscosity of the reaction medium we may expect drastic changes in the product composition if such fragmentations are performed at low temperature, in a plastic film, or in the crystalline phase[12] instead of under normal conditions, *i.e.* under conditions which should not oppose a light-induced denitrogenation but might obstruct a heat-induced reaction.

2.1. Crystal Lattice-Induced Cage Effect Determines Simplicity of Photoproduct

Photo-denitrogenation or -decarbonylation of the compounds shown in Figure 3 affords hydrocarbon products whose composition becomes more and more simple the greater the role played by the cage effect during the combination of transiently formed radicals[13].

Irradiation of a benzene solution of 1,1,3-triphenylacetone at 13 °C with 313-nm light gives a hydrocarbon mixture containing 1,2-diphenylethane, 1,1,2-triphenylethane, and 1,1,2,2-tetraphenylethane in the ratio 1:2:1, *i. e.* no coupling of phenylated methyl radicals takes place in the solvent cage: $a=0$. Irradiation of the crystalline compound under otherwise identical conditions leads exclusively to 1,1,2-triphenylethane: $a=1$. That the carbonyl compound reacts more sensitively than the corresponding azo compound to the crystal lattice-



Conditions / Reactant	In Benzene		Crystal	
	a	*T* [°C]	*a*	*T* [°C]
Azo-Compound	0.28	27	1.0	-196
Carbonyl-Compound	0.0	13	1.0	13

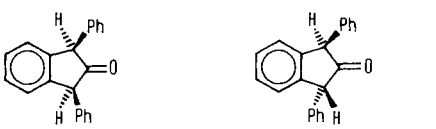
A 88.3

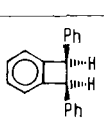
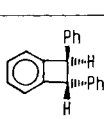
Fig. 3. The cage effect is enhanced when the light-induced denitrogenation of diphenylmethylazotoluene or the light-induced decarbonylation of 1,1,3-triphenylacetone occurs in the crystalline phase instead of in solution [13].

induced cage effect has its reason in the stepwise liberation of CO as opposed to the one-step release of N_2.

2.2. Crystal Lattice-Induced Viscosity Effect Determines Stereoselectivity of Product Formation

If a diradical appears as an intermediate instead of a radical pair during analogous fragmentations, an increase in stereoselectivity is to be expected on transition from solution to the crystalline phase owing to the increase in viscosity. This postulate is confirmed in convincing manner by the photodecarbonylation of the configurationally isomeric 2-indanone derivatives depicted in Figure 4 in ether and, under otherwise identical conditions, in the crystalline state[13].



Product / Reactant			Conditions
cis-Ketone	11	89	Solution
	95	5	Solid
trans-Ketone	5	95	Solid
	13	87	Solution

A 88.4

Fig. 4. The stereoselectivity of photodecarbonylation is enhanced when the stereoisomeric 1,3-diphenyl-substituted 2-indanone derivatives react in the crystalline phase instead of in solution [13].

Here we are dealing only with the restricted mobility of primary reaction products which can, in principle, also be effected by a highly viscous non-crystalline medium. Since a crystalline network

- contains the individual molecules in a low number of conformations and in particular mutual arrangements,
- may be chiral, even in cases of molecular achirality,

the specific effects that a solid of particular crystal structure can exert on a reaction course should at least be mentioned[12].

Light-induced reactions command special interest in organic solid state chemistry because

- the "reagent light" can penetrate to sufficient depth in the crystal lattice
- they are characterized by low activation enthalpies such that they proceed at temperatures for which fusion of the crystals can be ruled out.

If, as in the first case, the light- and the heat-induced reaction lead to the same kind of product then the thermal reaction will generally be preferred. This can change if the photoreaction occurs under conditions permitting selection of particular compounds from among the range of possible products.

3. Case II: Two Electronic Isomers of a Reactant Afford Two Different Products

Thermo- and photochemical reaction of a compound generally yield different kinds of products. Tetraphenyl-*o*-quinonodimethane may serve to illustrate this second case (see Fig. 5)[14]. Under the mildest possible conditions for a thermal reaction the kinetically unstable compound cyclizes exclusively and completely to tetraphenylbenzocyclobutene. On exposure to 519-nm-light at the temperature of liquid nitrogen, however, the *o*-quinodimethane derivative cyclizes exclusively and completely to triphenylisodihydroanthracene.

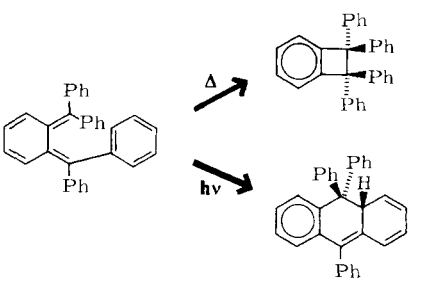


Fig. 5. The diverse products of thermo- and photocyclization of 7,7,8,8-tetraphenyl-*o*-quinodimethane [14].

3.1. A Semantic Excursion: Electronic and Spin Isomerism

Tetraphenyl-*o*-quinodimethane in its electronic ground state and tetraphenyl-*o*-quinodimethane in its first excited state accordingly display different reaction behavior. Both species possess the same constitution but most probably differ in their geometry; they could fittingly be described as stereoisomers but one is well advised to abstain from doing so. Stereoisomerism and constitutional isomerism refer to the topological aspect but not to the electronic aspect of molecular structure. The terms "constitutional isomer" and "stereoisomer" satisfy the organic chemist's need to classify structural isomers altogether, which does not, of course, preclude stereoisomers' being further subdivided unambiguously into enantiomers and diastereomers, or equivocally[15] into configurations and conformations (cf. Fig. 6). However, the organic photochemist lacks a clear delineation of those structures which differ in their electronic state, which will henceforth be designated as electronic isomers; moreover, he lacks a subclassification of electronic isomers which differ in their spin state, which will be termed spin isomers (Fig. 6). Accordingly, *e.g.* acetone in the electronic ground state, acetone in the first excited state, and acetone in the second excited

state are three related electronic isomers; acetone in the first excited singlet state and acetone in the first excited triplet state are the two corresponding spin isomers.

Structural Isomerism

Topological	Aspect	Electronic
Constitutional Stereo	Isomerism	Electronic Spin

A 86.6

Fig. 6. Classification of structural isomers taking account of topological or electronic aspects.

Turro put forward a similar proposal several years ago:

> For each excited electronic configuration there exist two states, S_1 and T_1, that are "electronic isomers" of the ground state. The singlet and triplet are "spin isomers" of each other[16].

The term "electronic isomerism" appeared in *Staab*'s "Einführung in die theoretische organische Chemie", but was used in the sense of our spin isomerism rather than our electronic isomerism:

> Der Singulettzustand und der Triplettzustand stehen zueinander im Verhältnis der "Elektronenisomerie", für die ein diskontinuierlicher Übergang zwischen zwei selbständigen, durch ihre Elektronenkonfiguration unterschiedenen Molekelformen charakteristisch ist. Diese Elektronenisomerie ist also etwas ganz anderes als die Mesomerie[17].

Recent publications by *Dewar et al.* employ the term "orbital isomerism" in the sense of our spin isomerism:

> A general type of isomerism which may be termed orbital isomerism involves alternative occupation of distinguishable orbitals by electrons[18].

Since observables of a system, *e. g.* the number and structure of isomers of the compound CH_2, are to be correlated with the relevant state it is to be feared that widespread use of the concept of "orbital isomerism" for classification would above all promote division in the ranks of chemists.

Inclusion of this semantic discourse might seem rather strange. However, anybody sharing *Wittgenstein*'s view that language is the vehicle of thought will desire a clear mode of expression in language and formula in the chemistry of electronically excited compounds, commonly known as photochemistry. Students and taxpayers will warmly welcome such a move. The former because they will register fewer "bumps inflicted on the mind by running up against the frontiers of language"[19]; the latter because they would be grateful for any help, however slight, in seeing their own advantage in financing fundamental research.

With that in mind it hardly seems necessary to mention that the formulation of the two cyclization reactions accounts not only for the *o*-quinodimethane derivative in the electronic ground state but also—at least symbolically—for the electronic isomer which arises on absorption of light (see Fig. 7). In general, its electronic structure is uncertain *a priori*; however, there can be little doubt in the present case. The long-wavelength absorption of the conjugated unsaturated alternant hydrocarbon—maximum at 519 nm—corresponds to an electronic transition from the highest occupied MO to the lowest unoccupied MO in the Kasha notation[20], *i. e.* to a π^*,π transition in this case.

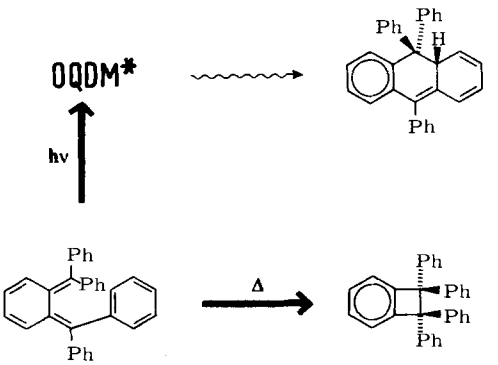
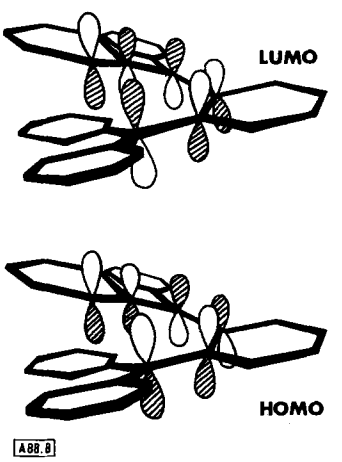


Fig. 7. Electronic isomers of 7,7,8,8-tetraphenyl-*o*-quinodimethanes in the ground state and first excited state (OQDM*) undergo regioselective cyclization to give constitutionally isomeric products [14].

3.2. Matrix Photochemistry and Matrix Absorption Spectroscopy at Low Temperatures

At first glance the electrocyclic reactions of tetraphenyl-*o*-quinodimethane would appear open regarding both the stereochemistry of the mode of cyclization—conrotatory or disrotatory—and the constitution of the cyclization product—benzocyclobutene or isodihydroanthracene derivative. In fact, the two electronic isomers each cyclize with a remarkable regioselectivity which can be intelligibly deduced from the nodal properties of their frontier orbitals (Fig. 8).



A 88.8

Fig. 8. The regioselectivity of thermo- and photocyclization can be deduced from the nodal properties of the frontier orbitals of 7,7,8,8-tetraphenyl-*o*-quinodimethane [14].

Before viewing these pictures in detail it should be borne in mind that tetraphenyl-*o*-quinodimethane possesses a helical structure owing to steric hindrance between the two inwardly oriented phenyl groups. As a result conrotatory cyclization will be favored over the disrotatory mode because of a diminished interaction between these phenyl groups. Under this condition it follows from the nodal properties of the HOMO that the electronic isomer of the ground state closes to give a four-membered ring; the nodal properties of the

LUMO show that the electronic isomer of the π^*,π excited state furnishes a new six-membered ring.

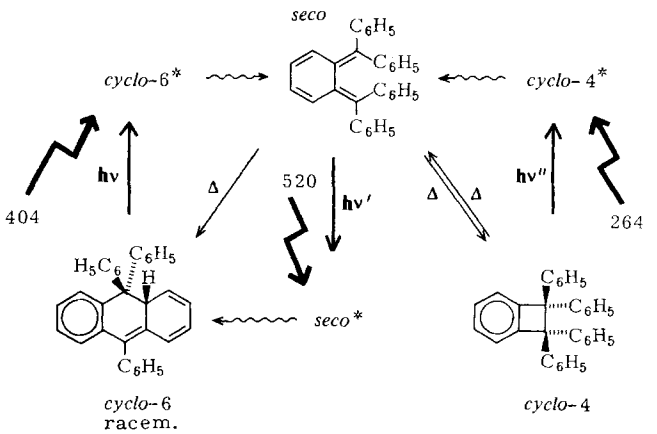


Fig. 9. A complex photochromic system the components of which were established from their characteristic absorption (see Fig. 10) and their dynamic interrelationships by kinetic spectrophotometry (see Fig. 12) [14].

As shown in Figure 9, there are more mutual interrelations between the *seco* isomer and its two *cyclo* isomers than have been mentioned so far. Instead of delving further into these let us restrict our attention to the kinetic stability of the three constitutional isomers. Only the yellow isodihydroanthracene derivative can be handled at room temperature. The colorless benzocyclobutene derivative and the purple *o*-quinodimethane isomer are accessible to conventional methods of study only below -25 and -110 °C respectively. In such cases, low temperature glassy media in which compounds kinetically unstable at room temperature can be generated by light-induced processes, preserved by freezing, and identified by spectroscopy prove to be extremely valuable tools in the photochemist's workshop.

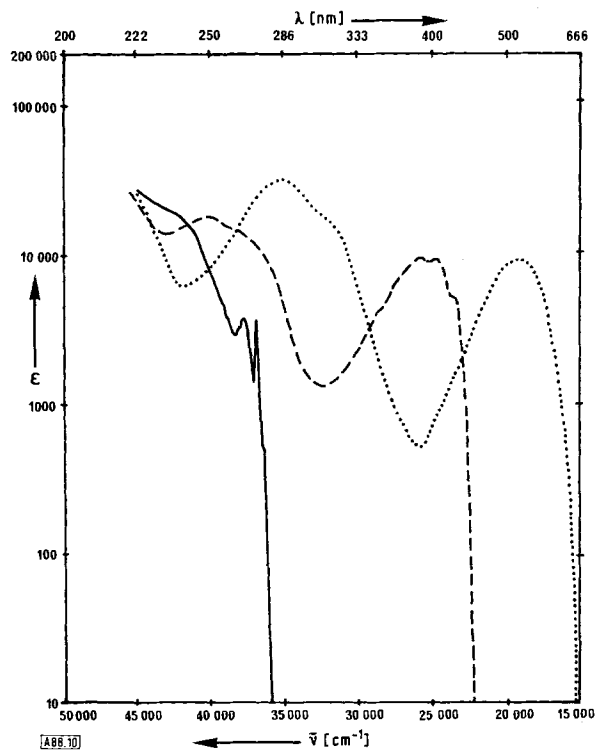


Fig. 10. Electronic absorption spectra of tetraphenylbenzocyclobutene (——), triphenylisodihydroanthracene (------), and tetraphenyl-*o*-quinodimethane (·····) at *ca.* -185 °C in methylcyclohexane/isopentane (1:4) [14].

The electronic absorption spectra of tetraphenylbenzocyclobutene, triphenylisodihydroanthracene, and tetraphenyl-*o*-quinodimethane recorded in a methylcyclohexane/isopentane glass at -185 °C are reproduced in Figure 10. A skeptic could ask whether the same isomerizations observed by spectroscopy at low temperature also occur at room temperature. Spectroscopic analysis of flash photolysis experiments will provide him with a convincing answer.

3.3. The Matrix and Flash Techniques Are Complementary

A highly suitable experimental method is to be found in kinetic spectrophotometry, in which "flashed" solutions of a substrate are examined one wavelength at a time over a variable period of time (see Fig. 11)[21]. The yellow isodihydroanthracene derivative, the only member of the present set of constitutionally isomeric hydrocarbons to possess sufficient kinetic stability at room temperature, is a suitable substrate.

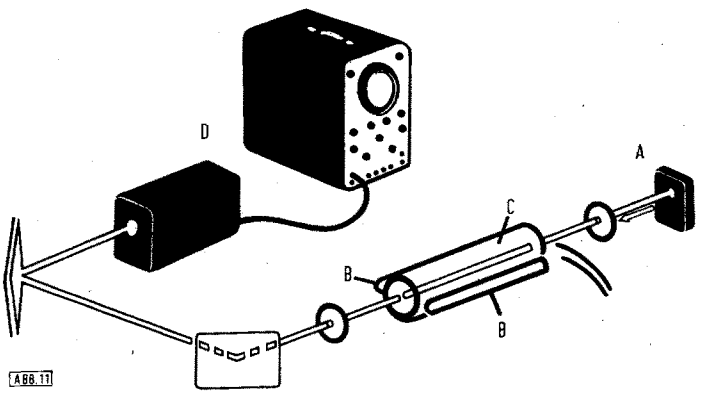


Fig. 11. Apparatus for kinetic spectrophotometry (schematic). A, analysis lamp; B, flash lamp; C, cell; D, monochromator and detector.

A time-consuming analysis performed by point-by-point development on a methylcyclohexane solution at -35 °C for numerous wavelengths affords the absorption spectrum of the transient *seco* isomer already encountered in Figure 10.

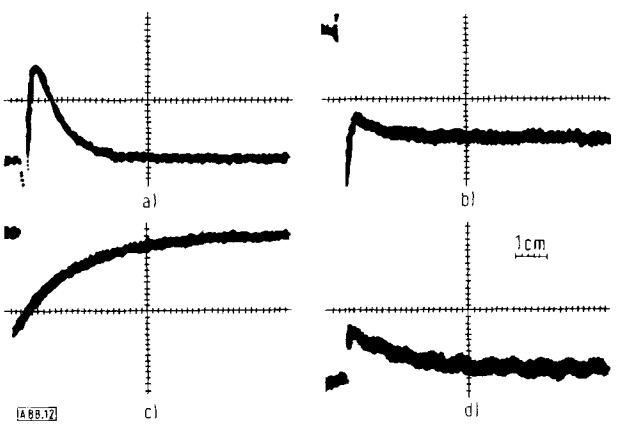


Fig. 12. Oscillograms of flash photolysis of a 1.66×10^{-5} M solution of triphenylisodihydroanthracene (a to c) and of tetraphenylbenzocyclobutene (d) in methylcyclohexane. See text and ref. [21] for an explanation of the individual traces. a) $\lambda = 450$ nm, $t = 0.05$ ms cm^{-1}; b) $\lambda = 400$ nm, $t = 0.05$ ms cm^{-1}; c) $\lambda = 400$ nm, $t = 1000$ ms cm^{-1}; d) $\lambda = 400$ nm, $t = 10$ ms cm^{-1}.

The oscilloscope traces shown in Figure 12 contain time-dependent decay curves of intermediates generated from the respective reactants by flash photolysis.

Oscillograms a) and b) inform about the *cyclo* isomerization of tetraphenyl-*o*-quinodimethane which absorbs more intensely than the reactant (triphenylisodihydroanthracene) at 450 nm but less strongly at 400 nm (cf. Fig. 10). The isomerization proves to be a first order reaction, the half-life of the *seco* isomer is 3.6×10^{-5} s at 23 °C in methylcyclohexane solution, and the Arrhenius parameters E and A amount to 15.3 kcal/mol and $3.2 \times 10^{15}\,s^{-1}$ respectively. On changing the wavelength of the analyzing monochromator (Fig. 11) from 450 nm [see a) in Fig. 12] to 400 nm [see b) in Fig. 12] the primary cyclization product is seen to be the benzocyclobutene derivative, being non-identical with the reactant. Expanding the time scale by a factor of 20000 [see c) in Fig. 12] returns us to the situation prior to flashing. Accordingly, the benzocyclobutene derivative is the kinetically preferred *cyclo* isomer, while the isodihydroanthracene derivative is the thermodynamically favored one. The last oscillogram [see d) in Fig. 12] demonstrates the thermo-reversible ring opening of tetraphenylbenzocyclobutene to the corresponding *seco* isomer on UV irradiation at −35 °C.

Together, this means

- *specifically* that structural modifications observed at low temperatures also occur at room temperature
- *generally* that the matrix and flash techniques are complementary.

The essential point to remember about the case just considered is that irradiation of a compound with suitable light generates an excited electronic isomer from the ground state electronic isomer. Since the two species differ of course in their energy content, and frequently also in their topology and their reactions, they are in fact different compounds. Hence, a method of unparalleled simplicity for the synthesis of new compounds utilizes the reagent light.

4. Case III: Three Electronic Isomers of a Reactant Afford Three Different Products

2,4,6-Trimethyl-6-acetoxy-2,4-cyclohexadienone[22] behaves even more like a chameleon than 7,7,8,8-tetraphenyl-*o*-quinodimethane: three of its electronic isomers react to give three different products. This substance belongs to a class of compounds the intense study[23, 24] of which initiated the development of a simple concept[25, 26] which helps to trace the fate of structurally related electronic and spin isomers on diverse energy surfaces.

On gentle heating in a polar solvent the lead(IV) acetate oxidation product of mesitol isomerizes to the cross-conjugated cyclohexadienone (Fig. 13)[22a]. The excited electronic isomer mainly of π*,n character undergoes complete ring opening to give the stereoisomeric dienylketenes, which thermo-recyclize to the reactant in the absence of protic nucleophiles at room temperature (see Fig. 13). The excited electronic isomer predominantly of π*,π character rearranges to a bicyclo[3.1.0]-hexenone derivative (see Fig. 13).

Two questions arise here: First, how can one selectively obtain the electronic isomer of the linearly conjugated cyclohexadienone mainly of π*,n character or its electronic isomer predominantly of π*,π character and, secondly, how can their different chemistry be interpreted?

4.1. Wavelength- and/or Medium-Dependent Photochemistry

With regard to the first question it would appear appropriate to try to initiate a wavelength-dependent photochemistry by selective irradiation into the π*,n or π*,π absorption band. However, the success of the method depends upon whether the constitutional isomerization of the higher excited dienone electronic isomer is much faster than deactivation to the lower excited dienone electronic isomer. Since both 365-nm and 313-nm light effect *seco* isomerization with the same quantum yield (convenient and reliable evidence for the intermediacy of a dienylketenic transient is obtained by low temperature UV, IR, and NMR spectroscopy[23, 24]) the above premise is clearly not met in the present instance. Hence, it may safely be assumed that in both cases, reaction proceeds from the dienone electronic isomer mainly of π*,n character as the lowest excited electronic isomer.

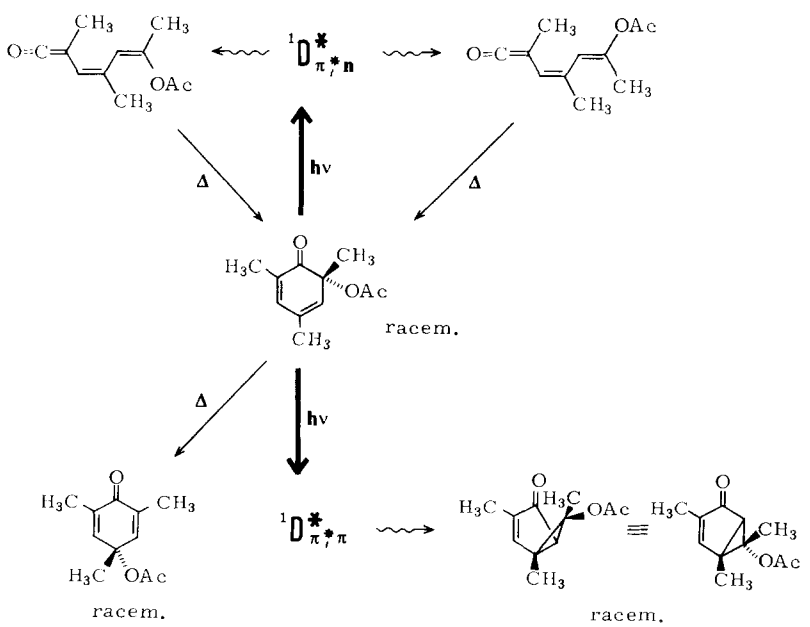


Fig. 13. Separate reaction pathways lead from three electronically isomeric 2,4,6-trimethyl-6-acetoxy-2,4-cyclohexadienones (of the ground state, the excited state having mainly π*,n character, and the excited state predominantly of π*,π character) to products of different constitution [22, 24].

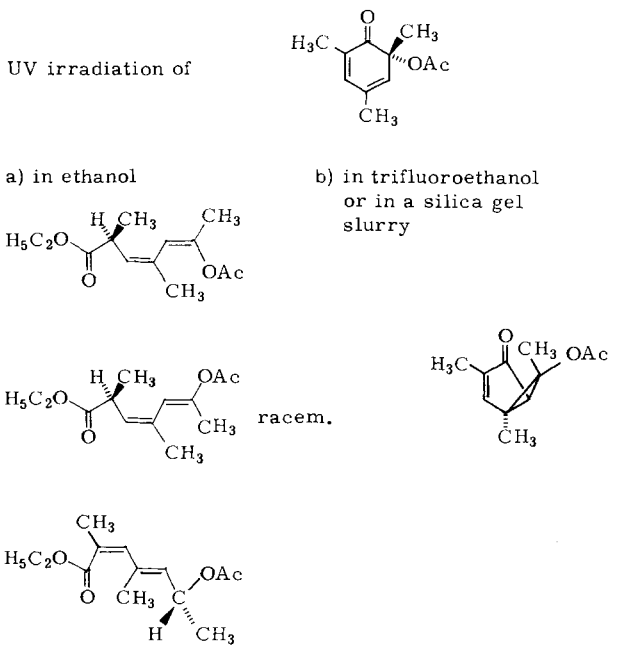


Fig. 14. Medium-dependent photoproducts arising from 2,4,6-trimethyl-6-acetoxy-2,4-cyclohexadienone on UV irradiation in a) ethanol (by 1,2 or 1,6 addition of solvent to primary dienylketene stereoisomers) or b) in trifluoroethanol or a slurry of silica gel in cyclohexane [22, 24].

Alternatively, an attempt can be made to induce the participation of both electronic isomers by choice of a suitable reaction medium. Since each of the related electronic isomers reacts to its surroundings in an individual manner, the character of a photochemical reaction can, in principle, be modified by variation of the molecular environment. Thus, if it were to prove possible to change the sequence of electronic isomers valid for a given medium by use of a different medium, a drastic change in the course of reaction would be expected under the appropriate conditions. The observation (see Fig. 14) that irradiation of 2,4,6-trimethyl-6-acetoxy-2,4-cyclohexadienone gives

- three esters in ethanol
- a bicyclo[3.1.0]hexenone derivative in trifluoroethanol or in a slurry of silica gel in cyclohexane

has already[22-24] been interpreted in this sense. Accordingly, medium-dependent photochemistry is feasible here because

- in a relatively non-polar environment the electronic isomer mainly of π^*,n character is the lowest excited electronic isomer, while in a relatively polar environment it is the one predominantly of π,π character[27];
- the photochemical reaction always starts from the lowest excited electronic isomer.

Our test compound from the family of linearly conjugated cyclohexadienones has revealed the existence of three isomerizations taking place on different energy surfaces[27a]. Knowing the electronic isomer of the reactant from which reaction starts in each case, a search for further details of the individual energy surfaces can be instigated.

4.2. α-Cleavage of Electronically Excited 2,4-Cyclohexadienones

Figure 15 summarizes our knowledge about light-induced *cyclo/seco* isomerization of linearly conjugated cyclohexadienones. The stereoisomeric dienylketenes appear as precursors of the respective stereoisomeric carboxylic acid derivatives. The two *seco* isomers of the cyclic reactant are readily formed—by rotation in one and in the opposite direction about the 5,6 bond—from a diradical generated as the normal α-cleavage product from the electronic isomer of the cyclohexadienone mainly of π^*,n character.

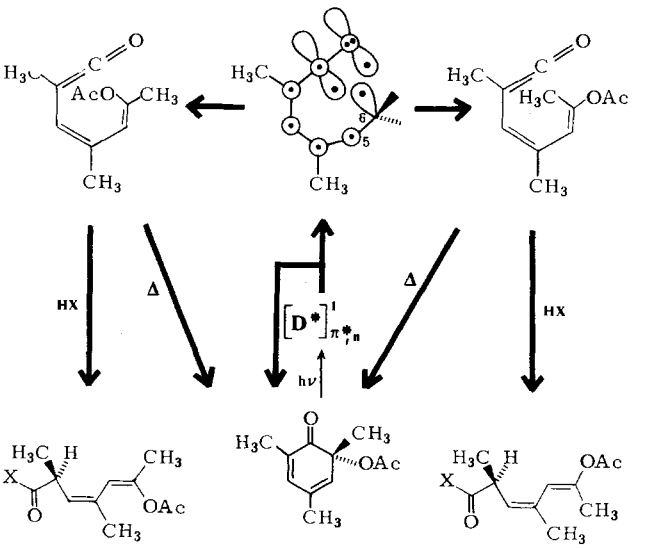


Fig. 15. Concerning the chemistry of the electronic isomer of 2,4,6-trimethyl-6-acetoxy-2,4-cyclohexadienone having mainly π^*,n character and its dienylketenic stereoisomers [22, 24]. The *cyclo/seco* isomerization probably occurs from the singlet spin isomer; if the triplet spin isomer is very short-lived and therefore cannot be quenched by conjugated dienes then it may also play a role.

A definite electronic structure is assigned to the diradical (cf. Fig. 15). Accepting simplifications as the price to pay for emphasis of the difference in nature from other possible electronic structures, the present species can be described as a diradical α-cleavage product with σ,π character. It has of course then been tacitly assumed that the cyclohexadienone possesses a plane of molecular symmetry which is retained during the primary reaction and permits distinction between π-electrons and σ-electrons directly involved in the reaction.

To *Salem* must go the credit for undertaking, on the basis of our views on the α-cleavage of linearly conjugated cyclohexadienones[23, 24],

- a classification of photochemical processes, taking account of the difunctional primary products[26, 28]
- initially a discriminating discussion of the mutually related diradical and zwitterionic electronic isomers[29].

The resulting progress in our understanding of photochemical reactions becomes clear on considering the previous situation:

> The understanding of photochemical reaction mechanisms has been hindered by ignorance of the electronic states of the chemical intermediates. In many photochemical reactions a diradical or zwitterionic intermediate is postulated even though the nature of the electronic surface to which this intermediate belongs is shrouded with mystery[25].

Electronic isomers and discussions about their correct energetic sequence are therefore encountered not only on the linearly conjugated cyclohexadienone side but also on that of the α-cleavage product. Correlating each electronic isomer on the reactant side with the corresponding electronic isomer

on the product side affords the Salem correlation diagram for α-cleavage of linearly conjugated cyclohexadienones (Fig. 16).

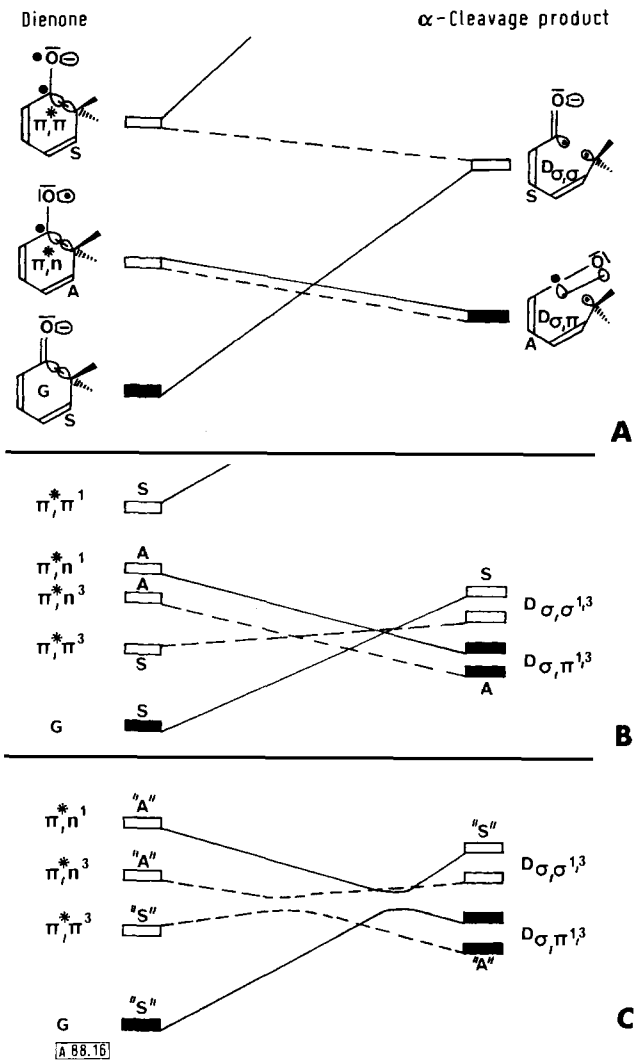


Fig. 16. Qualitative state correlation diagrams for α-cleavage of linearly conjugated cyclohexadienones in the unperturbed case (in a relatively nonpolar molecular environment) [26, 28]. A, planar reaction geometry; account taken of electronic isomers, each symbolized by a single characteristic resonance structure. B, planar reaction geometry; account also taken of spin isomers. C, correlation diagram B modified by helical reaction geometry. The correlation lines between corresponding singlet structures (triplet structures) of the same symmetry character are shown as solid (broken) lines [29a].

On the left-hand side of Figure 16A are seen the electronic isomers of the cyclohexadienone arranged from bottom to top in the order of increasing energy and each symbolized by a definite resonance structure: at the bottom the electronic isomer of the ground state, in the middle that of the π*,n excited state, and above it that of the π*,π excited state.

On the right-hand side of Figure 16A we see at the bottom the diradical electronic isomer of the α-cleavage product already mentioned; it has σ,π character (cf. Fig. 15). Above it is located the diradical electronic isomer having σ,σ character. The series could be continued as far as electronic isomers having zwitterionic character; however, we shall stop here for the time being.

The simplest way of finding the correlation partner on the product side is to take a particular electronic isomer of the reactant and stretch that CC single bond designated to be cleaved without introducing any additional unnecessary changes in the electronic structure of the reacting molecule. In this way one obtains pairs having the same number of π- and σ-electrons participating directly in the reaction and hence with the same symmetry.

The ground state electronic isomer of the cyclohexadienone correlates with the diradical electronic isomer of the α-cleavage product having σ,σ character; both are symmetrical and possess six π- and four directly participating σ-electrons. The electronic isomer of the cyclohexadienone with π*,π character is again symmetrical. Its triplet spin isomer correlates with the diradical triplet spin isomer having σ,σ character, and its singlet spin isomer with a symmetrical singlet spin isomer having zwitterionic character (not shown in Fig. 16).

Correlation diagram B in Figure 16 corresponds to correlation diagram A. It appears clearer now because the symbolic representation of electronic isomers by a characteristic resonance structure each has been dropped, it is more complex because an attempt has been made to adjust to physical reality by taking account of the energy separations between related spin isomers on the ketone side. This plays a greater role for electronic isomers having π*,π than for those with π*,n character.

For anybody[23] regarding a photochemical reaction merely as a special case of radiationless deactivation of an electronically excited compound and who considers any distinction between physical and chemical deactivation processes as artificial, a Salem correlation diagram is a Jablonski diagram extended by the hitherto neglected dimension of an appropriate reaction coordinate. It helps the photochemist with an interest in mechanisms, who is eagerly looking for detailed information about the dynamic behavior of a molecule on a complex energy surface, to find his way around the field of multisurface chemistry *grosso modo* with the aid of a qualitative physical model[30].

In the photochemistry of linearly conjugated cyclohexadienones, interest attaches to the following questions: Starting from what electronic isomer (spin isomer) of the reactant will lead to what electronic isomer (spin isomer) of the product? What can be said about the reactivity and about the quantum yield? What influence does the nature of the reaction medium have on the kind of photoproduct?

Assuming that the stereoisomeric dienylketenes arise from the electronic isomer of the diradical α-cleavage product having σ,π character (cf. Fig. 15), then Figure 16 suggests that the electronic isomer of the diradical α-cleavage product having (mainly) σ,π character (both spin isomers) is accessible from the cyclohexadienone electronic isomer mainly of π,n character (both spin isomers). For a planar reaction geometry (Fig. 16B) each process is adiabatic; the energy surface containing the two antisymmetric electronic isomers of the reactant and the primary product crosses the energy surface containing the symmetrical electronic isomers of reactant and primary product. For a helical reaction geometry (Fig. 16C) the two energy surfaces repel each other (non-crossing rule) without diminishing the high reactivity (energy surface pointing downwards) or the high quantum yield (internal conversion is faster for small distance between the two energy surfaces crossing for planar reaction geometry than relaxation of the molecule in the energy minimum on the upper surface).

The triplet spin isomer belonging to the electronic isomer of the diradical α-cleavage product with (mainly) σ,π character

can also arise from the triplet spin isomer of the cyclohexadienone electronic isomer with (predominantly) π*,π character; for planar reaction geometry (Fig. 16B) by transition from the symmetrical triplet energy surface to the antisymmetrical triplet energy surface, and for helical reaction geometry (Fig. 16C) by remaining on the lowest triplet energy surface. The reactivity is now lower than in the case discussed above since the triplet energy surface which contains the triplet spin isomer belonging to the electronic isomer of the cyclohexadienone having mainly π*,π character falls off less steeply (cf. ref. [29a]); the quantum yield should be of about the same order of magnitude.

A strongly polar medium, which as already mentioned (see Fig. 14) exerts a far-reaching influence on the nature of the photoproduct from 2,4-cyclohexadienones modifies the energy surfaces in multidimensional space. The energetic location of the electronic isomers on both the reactant side and the product side of the α-cleavage will change; if this should go so far as to lead to a regrouping in the packing order of electronic isomers then the consequences can be read off from a qualitative correlation diagram. Figure 17 contains

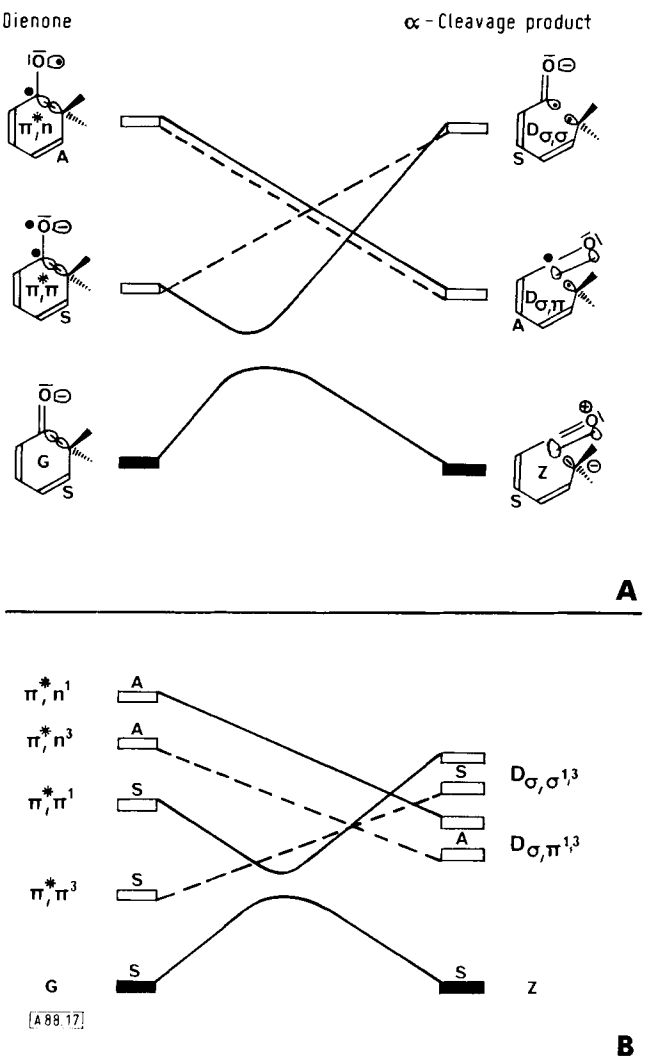


Fig. 17. Qualitative state correlation diagrams for α-cleavage of linearly conjugated cyclohexadienones in the perturbed case (in strongly polar environment) for planar reaction geometry [26, 28]. A, taking account of electronic isomers, each symbolized by a single characteristic resonance structure. B, account also taken of spin isomers. The correlation lines between corresponding singlet structures (triplet structures) of the same symmetry character are shown as solid (broken) lines [29a].

such diagrams for the α-cleavage of linearly conjugated cyclohexadienones in a strongly polar molecular environment. The electronic isomer having π*,π character (both spin isomers) on the reactant side now lies below that having π*,n character (cf. Section 4.1). On the side of the α-cleavage product the diradical electronic isomers will be affected only slightly but the zwitterionic electronic isomers to a much greater extent. In an extreme case, this "perturbation" can lead to a situation where a zwitterionic electronic isomer represents the ground state electronic isomer and is possibly the decisive reason for the medium-dependent photochemistry of linearly conjugated cyclohexadienones (see Fig. 14), more important than the fact that the cyclohexadienone electronic isomer having π*,π character lies lower than the electronic isomer having π*,n character (cf. Section 4.1).

During incipient stretching of the CC bond undergoing cleavage the electronic isomers of the linearly conjugated cyclohexadienone at first tend, also in strongly polar reaction media, to correlate with the same electronic isomers of the α-cleavage product as in the unperturbed case (Fig. 16). However, as reaction proceeds further, crossing of the two energy surfaces linking mutually symmetric electronic isomers of reactant and product is avoided. The diagrams in Figure 17 suggest above all that the singlet spin isomer corresponding to the cyclohexadienone electronic isomer having π*,π character reacts with high reactivity[29a] and possibly high quantum yield—after switching from the upper to the lowest singlet surface ("internal conversion")—to give the ground state electronic isomer of the α-cleavage product with zwitterionic character and thence to the bicyclo[3.1.0]hexenone derivative.

We can summarize the third case as follows: The chemistry of compounds in their respective electronic ground state is a unisurface chemistry. Contact with photochemical reactions opens the way to multisurface chemistry. Salem correlation diagrams are valuable signposts. They do not render experimentation unnecessary but instead permit more precise expression of the questions to be answered and hence provide a valuable navigational aid through the jungle of multisurface chemistry. They motivate the experimental photochemist to observe the different meaning of reactivity parameters and quantum yields and to determine their numerical values as a means of testing energy surface structures deduced more or less intuitively. They point to the eminent significance that solvent and of course substituent effects may have on any decision in favor of one of several possible reaction pathways[31]. And finally, they open up a broad field of activity to the theoretical photochemist and encourage him to calculate the correct sequence of electronic and spin isomers on the reactant and product sides and to establish the detailed topology[32] of the energy surfaces, which is so much more complex than the crude predictions of qualitative correlation diagrams would appear to indicate.

4.3. Synthetic Utilization of α-Cleavage of Linearly Conjugated Cyclohexadienones

The financial means invested by the taxpayer in Great Britain, France, the USA, and the Federal Republic of Germany more or less indirectly in those laboratories actively engaged in studying the photochemistry of linearly conjugated cyclohexadienones justify an enquiry as to the tangible returns

registered so far. Now the results of pure research are quite rightly entered into any generation's credit column of the internationally intermeshed cultural balance. Wherever they appear in doctoral theses issuing from university laboratories, their discovery has already contributed to the education of chemists.

Furthermore, the example of the study of electronically excited 2,4-cyclohexadienones clearly demonstrates how investigations initially based on the mere hunch that such compounds which absorb in the experimentally convenient wavelength range should undergo chemical changes on exposure to suitable light popularized low temperature methods[33] formerly uncommon in the organic chemistry laboratory and made a not inconsiderable contribution to a better understanding of photochemical reactions.

If the statement

> In the last decade photochemistry has grown from a minor to a major activity in organic chemical laboratories. Many striking and (thermally) unusual processes can be observed and the mechanistic problems posed in their interpretation demand new dimensions in organic chemical thought. However, in spite of the large number of new photochemical reactions which have been discovered in recent years, rather few have yet found use in organic synthesis and fewer still have been of economic value in industry[34].

is understood not so much as a contemplative analysis but rather as a challenge to change the situation, then one will be spurred on to exploit the preparatively feasible ring cleavage of linearly conjugated cyclohexadienones—and since they are conveniently accessible by several methods from phenols, in effect the ring cleavage of benzenoid compounds to give substituted hexadienoic acid derivatives—for the synthesis of a product having potential economic interest. This goal has now been accomplished by implementation of a synthetic concept[35] for the preparation of dimethylcrocetin, a naturally occurring "lemon yellow" food colorant.

The synthesis[36] has the following features:

- overall yield in excess of 15%,
- only few reaction steps,
- light-induced α-cleavage of a 2,4-cyclohexadienone as key reaction (Fig. 18).

The initial phase starts from the two inexpensive compounds 2,6-dimethylphenol and 1,4-dibromo-2*E*-butene and attaches the cyclic moiety to each end of the chain structural unit by double CC linkage. This $C_8+C_4+C_8$ building principle affords a product already containing all 20 C atoms of crocetin. Since not only the desired CC alkylation, but also OO and statistically favored CO alkylations take place, the yield of the two possible stereoisomeric bisdienones is not expected to be very high from the outset. Execution of the reaction as a heterogeneous process in benzene at 10–15 °C and use of a 10% excess of sodium phenoxide gives a yield of 28%. Separation of the three constitutional isomers having the molecular formula $C_{20}H_{24}O_2$ is accomplished fairly easily by a single chromatographic run over a column of silica gel. Separation of the two stereoisomeric bisdienones, performed for identification purposes although unnecessary for the course of synthesis, is achieved with extensive losses by tedious plate chromatography over silica gel.

The two stereoisomers, of which one is achiral and the other chiral, can be distinguished by NMR spectroscopy with the aid of an optically active lanthanoid shift reagent.

In the second phase, the two terminal dienone rings are opened to give the entire C_{16} chain with the four methyl branches of crocetin and, if reaction has been performed in methanol which adds to the initially formed ketene group, the terminal methyl ester groups of dimethylcrocetin. UV irradiation of bisdienone (in the form of individual or mixed diastereoisomers) affords a 95% yield of a stereoisomer mixture of a tetrahydrodimethylcrocetin having absorption maximum at 244 nm. Gas chromatography reveals three components in the ratio 17:3:1. According to their NMR spectra, these are each due to a pair of stereoisomers having different relative arrangements of the ligands on the chirality centers C^2 and $C^{2'}$ and either *ZZEZZ*, *ZZEEZ*, or *ZEEEZ* orientation of the five CC double bonds.

The third phase completes the entire conjugation of the polyene system. Dehydrogenation with dichlorodicyano-*p*-benzoquinone transforms the stereoisomeric pairs (individually or as a mixture) into all-*E*-dimethylcrocetin in 41% yield[36a].

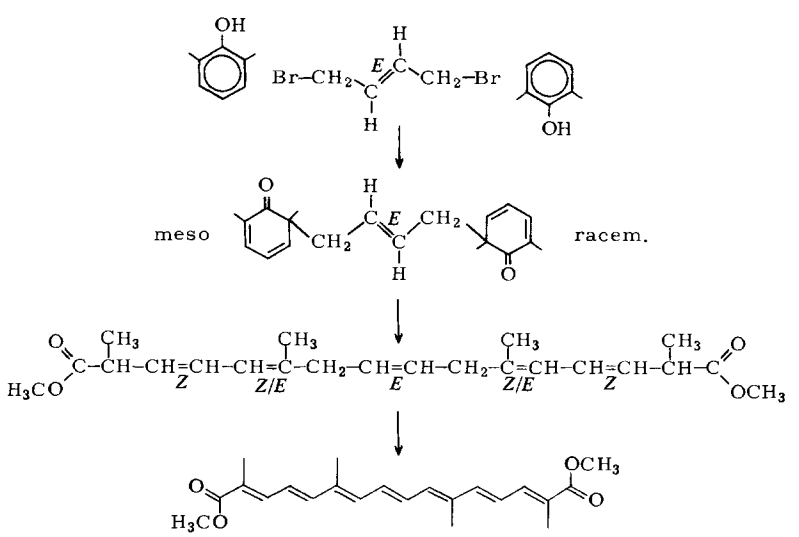


Fig. 18. Scheme of a simple dimethylcrocetin synthesis embodying a photochemical key reaction.

5. Final Comments

The question of what happens when a compound is supplied the energy necessary for chemical reaction by an irradiation lamp instead of by a Bunsen burner has been attracting steady attention for about ten years; since *Woodward* and *Hoffmann*[37] discovered that agreement between the nodal properties of the molecular orbitals of reactant and product is a criterion for smooth occurrence of light- or heat-induced synchronous reactions, and thus overcame conceptual barriers not only in the field of "no mechanism" reactions[38] but also in the development of the theory of organic reactions *in toto*. Since that time there has been no justification whatsoever for a special status for electronically excited compounds and their chemical reactions in organic chemistry. This becomes all the clearer when it is recalled that the motivation leading to the rules concerning the direction of stereospecificity of electrocyclic thermo- and photoreactions[39] was studies on the synthesis of vitamin B_{12}, and the uncomfortable situation that existed prior to their formulation in which it was impossible to interpret the different modes of cyclization of precalciferol depending upon whether it is activated thermally or photochemically[40]. Both synthetically and mechanistically oriented chemists have long accepted this fact to the benefit of their own research work. Authors of textbooks or introductory lecture courses are well advised to show the same degree of insight.

The co-workers mentioned in the references cited[13, 14, 21–24, 33, 36] *participated in the work proceeding from our laboratory. Miss G. Stracke assisted in the synthesis of dimethylcrotecin, and Mrs. U. Dörr provided for spectroscopically pure solvents. The flash photolysis experiments were performed under the direction of Dr. K. H. Grellmann, Max-Planck-Institut für Biophysikalische Chemie, Göttingen. Financial support of our studies by Hoechst AG, BASF AG, Schering AG, the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Max-Buchner-Forschungs-Stiftung is gratefully acknowledged.*

Received: March 13, 1975 [A 88 IE]
German version: Angew. Chem. *87*, 851 (1975)

[1] *W.-D. Stohrer, P. Jacobs, K. H. Kaiser, G. Wiech,* and *G. Quinkert,* Fortschr. Chem. Forsch. *46*, 181 (1974).
[2] For a biography, see *R. Fabre* in *E. Farber:* Great Chemists. Wiley-Interscience, New York 1961, p. 1085.
[3] *G. Ciamician,* Science *36*, 385 (1912).
[4] *P. de Mayo,* Adv. Org. Chem. *2*, 367 (1960).
[5] *J. M. Mellor, D. Phillips,* and *K. Salisbury,* Chem. Br. *10*, 160 (1974).
[6] *A. L. Hammond, W. D. Metz,* and *Th. H. Maugh II:* Energie für die Zukunft. Umschau Verlag, Frankfurt am Main 1974; unsigned articles in Nachr. Chem. Tech. *20*, 391 (1972) and in Chem. Eng. News 17 (1973).
[7] Concerning the relation between chemical yield, efficiency, and reactivity in a photochemical reaction, see *N. J. Turro,* J. Chem. Educ. *44*, 536 (1967); for the definition of the reactivity of electronically excited molecules see, in particular, *G. Porter,* Reactiv. Photoexcited Org. Mol., Proc. Conf. Chem. 13th 1965 (Publ. 1967).
[8] *H. E. Zimmerman, D. P. Werthemann,* and *K. S. Kamm,* J. Am. Chem. Soc. *96*, 439 (1974).
[9] Regarding the problems of analogous or trivial research, see *D. H. R. Barton,* Inaugural Lecture, Imperial College of Science and Technology, December 3rd., 1967.
[10] *J. P. Simons:* Photochemistry and Spectroscopy. Wiley-Interscience, London 1971.
[11] *P. D. Bartlett,* Q. Rev. Chem. Soc. *24*, 473 (1970).
[12] Regarding the photochemistry of organic solids, see *M. D. Cohen,* Pure Appl. Chem. *9*, 567 (1964); *J. Z. Gougoutas, ibid. 27*, 305 (1971); *G. M. J. Schmidt, ibid. 27*, 647 (1971); *M. D. Cohen* and *B. S. Green,* Chem. Br. *9*, 490 (1973); *M. D. Cohen,* Angew. Chem. *87*, 439 (1975); Angew. Chem. internat. Edit. *14*, 386 (1975).
[13] *G. Quinkert, T. Tabata, E. A. J. Hickmann,* and *W. Dobrat,* Angew. Chem. *83*, 212 (1971); Angew. Chem. internat. Edit. *10*, 198 (1971).
[14] *G. Quinkert, W.-W. Wiersdorff, M. Finke, K. Opitz,* and *F.-G. von der Haar,* Chem. Ber. *101*, 2302 (1968).
[15] See Appendix 1 to IUPAC Tentative Rules for the Nomenclature of Organic Chemistry, J. Org. Chem. *35*, 2862 (1970).
[16] *N. J. Turro,* Chem. Eng. News 84 (1967).
[17] *H. A. Staab:* Einführung in die Theoretische Organische Chemie, 3rd. Edit. Verlag Chemie, Weinheim 1962, p. 464.
[18] *M. J. S. Dewar, S. Kirschner,* and *H. W. Kollmar,* J. Am. Chem. Soc. *96*, 5240 (1974).
[19] *L. Wittgenstein:* Philosophische Untersuchungen, Satz 119, Edit. *G. E. M. Anscombe* and *R. Rhees.* Basil Blackwell, Oxford 1953.
[20] *M. Kasha,* Discuss. Faraday Soc. *9*, 14 (1950).
[21] *K. H. Grellmann, J. Palmowski,* and *G. Quinkert,* Angew. Chem. *83*, 209 (1971); Angew. Chem. internat. Edit. *10*, 196 (1971).
[22] *G. Quinkert, B. Bronstert,* and *K. R. Schmieder,* Angew. Chem. *84*, 638 (1972); Angew. Chem. internat. Edit. *11*, 637 (1972).
[22a] *D. H. R. Barton, P. D. Magnus,* and *M. J. Pearson,* J. Chem. Soc. *C 1971*, 2231.
[23] *G. Quinkert,* Angew. Chem. *84*, 1157 (1972); Angew. Chem. internat. Edit. *11*, 1072 (1972).
[24] *G. Quinkert,* Pure Appl. Chem. *33*, 285 (1973).
[25] *L. Salem, W. G. Dauben,* and *N. J. Turro,* J. Chim. Phys. *70*, 694 (1973).
[26] *L. Salem,* J. Am. Chem. Soc. *96*, 3486 (1974).
[27] *J. Griffiths* and *H. Hart,* J. Am. Chem. Soc. *90*, 5296 (1968).
[27a] The singlet and triplet spin isomers belonging to each of the discussed electronic isomers may, of course, distinguish themselves by their characteristic chemistry. According to unpublished observations by *H.-Ch. Steinmetzer* the light-induced rearrangement of 2,4,6-trimethyl-6-acetoxy-2,4-cyclohexadienone to acetoxymesitol [cf. *D. H. R. Barton* and *G. Quinkert,* J. Chem. Soc. *1960*, 1] can be achieved by triplet/triplet energy transfer in the absence of any protic nucleophile with low quantum yield ($\Phi \leq 10^{-2}$). As sensitizers with a triplet energy as low as 42 kcal/mol are still active as donors, the triplet spin isomer from which the isomerization starts no doubt belongs to the electronic isomer of the dienone predominantly of π^*,π-character; the corresponding singlet spin isomer undergoes an oxa-di-π-methane rearrangement to the discussed bicyclo[3.1.0]hexenone derivative.
[28] *W. G. Dauben, L. Salem,* and *N. J. Turro,* Acc. Chem. Res. *8*, 41 (1975).
[29] Regarding the diradical or zwitterionic character of electronically excited diradicals, see *L. Salem* and *C. Rowland,* Angew. Chem. *84*, 86 (1972); Angew. Chem. internat. Edit. *11*, 92 (1972).
[29a] Correlation lines obtained in the indicated manner are just straight lines; as two-dimensional cross sections of polydimensional hypersurfaces, they "generously" ignore existing maxima or minima. This is especially awkward if such irregularities occur at the beginning of an elementary reaction. They can be detected as Woodward/Hoffmann energy barriers if a given correlation is forbidden from the orbital point of view although allowed from the standpoint of state symmetry. This is true, for example, for the correlation between π^*,π and $D_{\sigma,\sigma}$ (cf. Fig. 16A) or π^*,π^3 and $D^3_{\sigma,\sigma}$ (cf. Fig. 16B). Similarly, a barrier appears at the onset of the surface connecting π^*,π^1 and $D^1_{\sigma,\sigma}$ (cf. Fig. 17) as that electronic isomer on the α-cleavage product having zwitterionic character correlates orbitalwise with the singlet spin isomer belonging to the dienone electronic isomer having σ^*,n-character.
[30] A physical model has been lucidly described in detail by *J. Michl* [Fortschr. Chem. Forsch. *46*, 1 (1974)]; cf. also refs. [26, 28].
[31] Concerning modification by polar solvents, see *L. Salem* and *W.-D. Stohrer,* J. C. S. Chem. Commun. *1975*, 140.
[32] Cf. references cited in [30].
[33] *G. Quinkert,* Photochem. Photobiol. *7*, 783 (1968) and also ref. [24], and references cited therein.
[34] *D. H. R. Barton,* Pure Appl. Chem. *16*, 1 (1968).
[35] *D. H. R. Barton* and *G. Quinkert,* US-Pat. No. 3 173 942 (1965).
[36] *K. R. Schmieder,* Dissertation, Universität Frankfurt am Main 1975; *K. Hache,* Dissertation, Technische Universität Braunschweig 1973.
[36a] In a variant form of the synthesis the derivative brominated in position 4 is used instead of 2,6-dimethylphenol. In this way it is possible to substitute the dehydrogenation, which occurs in only modest yield, by the more effective dehydrobromination.
[37] *R. B. Woodward* and *R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).
[38] *W. v. E. Doering* and *W. R. Roth,* Tetrahedron *18*, 67 (1962).
[39] *R. B. Woodward:* Aromaticity. Spec. Publ. No. 21, The Chemical Society London 1967, p. 217.
[40] *E. Havinga* and *J. L. M. A. Schlatmann,* Tetrahedron *16*, 146 (1961)

Tertiary Phosphane/Tetrachloromethane, a Versatile Reagent for Chlorination, Dehydration, and P—N Linkage

New synthetic methods (13)

By Rolf Appel[*]

In this review the processes occurring on the treatment of triphenylphosphane with tetrachloromethane are first reported; a key role is played here by (trichloromethyl)phosphonium chloride which reacts with a further amount of the phosphane to give the stable salt [chloro(triphenylphosphoranediyl)methyl]triphenylphosphonium chloride by way of dichlorophosphorane and (dichloromethylene)phosphorane that is detectable only as an intermediate. The preparative application of the two-component system as a chlorinating, dehydrating, and P—N-linking reagent is ascribable to "phosphorylation"[**] of the substrate in question through several reactive species. In these applications the reactions with the substrate compete with reactions of the two-component system with itself, so that the overall course of the reaction is in nearly all cases much more complex than was previously assumed. Nevertheless, very good results can be achieved by the use of this reagent, high yields and mild reaction conditions being characteristic.

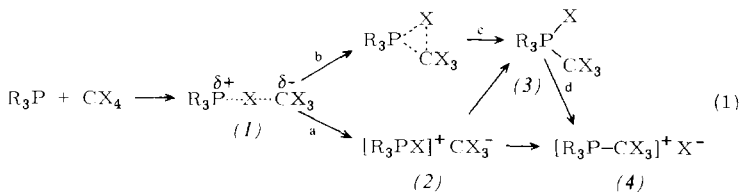
1. Introduction

In combination with a tetrahalomethane, tertiary phosphanes provide reagents that have manifold uses and are finding increasing application in preparative chemistry for halogenation, dehydration, and P—N-linking reactions[1, 2]. The reactivity of a two-component system of such composition can be varied within wide limits by the choice of substituents on the phosphorus and the halogen atoms on the carbon atom. For example, trialkylphosphanes react explosively with tetrachloromethane[3], whereas very pure triphenylphosphane appears at first not to react at all with CCl_4 even in great excess[4]. Such very different observations are probably the reason why the whole range of synthetic applications of this reagent has not previously been explored in spite of its ready accessibility in every laboratory.

Of the various possibilities for the preparation of the reagent and for its treatment with substrates, only that with the easily prepared and most conveniently handled two-component system, namely triphenylphosphane/CCl_4, will be treated in detail in this progress report. In addition, however, the combination tris(dimethylamino)phosphane/CCl_4 will be discussed, as it is occasionally used because of its well developed nucleophilic character. The considerations developed within the limits of these two systems below can, it is believed, be applied also to other combinations. However, the reactions of phosphites with tetrahalomethanes and third components will not be treated in the present review.

2. The Two-Component System Phosphane/CCl_4

The processes occurring in the two-component system are a key factor in the understanding of the preparative use of multicomponent reactions. As UV-irradiation and the addition of radical-trapping reagents exert no effect on the course of the reactions[5], all workers in this field are now agreed that an ionic mechanism lies at the root of phosphane-tetrahalomethane interactions. It is initiated by the polarizing action of the permanent dipole phosphane on the symmetrical but readily polarizable tetrahalomethane, and in accord with eq. (1) it leads to heterolytic bond cleavage by a direct interaction between the phosphorus atom and a halogen atom.



(1)

The amount of charge transfer in the dipolar associate *(1)* then depends on the substituents carried by the phosphorus atom. With strongly basic amino groups this tendency is so great that in the case of tris(dimethylamino)phosphane the primary complex already exists largely as the ion pair *(2)*. With more weakly basic phosphanes the charge transfer to the CX_4 molecule is much less pronounced, so that in these cases the ion pair *(2)* has only the subordinate importance of a canonical limiting form of a bonding state.

The ion pair *(2)* with its trihalomethanide ion has not yet been demonstrated in any phosphane/CX_4 system, but its existence as an intermediate is shown by all the subsequent reactions with proton-active substrates. Appreciably more stable than *(2)* is the (trichloromethyl)phosphonium chloride *(4)* that is produced by rearrangement, presumably by way of a pentavalent phosphorane stage *(3)*; it was first detected for certain in the system $[(CH_3)_2N]_3P/CCl_4$[6] and was recently isolated from the system Ph_3P/CCl_4[7].

[*] Prof. Dr. R. Appel
Anorganisch-Chemisches Institut der Universität
53 Bonn, Max-Planck-Strasse 1 (Germany)

[**] Here and below, "phosphorylation" is used to mean in general the formation of a phosphorus derivative. In the narrower sense this term denotes the introduction of phosphoryl groups P(O)≤.

2.1. Triphenylphosphane/CCl_4

The course of the reaction leading to the salt *(4)*, sometimes called "phosphonium salt formation of the second kind"[8], is presumably valid for all phosphanes. The subsequent reactions have hitherto been studied in detail only for triphenylphosphane[7]. In this case the rate of formation of the salt *(4)* is so slow that some unchanged triphenylphosphane is always still present after the formation of *(4)*, even if a large excess of the CCl_4 has been employed. It was recently shown that the phosphane reacts instantaneously with the (trichloromethyl)phosphonium chloride by dechlorination to yield the (dichloromethylene)phosphorane *(5)* and the dichlorophosphorane *(6)*.

$$[Ph_3P{-}CCl_3]^+Cl^- + Ph_3P \longrightarrow \underset{(5)}{Ph_3P{=}CCl_2} + \underset{(6)}{Ph_3PCl_2} \quad (2)$$

Contrary to an earlier postulate, the reaction according to eq. (2) does not, however, lead to a stable end state. In this system the ylide *(5)* can be regarded only as a very reactive intermediate that cannot be detected by ^{31}P-NMR spectrometry but reacts very rapidly according to eq. (3), or probably according to eq. (4), to afford the [chloro(triphenylphosphoranediyl)methyl]triphenylphosphonium chloride *(7)*.

$$Ph_3P{=}CCl_2 + Ph_3P \longrightarrow \underset{(7)}{[Ph_3P{=}C(Cl){=}PPh_3]^+Cl^-} \quad (3)$$

$$Ph_3\overset{\oplus}{P}{-}\overset{\ominus}{C}Cl_2 + Ph_3PCl_2 + Ph_3P \longrightarrow \left[\begin{array}{c} Cl \\ | \\ Ph_3P{-}C{-}PPh_3 \\ | \\ Cl \end{array}\right]^{2+} 2\,Cl^- + Ph_3P \longrightarrow \quad (4)$$

$$[Ph_3P{=}C(Cl){=}PPh_3]^+ Cl^- + Ph_3PCl_2$$

$$3\,Ph_3P + CCl_4 \longrightarrow (7) + (6) \quad (5)$$

Interaction of triphenylphosphane with tetrachloromethane ends in the stable products *(6)* and *(7)*, to a large extent independently of the molar proportions of the reactants. The overall reaction can therefore be described by eq. (5). This result agrees with early investigations of the triethylphosphane/CCl_4 system, which led to the same stoichiometry as a result of quantitative determination of the ionic chlorine measurable after hydrolysis[9]. It is therefore not unlikely that the reaction series given by eqs. (3) to (5), first established only for triphenylphosphane, also applies to other triorganylphosphanes.

2.2. Solvent-Dependence in the Ph_3P/CCl_4 System

Very remarkably, an enormous solvent-dependence is observed for the reactions occurring in the Ph_3P/CCl_4 two-component system. This becomes clear from a comparison of the rate constants at 25 °C listed in Table 1[10].

The reaction in acetonitrile is extremely fast, but in CCl_4 alone it is so slow that one can understand why some authors reported no reaction in this system. There is also the striking finding that, in spite of its large dipole moment, benzonitrile (not mentioned in Table 1) leads to a reaction scarcely faster than that in CCl_4[10]; thus, the relation between the reaction rate and the dipole moment or dielectric constant of the solvent, which can be discerned in the above table, appears not to be the sole determinant; the solvation capacity of the solvent, which cannot always be correlated with ε, seems to be equally important[11].

Table 1. Influence of the solvent on reactions occurring in the Ph_3P/CCl_4 system.

Solvent component in addition to CCl_4	Dielectric constant ε	Dipole moment μ [D]	k_{25} [s^{-1}]	k_∞ [s^{-1}]	$\Delta S^{\neq}$ [a] [e.u.]
CCl_4 alone	2.238	0.00	4.2×10^{-9}	1.7×10^{7}	−37
CH_2Cl_2	9.08	1.55	7.5×10^{-5}	4.5×10^{4}	−43
$ClCH_2{-}CH_2Cl$	10.65	2.06	2.6×10^{-5}	4.5×10^{6}	−37
CH_3CN	35.85	3.37	1.65×10^{-3}	1.6×10^{5}	−29

[a] Activation entropy, calculated according to ref. [11].

These findings indicate that charge separation is the rate-determining step. In apolar media, which exert coulombic forces having a reversing effect, the formation of an ion pair or even dissociated ions requires higher energies than does homolytic cleavage of a bond. The cleavage energy forms part of the activation energy and thus influences the rate constants. Solvation effects weaken the electrostatic field and thus decrease the coulombic portion of the activation energy. It thus becomes understandable why the rate of the reactions formulated in eq. (1), which parallel charge separations, depends markedly on the solvation properties of the solvent[12–14].

3. Basis of the Preparative Application of Multicomponent Reactions

In all preparatively useful reactions in which the Ph_3P/CCl_4 reagent was treated with a proton-active substrate it was at first assumed that the highly active agent responsible for phosphorylating the substrate had to be sought among the intermediates shown in eq. (1). From this point of view it seemed advisable to bring the phosphane and the CCl_4 into reaction in the molar ratio of 1:1; stoichiometry exceeding this molar ratio would favor the subsequent reactions of the two-component system according to eq. (3), which lead to the compound *(7)* inactive as a phosphorylating agent. Furthermore, because of this very rapid reaction it seemed advisable to mix the two components only in the presence of the substrate; this can be done, for example, by adding the easily measurable CCl_4 to a premixed solution of phosphane and substrate. The reaction time can be considerably influenced by proper choice of the solvent; it increases in the order acetonitrile, dichloromethane, benzene; mixtures of polar solvents with benzene or other inert apolar solvents are equally suitable. Even with a large excess of CCl_4, which acts at the same time as a solvent, satisfactory results are obtained in multicomponent reactions. This does not contradict the above-mentioned unreactivity of the system Ph_3P/CCl_4[4], as in this case the polar substrate functions first as a solvating agent and thus initiates the reactions shown in eq. (1). All the reactive intermediates are very susceptible to hydrolysis, making it necessary to use a carefully dried solvent.

3.1. Mechanism of the Three-Component Reaction

The mechanism of the three-component reaction phosphane/CCl_4/alcohol, the first to be studied in detail, was initially interpreted exclusively in the sense of eq. (6) and was later applied also to other multicomponent systems[15–23].

$$R_3P + CCl_4 \longrightarrow [R_3PCl]^+CCl_3^- \xrightarrow{+R'OH} [R_3POR']^+Cl^- + HCCl_3 \quad (6)$$

The chlorophosphonium trichloromethanide was taken to be the phosphorylating agent, its cation phosphorylating the alcohol to the alkoxyphosphonium salt and the extremely nucleophilic anion reacting with the proton to give chloroform. However, the alkoxyphosphonium salts expected from reactions of aliphatic alcohols are unstable, decomposing in the manner of an Arbuzov rearrangement to phosphane oxide and alkyl chloride. These concepts are also convincingly valid for reactions of tris(dimethylamino)phosphane because of the extensive charge transfer to give the ion pair *(2)* and because of the ability of the cation to mesomerize[20], but they do not apply to the triphenylphosphane/CCl_4 system.

Kinetic measurements based on quantitative determinations of the consumption of CCl_4 and the increase in the $CHCl_3$ content indicate that the formation of trichloromethylphosphonium chloride *(4)* as formulated in eq. (1) does not occur at all—or only slightly—by way of the ion pair *(2)* (route a), but instead by an intramolecular rearrangement of the dipolar complex *(1)* (route b, c, d)[24]. In this case the chloroform is formed already by reaction of the proton-active substrate with the dipolar associate *(1)* and only to a minor extent by reaction of the trichloromethylphosphonium chloride *(4)*[7, 24]. The main reaction shown in eq. (7) will be denoted below as the "A reaction".

A-Reaktion:

$$Ph_3P^{\delta+}\cdots Cl\cdots CCl_3^{\delta-} \longrightarrow [Ph_3P\text{–Substrate}]^+Cl^- + CHCl_3 \quad (7)$$

$$+ \text{Substrate-H}$$

According to stereochemical investigations with the chiral methyl-phenyl-*n*-propylphosphane which was treated with amines as substrate, the reaction occurs with racemization by way of pentavalent phosphorane stage *(8)*[25].

$$R''(R')(R''')P\cdots Cl\cdots CCl_3 \xrightarrow[-CHCl_3]{+HNR_2} R''(Cl)(R')(R''')P(NR_2) \longrightarrow \left[R''(R')(R''')P\text{–}NR_2\right]^+ Cl^- \quad (8)$$

(8)

Reaction of *(1)* [this may be a side-reaction of *(4)*] with a substrate XH is only slow when compared with that of the highly reactive ion pair *(2)*. It thus competes with the naturally occurring subsequent reactions of the two-component system Ph_3P/CCl_4 according to eq. (2). It affords, as is well known, the dichlorophosphorane *(6)*, which can react as an excellent phosphorylating agent for many substrates, yielding the same end-products as are obtained from triphenylphosphane/CCl_4, while the (dichloromethylene)phosphorane *(5)* acts as HCl-acceptor. In this way is formed the (dichloromethyl)phosphonium chloride *(9)*, which reacts with a further amount of phosphane to give the ylide *(10)* and the dichlorophosphorane *(6)*. Renewed reaction of the re-formed *(6)* as in eq. (9) and trapping of the liberated hydrogen chloride by the (chloromethylene)phosphorane *(10)* leads to the stable (chloromethyl)triphenylphosphonium chloride *(11)* and the salt composed of the phosphane and the deprotonated substrate. The latter salt is stable when XH = amine, but in the reaction with other substrates it decomposes further in the characteristic manner. Eq. (13) thus represents the overall reaction in this, the "B reaction", specifically for triphenylphosphane and CCl_4 as the starting materials[7, 24].

B Reaction:

$$\underset{(6)}{Ph_3PCl_2} + XH \longrightarrow [Ph_3P\text{–}X]^+Cl^- + HCl \quad (9)$$

$$\underset{(5)}{Ph_3P{=}CCl_2} + HCl \longrightarrow \underset{(9)}{[Ph_3P\text{–}CHCl_2]^+Cl^-} \quad (10)$$

$$\underset{(9)}{[Ph_3P\text{–}CHCl_2]^+Cl^-} + Ph_3P \longrightarrow \underset{(10)}{Ph_3P{=}CHCl} + \underset{(6)}{Ph_3PCl_2} \quad (11)$$

$$\underset{(10)}{Ph_3P{=}CHCl} + HCl \longrightarrow \underset{(11)}{[Ph_3P\text{–}CH_2Cl]^+Cl^-} \quad (12)$$

$$3\ Ph_3P + CCl_4 + 2\ XH \longrightarrow 2\ [Ph_3P\text{–}X]^+Cl^- + [Ph_3P\text{–}CH_2Cl]^+Cl^- \quad (13)$$

In all the reactions with Ph_3P/CCl_4, and independently of the nature of the third component, the phosphorylations are effected in part by the dichlorophosphorane formed as an intermediate, which explains why most of the reactions discussed below can also be effected directly by means of Ph_3PCl_2. If the atom phosphorylated in the substrate is oxygen or sulfur, there are usually subsequent rearrangements; these will be discussed in greater detail for the individual examples below.

For preparative application it is important that in the reaction route B one-third of the phosphane used is withdrawn as $[Ph_3PCH_2Cl]Cl$ from the phosphorylating reaction, and for the use of Ph_3P/CCl_4 this requires a small correction of the 1:1 stoichiometry derived in Section 3; on the assumption that each of the two reaction routes A and B accounts for half of the total reaction, a molar ratio of 1.2:1 is advisable[24]. A recent observation that the reaction of enolizable ketones with Ph_3P/CCl_4 proceeds to the extent of 95% *via* path B[24a] will certainly only be valid for this specific system and not be applicable to other multicomponent reactions.

The multiplicity of the processes occurring with the Ph_3P/CCl_4 system may be perplexing at first sight and may make its application appear less advisable than that of the reagents $[(CH_3)_2N]_3P/CCl_4$ or Ph_3PCl_2. Such doubts are, however, insignificant, since the desired reaction products are formed by both route A and route B, and the total yield is therefore generally very good. Special advantages of this system can be seen in its ready accessibility and ease of handling; it may further be advantageous that the ylide *(5)* formed as an intermediate is a strong base, and that therefore the addition of a foreign base is often superfluous or required only in small amount.

4. Chlorinations

4.1. Chlorination Reactions of O-Functional Compounds

4.1.1. Alcohols and Thiols

The predominant reaction of tertiary phosphanes and tetrachloromethane with alcohols[15-23a] or thiols[21,26-28a] occurs in the sense of eq. (14), yielding the salt *(12)* and chloroform.

$$R_3P + CCl_4 + R'-XH \longrightarrow [R_3P-X-R']^+Cl^- + CHCl_3 \quad (14)$$
(12), X = O, S

$$[R_3P-X-R']^+Cl^- \longrightarrow R_3P=X + R'-Cl \quad (15)$$

The phosphonium chlorides *(12)* in which R = Ph and R' = alkyl decompose in a rapid Arbuzov rearrangement to the phosphane oxide or sulfide and alkyl chloride [eq. (15)]. The reaction according to eqs. (14) and (15) is thus a method of converting alcohols into alkyl chloride that can be effected under very mild conditions.

The process is so mild that it is suitable for, *e.g.*, conversion of the hydroxyl groups of 5-spiro[3.4]octen-7-ol[28b] and, among natural products, of glycerides[29b], carbohydrates[16,17,29a,c], lincomycins[29d], or geraniol[30] into the corresponding chloro derivatives; it has also been used for mild halogenation of OH groups in ribose bound in nucleosides[31].

The stereochemistry of this reaction has been clarified by experiments with optically active alcohols[21,22,22a,28b,32]: it is largely stereoselective, with inversion.

The phosphonium ion from tris(dimethylamino)phosphane is considerably more stable, so that it can be isolated as perchlorate or hexafluorophosphate[19,23]. If such alkoxyphosphonium perchlorates are treated with alkali-metal halides or pseudohalides, the Arbuzov rearrangement is enforced and covalent halogen or pseudohalogen compounds are obtained[32,33], *e.g.*:

$$[(CH_3)_2N]_3POR]^+ClO_4^- + NaN_3 \longrightarrow [(CH_3)_2N]_3PO + RN_3 + NaClO_4 \quad (16)$$

Primary and secondary alcohols can similarly be converted into the corresponding carbonitriles; these are formed when the alcohols are heated with Ph_3P/CCl_4 and NaCN in dimethyl sulfoxide (DMSO)[34]:

$$CH_3-(CH_2)_6-\underset{OH}{CH}-CH_3 \xrightarrow[DMSO]{Ph_3P/CCl_4/NaCN} CH_3-(CH_2)_6-\underset{CN}{CH}-CH_3 \quad (17)$$

The aryloxy- and arylthiophosphonium salts *(12)* (R' = aryl) prove markedly more stable than the alkoxy- and alkylthiophosphonium salts, and when R = Ph they can be isolated as chlorides[28a] or hexachloroantimonates[27]. The phenoxy- and phenylthiotriphenylphosphonium chlorides are extremely sensitive to hydrolysis and decompose immediately even in air to HCl, triphenylphosphane oxide and phenol or thiophenol; when they are treated with an alcohol, the corresponding alkyl halide is formed together with the phosphane oxide and phenol or thiophenol. Alkanethiols decompose these salts analogously with formation of the phosphane sulfide[28a].

As in all such three-component reactions, the side reaction (B reaction) according to eq. (18) occurs alongside the main reaction [A reaction; eq. (14)].

$$3\ Ph_3P + CCl_4 + 2\ R'-XH \longrightarrow 2\ [Ph_3P-X-R']^+Cl^- + [Ph_3P-CH_2Cl]^+Cl^- \quad (18)$$
(12), X = O, S

4.1.2. Aldehydes, Ketones, and Epoxides

The two systems tris(dimethylamino)phosphane/CCl_4 and triphenylphosphane/CCl_4 behave very differently with aldehydes. The cause of this is the differing charge transfer, which was discussed in Section 2 and which leads to significant amounts of the ion pair *(2)* and the trichloromethanide ion only in the case of the tris(dimethylamino)phosphane. The overall reaction expressed in eq. (19) is based on a multistep mechanism [eqs. (19a–c)], in which the first step is nucleophilic attack of the CCl_3^- ion on the carbonyl carbon[35-38].

$$[R_3PCl]^+CCl_3^- + R'-CHO \longrightarrow \underset{(13)}{[R_3PCl]^+\ R'-\underset{CCl_3}{CH}-O^-} \quad (19a)$$
(2), R = $N(CH_3)_2$

$$(13) \longrightarrow \left[R_3P-O-\underset{CCl_3}{CHR'}\right]^+Cl^- \quad (19b)$$
(14)

$$(13) + (14) \longrightarrow \left[R_3P-O-\underset{CCl_3}{CHR'}\right]^+\ R'-\underset{CCl_3}{CH}-O^- + R_3PCl_2 \quad (19c)$$
(15)

$$2\ R_3P + 2\ CCl_4 + 2\ R'-CHO \longrightarrow (15) + R_3PCl_2 \quad (19)$$

On hydrolysis, the alkoxyphosphonium salt *(15)* affords α-substituted trichloroethanols[36-38]. If, however, the starting materials are used in the ratio phosphane/CCl_4/aldehyde = 2:1:1, then 1,1-dichloroolefins are obtained in accordance with eq. (20).

$$[R_3PCl]^+CCl_3^- + R'-CHO \longrightarrow \underset{(13)}{[R_3PCl]^+\ R'-\underset{CCl_3}{CH}-O^-} \quad (20a)$$
(2), R = $N(CH_3)_2$

$$(2) + (13) \longrightarrow R_3PCl_2 + \left[R_3P-O-\underset{CCl_3}{CHR'}\right]^+CCl_3^- \quad (20b)$$
(16)

$$(16) \longrightarrow R_3PO + R'-CH=CCl_2 + CCl_4 \quad (20c)$$

$$2\ R_3P + CCl_4 + R'-CHO \longrightarrow R_3PO + R_3PCl_2 + R'-CH=CCl_2 \quad (20)$$

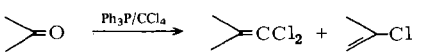
By analogy with the reaction of triphenylphosphane with CCl_4 [cf. eq. (2)], the (dichloromethylene)phosphorane *(5)* containing $N(CH_3)_2$ in place of Ph might arise by an ylide mechanism and react with the carbonyl compound by a Wittig-type reaction; this, however, is excluded, presumably because the (trichloromethyl)phosphonium chloride *(4)*, R = $N(CH_3)_2$, formed as intermediate is not dechlorinated by further amounts of the phosphane, as it is in the case of *(4)* where R = Ph[6]. The ylide mechanism is also opposed by the fact that not only aldehydes but also α-(trichloromethyl)alcohols can be

converted into 1,1-dichloroolefins in good yields[36]. Formation of the dichloroolefin probably results directly from dechlorination of the alkoxyphosphonium salt *(16)*.

None of the intermediates formulated in eq. (1) plays a significant part in the reaction of the Ph_3P/CCl_4 reagent with carbonyl compounds. The reaction occurs only through the (dichloromethylene)phosphorane *(5)* and the dichlorophosphorane *(6)* that are formed according to eq. (2) and leads to 1,1-dichloroolefins and dichloromethylene compounds[5, 7, 39]:

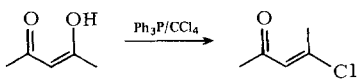
$$\underset{(5)}{Ph_3P{=}CCl_2} + \underset{(6)}{Ph_3PCl_2} + 2\ O{=}C\!\!\!\diagup\!\!\!\diagdown \longrightarrow Cl_2C{=}C\!\!\!\diagup\!\!\!\diagdown + Cl_2C\!\!\!\diagup\!\!\!\diagdown + 2\ Ph_3PO \qquad (21)$$

On reaction with Ph_3P/CCl_4, enolizable ketones also afford 1,1-dichloroolefins, but the chlorine-substitution product of the enol is also formed[40]. Among the five-membered ring ketones the dichloroolefin predominates very greatly, whereas the reverse is true for six membered ring ketones.



(22)

Good yields of β-chloro α,α-unsaturated ketones are obtained from 1,3-diketones[40a].



(22a)

With epoxides the Ph_3P/CCl_4 reagent gives dichloroalkanes in accordance with eq. (23); this reaction of cycloalkene oxides leads stereospecifically to *cis*-1,2-dichlorocycloalkanes[41].

$$2\ Ph_3P + CCl_4 + \underset{\diagup\ \diagdown}{>C{-}C<}\!\!\!\!O \longrightarrow Ph_3PO + Ph_3P{=}CCl_2 + \underset{|\quad|}{\overset{Cl\,Cl}{-C-C-}} \qquad (23)$$

Presumably this reaction does not occur by the postulated ionic mechanism[41] but rather, by analogy with eq. (21), through the intermediates *(5)* and *(6)*, the dichlorophosphorane reacting with the epoxide in the known manner[42].

$$Ph_3PCl_2 + R_2C\underset{\diagup\ \diagdown}{-}CR_2\!\!\!\!O \longrightarrow Ph_3PO + \overset{Cl\,Cl}{R_2C{-}CR_2} \qquad (24)$$

4.1.3. Carboxylic Acids and Oxophosphoric Acids

Similarly to the conversion of alcohols into alkyl chlorides, carboxylic acids can be easily converted by Ph_3P/CCl_4 into acyl chlorides [cf. eqs. (14) and (15); X=O, R'=C(O)R][43]. In contrast to the usual methods of preparing acid chlorides by means of thionyl chloride, phosphorus pentachloride, oxalyl chloride, or phosgene, the reaction medium is neutral, which is advantageous in the case of substances sensitive to acidic conditions.

The obvious thought of using this process for the synthesis of acid chlorides from other than carboxylic acids was recently realized for the acid chlorides from phosphoric esters and phosphinic acids[44]: 50—60% yields of the corresponding acid chlorides were obtained by the reaction of dimethyl- or diphenylphosphinic acid or of dibutyl hydrogen phosphate in acetonitrile, as shown in eq. (25).

$$Ph_3P + CCl_4 + R_2P(O)OH \longrightarrow R_2P(O)Cl + CHCl_3 + Ph_3PO \qquad (25)$$

$R = CH_3,\ C_6H_5,\ n\text{-}OC_4H_9$

Phosphoric monoesters can be converted into phosphoric ester dichlorides $ROP(O)Cl_2$, $R = i\text{-}C_3H_7$ or C_6H_5, in the same way.

For these cases it has been proved that chlorination does not occur exclusively according to eq. (25) with the formation of chloroform; here the B reaction also occurs [cf. eq. (13)]:

$$3\ Ph_3P + CCl_4 + 2\ R_2P(O)OH \longrightarrow 2\ R_2P(O)Cl + 2\ Ph_3PO + [Ph_3P{-}CH_2Cl]^+Cl^- \qquad (26)$$

Although participation of the B reaction in the synthesis of carboxylic acid chlorides has not been proved experimentally, it can be assumed that it does so in that case too, as usually occurs in reactions of the Ph_3P/CCl_4 system with proton-active substrates.

The diethyl ester chloride of phosphoric acid is not obtainable by the mechanism of eq. (25), the anhydride being formed instead [eq. (27)][44].

$$2\ (C_2H_5O)_2P(X)OH + Ph_3P + CCl_4 \longrightarrow (C_2H_5O)_2\overset{X}{\overset{\|}{P}}{-}O{-}\overset{X}{\overset{\|}{P}}(OC_2H_5)_2 + Ph_3PO + CHCl_3 + HCl \qquad (27)$$

X = O, S

This anhydride is formed not by way of the acid chloride, but directly from the phosphoryloxyphosphonium salt as shown in eq. (28).

$$\left[Ph_3P{-}O{-}\overset{O}{\overset{\|}{P}}(OC_2H_5)_2\right]^+ Cl^- + {}^-O{-}\overset{O}{\overset{\|}{P}}(OC_2H_5)_2 + H^+ \xrightarrow[-\ Ph_3PO]{-\ HCl} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}{-}O{-}\overset{O}{\overset{\|}{P}}(OC_2H_5)_2 \qquad (28)$$

In the three-component system $[(CH_3)_2N]_3P/CCl_4$/R'COOH the reaction also leads directly to the acid anhydride, owing to the greater stability of the intermediate acyloxyphosphonium chloride *(18)*[45].

$$\underset{(2),\ R = N(CH_3)_2}{[R_3PCl]^+CCl_3^-} + R'{-}COOH \longrightarrow \underset{(17)}{[R_3PCl]^+R'{-}COO^\ominus} + CHCl_3 \qquad (29a)$$

$$(17) \longrightarrow \underset{(18)}{[R_3P{-}O{-}CO{-}R']^+Cl^-} \qquad (29b)$$

$$(17) + (18) \longrightarrow R'{-}CO{-}O{-}CO{-}R' + R_3PO + R_3PCl_2 \qquad (29c)$$

$$2\ R_3P + 2\ CCl_4 + 2\ R'{-}COOH \longrightarrow R'{-}CO{-}O{-}CO{-}R' + 2\ CHCl_3 + R_3PO + R_3PCl_2 \qquad (29)$$

4.2. Chlorination Reactions of —C(X)—NH-Functional Compounds (X=O or S)

4.2.1. Chloroformamidines from Trisubstituted Ureas

Chloroformamidines can be obtained in good yields by the action of Ph_3P/CCl_4 on *N,N,N'*-trisubstituted ureas[46].

Under the very mild reaction conditions compounds can be obtained that are accessible only with difficulty, if at all, by the usual methods, *e.g.* chloroformamidines containing one or two aryl groups on the disubstituted N atom. Purely aliphatic chloroformamidines can also be prepared by this method[47].

$$Ph_3P + CCl_4 + R{-}NH{-}CO{-}NR'R'' \longrightarrow R{-}N{=}\underset{Cl}{C}{-}NR'R'' + Ph_3PO + CHCl_3 \quad (30)$$

As with all —CO—NH-functional compounds, the phosphorylation occurs on the O atom, after which the *O*-phosphorylated salt decomposes to phosphane oxide and chloroformamidine by a kind of Arbuzov rearrangement [eq. (31)].

$$\left[R''R'N{-}\underset{O{-}PPh_3}{C}{=}NR\right]^+ Cl^- \longrightarrow R''R'N{-}\underset{Cl}{C}{=}NR + Ph_3PO \quad (31)$$

It has been proved that the B reaction also takes part in this method of chloroformamidine formation, the active agent being the intermediate dichlorophosphorane *(6)*; this reaction, which provides no chloroform, is expressed in eq. (32).

$$3\ Ph_3P + CCl_4 + 2\ R{-}NH{-}CO{-}NR'R'' \longrightarrow 2\ R{-}N{=}\underset{Cl}{C}{-}NR'R'' + 2\ Ph_3PO + [Ph_3P{-}CH_2Cl]^+\ Cl^- \quad (32)$$

4.2.2. Imidoyl Halides from Monosubstituted Carboxamides and by Beckmann Rearrangement of Ketoximes

As shown in eq. (33), which is analogous to eq. (30), imidoyl halides are obtained from *N*-monosubstituted carboxamides; these products are important intermediates for the preparation of amidines and imino ethers[48].

$$Ph_3P + CX_4 + R{-}CO{-}NH{-}R' \longrightarrow R{-}\underset{X}{C}{=}N{-}R' + Ph_3PO + CHCl_3 \quad (33)$$

X = Cl, Br

The mild conditions make it possible to synthesize imidoyl halides that are difficult to prepare by other methods[49]. The discussion of chloroformamidine formation (Section 4.2.1) applies here too to the mechanism and participation of the B reaction. A further method for the formation of imidoyl chlorides by the Ph_3P/CCl_4 reagent consists in the latter's reaction with aromatic or aliphatic ketoximes in accordance with eq. (34)[50].

$$Ph_3P + CCl_4 + \begin{matrix} R' \\ \diagdown \\ C{=}NOH \\ \diagup \\ R \end{matrix} \longrightarrow R{-}\underset{Cl}{C}{=}N{-}R' + Ph_3PO + CHCl_3 \quad (34)$$

It is not certain that this formation of imidoyl chlorides occurs in accordance with eq. (35) by way of the *N*-chloro compound; it is also conceivable that *O*-phosphorylated ketoxime itself undergoes a Beckmann rearrangement [see eq. (36)]. Because of the great sensitivity of most imidoyl chlorides to hydrolysis, chromatographic processes are rarely suitable

$$\left[\begin{matrix} R' \\ \diagdown \\ C{=}N{-}O{-}PPh_3 \\ \diagup \\ R \end{matrix}\right]^+ Cl^- \xrightarrow[-\,Ph_3PO]{} \begin{matrix} R' \\ \diagdown \\ C{=}N{-}Cl \\ \diagup \\ R \end{matrix} \xrightarrow{\ominus} R{-}\underset{Cl}{C}{=}N{-}R' \quad (35)$$

$$\left[\begin{matrix} R' \\ \diagdown \\ C{=}N{-}O{-}PPh_3 \\ \diagup \\ R \end{matrix}\right]^+ Cl^- \xrightarrow[-\,Ph_3PO]{\sim R'} [R{-}C{\equiv}N{-}R']^+\ Cl^- \longrightarrow R{-}\underset{Cl}{C}{=}N{-}R' \quad (36)$$

for the separation of the phosphane oxide; distillation under high vacuum often leads with these compounds, depending on the nature of the groups R and R', to complicated decompositions involving loss of HCl[51]. In such cases isolation of the imidoyl chloride is abandoned and the product is used directly, or it is hydrolyzed to the amide which can be readily separated from the phosphane oxide.

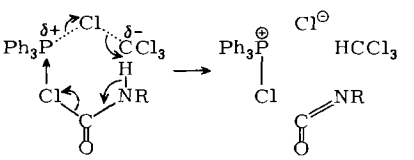
By hydrolysis of the crude products to the amides it has also been shown that dialiphatic ketoximes react to give imidoyl chlorides as expressed in eq. (34)[52]. As regards the migration tendency of the two groups R and R', the same rules are obeyed as for the Beckmann rearrangement by the usual reagents (H_2SO_4, PCl_5, or $COCl_2$). In diaromatic ketoximes the unsubstituted phenyl group migrates preferentially, and in aromatic-aliphatic compounds the aromatic group migrates[50].

4.2.3. Reaction with Carbamoyl Halides

Carbamoyl chlorides and fluorides do not react with Ph_3P/CCl_4 to give isocyanide dihalides in analogy with other reactions of —CO—NH-compounds, but instead isocyanates and dihalotriphenylphosphorane are obtained[53], *e.g.*:

$$Ph_3P + CCl_4 + R{-}NH{-}CO{-}Cl \longrightarrow R{-}N{=}C{=}O + Ph_3PCl_2 + CHCl_3 \quad (37)$$

In the case of carbamoyl fluoride a mixture of dichloro- and difluorotriphenylphosphorane is formed in place of the chlorofluorophosphorane. It is probable that in this reaction the halogen atom rather than the oxygen attacks the phosphorus of the charge-transfer complex *(1)* nucleophilically; in this way the electron density of the CCl_3 group is increased to such an extent that it deprotonates the carbamoyl halide [eq. (38)]:



(38)

From gas-chromatographic determinations of the increase in $CHCl_3$ concentration and decrease in that of CCl_4 in this three-component reaction it follows that here too, along with reaction according to eq. (37), the B reaction according to eq. (39) makes a considerable contribution to the overall conversion.

$$3\ Ph_3P + CCl_4 + 2\ R{-}NH{-}CO{-}Cl \longrightarrow 2\ R{-}N{=}C{=}O + 2\ Ph_3PCl_2 + [Ph_3P{-}CH_2Cl]^+\ Cl^- \quad (39)$$

4.2.4. Reaction with Thiocarbamic *O*-Esters

Whereas *N*-unsubstituted or *N*-monosubstituted carbamic esters afford stable *N*-phosphonium salts on treatment with Ph_3P/CCl_4[54], no phosphonium salt is detectable from the corresponding reaction of *N*-substituted thiocarbamic *O*-esters; the latter reaction leads directly to the phosphane sulfide, isocyanate, and alkyl chloride[55].

$$Ph_3P + CCl_4 + R{-}NH{-}\underset{\underset{S}{\|}}{C}{-}OR' \longrightarrow R{-}N{=}C{=}O + Ph_3PS + R'Cl + CHCl_3 \quad (40)$$

4.2.5. *N*-Phenylchlorothioformimidic Esters from Thiocarbamic *S*-Esters

Unlike the *O*-esters, the isomeric *S*-esters of thiocarbamic acid can be chlorinated by Ph_3P/CCl_4 with retention of the molecular skeleton on the carbonyl group[55]. The N-phenylchlorothioformimidic esters thus obtainable in 70—80% yield by the process of eq. (41) are pale yellow oils with an unpleasant odor, their thermal stability varying according to the nature of R'. When R'=*t*-butyl, complete

$$Ph_3P + CCl_4 + R{-}NH{-}\underset{\underset{O}{\|}}{C}{-}SR' \longrightarrow R{-}N{=}\underset{\underset{Cl}{|}}{C}{-}SR' + Ph_3PO + CHCl_3 \quad (41)$$

decomposition to isothiocyanate and *t*-butyl chloride takes place already during working up, but decomposition is of minor importance when R'=C_2H_5, *n*-C_3H_7 or *i*-C_3H_7.

As measured from the yield of chloroform, the products of the reaction of the *O*- and the *S*-esters are each formed to an extent of approximately 50% by the B reaction.

5. Dehydrations

5.1. Nitriles from Carboxamides and Aldoximes

The ability of the tertiary phosphane/CCl_4 system to remove water was discovered with carboxamides[56, 57]. In the presence of tertiary nitrogen bases such as triethylamine, pyridine, *etc.*, nitriles are thus formed in 80—90% yields. Thiocarboxamides react analogously.

$$Ph_3P + CCl_4 + R{-}C(X){-}NH_2 \xrightarrow[-[Et_3NH]Cl]{+Et_3N} R{-}C{\equiv}N + Ph_3PX + CHCl_3 \quad (42)$$
X = O, S

This nitrile synthesis can be applied equally well to aliphatic and aromatic carboxamides. It is also applicable to the production of such nitriles as 4,8-dioxoadamantane-2-carbonitrile[57] and 7-chloro-2,3-dihydro-1-methyl-2-oxo-5-phenyl-1*H*-1,4-benzazepine-3-carbonitrile[58], which are not accessible by the use of the usual strongly acidic dehydrating agents.

Again only about 50% of the nitrile is formed as shown in eq. (42), the other half being formed by dehydration of the dichlorophosphorane *(6)* occurring as an intermediate *via* a B mechanism. For this partial reaction eq. (43) summarizes the overall effect.

$$3\ Ph_3P + CCl_4 + 2\ R{-}C(X){-}NH_2 \xrightarrow[-2\,[Et_3NH]Cl]{+2\,Et_3N} 2\ R{-}C{\equiv}N + 2\ Ph_3PX + [Ph_3P{-}CH_2Cl]^+Cl^- \quad (43)$$

Removal of the phosphane oxide or sulfide occurs from the *O*- or *S*-phosphorylated salt in both reactions. This is also the case for the dehydration of aldoximes. By using deuterated acetaldoxime it has been shown that the hydrogen of the chloroform comes solely from the OH group[59].

$$Ph_3P + CCl_4 + DON{=}CHR \longrightarrow [Ph_3P{-}O{-}N{=}CHR]^+Cl^- + DCCl_3 \quad (44a)$$

$$[Ph_3P{-}O{-}N{=}CHR]^+Cl^- + Et_3N \longrightarrow R{-}C{\equiv}N + Ph_3PO + [Et_3NH]Cl \quad (44b)$$

5.2. Isocyanides from Monosubstituted Formamides

The Ph_3P/CCl_4 reagent can also be used with considerable success for the removal of water from *N*-substituted formamides. The process according to eq. (45), which represents a reaction partially analogous to that of eq. (43), affords alkyl and aryl isocyanides in yields of 90%[60], although so far it has been tested on only a few examples.

$$Ph_3P + CCl_4 + R{-}NH{-}CHO \xrightarrow[-[Et_3NH]Cl]{+Et_3N} R{-}\overset{\oplus}{N}{\equiv}\overset{\ominus}{C}: + Ph_3PO + CHCl_3 \quad (45)$$

5.3. Carbodiimides from *N,N'*-Disubstituted Ureas

The synthesis of carbodiimides from *N,N'*-disubstituted ureas or thioureas proceeds equally smoothly and with similarly high yields[61]:

$$Ph_3P + CCl_4 + R{-}NH{-}C(X){-}NH{-}R \xrightarrow[-[Et_3NH]Cl]{+Et_3N} R{-}N{=}C{=}N{-}R + Ph_3PX + CHCl_3 \quad (46)$$
X = O, S

The same considerations as described in Section 5.1 apply to its mechanism and participation of the two reaction routes A and B.

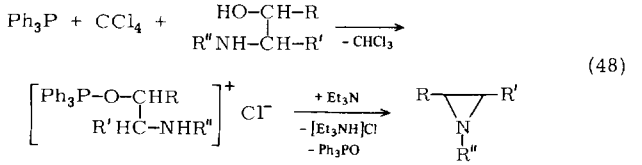
5.4. *C*-Ethoxycarbonyl-*C*-imidoylketene Imines from (Aminoalkylene)malonamic Esters

The (aminoalkylene)malonamic esters that can be obtained by the reaction of secondary enamines with isocyanates can be regarded as vinylogous ureas. They react, in the same way as *N,N'*-disubstituted ureas themselves, with Ph_3P/CCl_4 by undergoing dehydration to the very labile (ethoxycarbonyl)imidoylketene imines[62].

$$RNH{-}CR{=}\underset{\underset{CO_2Et}{|}}{C}{-}CO{-}NHR \xrightarrow[-H_2O]{} RN{=}CR{-}\underset{\underset{CO_2Et}{|}}{C}{=}C{=}NR \quad (47)$$

5.5. Aziridines from *N*-Substituted β-Amino Alcohols

An interesting aziridine synthesis derives from the action of Ph_3P/CCl_4 on *N*-substituted β-amino alcohols[63]. Unlike the usual methods of preparing aziridines in two stages by way of β-halo amines or β-amino sulfonic acids, this synthesis occurs in a single step under mild conditions and in good yields [see eq. (48)].

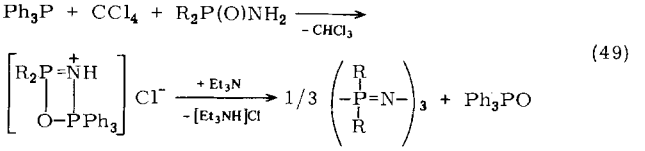


(48)

The ring closure from the alkoxyphosphonium salt occurs with inversion as in similar syntheses by means of Ph_3PBr_2[64]. Amino alcohols not substituted on the nitrogen undergo P—N linkage to a predominant extent, and this procedure is thus unsuitable for the synthesis of aziridines not substituted on the nitrogen.

5.6. Removal of Water from Phosphoramides and Phosphinamides

When phosphoramides or their diesters are treated with Ph_3P/CCl_4, linkage of P to N is usually observed (cf. Section 6.2). As exceptions to this, diethyl phosphoramidate and diphenylphosphinamide are dehydrated by this reagent to cyclotri-λ^5-phosphazenes[65]; formation of the cyclophosphazene in this way may involve a four-membered ring mechanism indicated in eq. (49).



(49)

R = Ph, OEt

The above reactions by no means exhaust the possible examples of the use of intramolecular elimination of water. This is apparent from the recently reported 1,1-dehydration of *N*-*p*-tolylhydroxylamine[65a], which affords mainly *p*-azotoluene, and the dehydration of *N*-acylphenylglycine esters which proceeds with concomitant cyclization to give the 5-alkoxyoxazole[65b].

5.7. Intermolecular Removal of Water

Examples of intermolecular removal of water by Ph_3P/CCl_4 were treated above in Section 4.1.3 concerning the formation of carboxylic anhydrides and phosphoric diesters or phosphinic anhydrides. Intermolecular dihydrations are also the basis for esterifications and amide formation, and this will be discussed in greater detail in Section 7 in connection with four-component reactions.

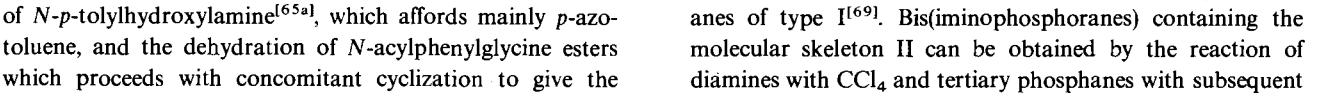
6. Reactions Providing P—N Linkage

Only in the first step does the action of the tertiary phosphane/CCl_4 system on ammonia and its derivatives occur analogously to the reaction with alcohols indicated in eq. (14). Unlike the alkoxyphosphonium salts, aminophosphonium chlorides do not readily rearrange, and this procedure is therefore particularly suitable for the formation of P—N bonds under mild conditions and in high yield. Similarly, the two-component system reacts with amides and imides of sulfur and phosphorus affording P—N linkage, processes that have the advantages of a smaller salt content in the product than after the reaction of phosphorus-halogen compounds with amines, and of less danger in the handling of the starting materials than in the chloramination or the azide method.

The reaction of a chiral phosphane with CCl_4 and an amine leads to loss of optical activity and thus, it is concluded, involves a pentavalent phosphorane intermediate[25]. It is also known that in all such reactions with the Ph_3P/CCl_4 system the B reaction participates alongside the main reaction that generates chloroform according to eq. (50); in most instances the reaction by route A is strongly predominant, and consequently, for simplification, the formulation of the B reaction is neglected in the discussion of the examples below.

6.1. Aminophosphonium Chlorides and Iminophosphoranes

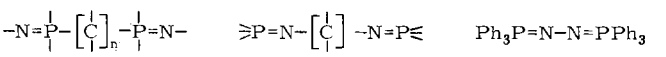
Ammonia and primary and secondary amines react smoothly with a tertiary phosphane and CCl_4 to yield aminophosphonium chlorides, and these can be readily deprotonated to iminophosphoranes by suitable bases[66, 67]. Because of the violent reaction of aliphatic phosphanes with CCl_4, the process shown in eq. (50) is effected with these phosphanes at $-50\,°C$[68], but in other cases best between 20 and $60\,°C$[66].



(50)

R', R'' = H, Alkyl, Aryl, $N(CH_3)_2$

On application of this reaction to ditertiary bisphosphanes with amines, bis(aminophosphonium) dichlorides are obtained, and on deprotonation by bases these afford bisiminophosphoranes of type I[69]. Bis(iminophosphoranes) containing the molecular skeleton II can be obtained by the reaction of diamines with CCl_4 and tertiary phosphanes with subsequent deprotonation[69]. Hydrazine behaves like a diamine toward Ph_3P/CCl_4: by twofold P—N linkage *N*,*N*'-bis(triphenylphosphonio)hydrazine chloride is formed, which is dehydrochlorinated even by liquid NH_3 to the bis(phosphoranediyl)hydrazine *(19)*[70, 71]. This product *(19)*, like the bisiminophosphoranes II, reacts smoothly with diketones undergoing O/N exchange, when energy-poorer N-heterocyclic systems are formed[71].



I II *(19)*

Only brief reference can be made here to the possibility of directed cyclocondensation of either biphosphanes or bifunctional amino compounds with CCl_4 to give diazadiphosphorines[72], triazadiphosphorines[73], or unambiguously differently substituted cyclotri- and cyclotetra-λ^5-phosphazenes[74]; other cyclic compounds, containing the atomic sequence —S—N—P—, can also be obtained by this method[72].

6.2. *N*-(Triphenylphosphoranediyl)amides of Sulfuric Acid, Sulfonic Acids, Alkyl Sulfates and Fluorosulfamides, as well as *N*-(Triphenylphosphoranediyl)-phosphoramidic Diesters and -phosphinamides

Unlike carboxamides, the amides of sulfonic acids or alkyl sulfates, *N*,*N*-dialkylsulfamic acids, and fluorosulfamic acid react with Ph_3P/CCl_4 not with dehydration but with P—N linkage[75, 76]. The primary products formed thereby are *N*-substituted aminophosphonium chlorides, which are converted, in some cases spontaneously and in others only on the addition of a base, into the corresponding iminotriphenylphosphoranes.

$$Ph_3P + CCl_4 + H_2N{-}SO_2{-}R \xrightarrow[-\,[Et_3NH]Cl]{+\,Et_3N} Ph_3P{=}N{-}SO_2{-}R + CHCl_3 \quad (51)$$

R = Alkyl, Aryl, $N(Alkyl)_2$, OAlkyl, F

The reaction of the three-component system triphenylphosphane/CCl_4 plus dialkyl phosphoramidates or phosphinamide has been observed to take a similar course[77], illustrated in eq. (52), but this process cannot be generalized since in analogous experiments with diethyl phosphoramidate and diphenylphosphinamide removal of water occurred, with the formation of cyclo-λ^5-phosphazenes (cf. Section 5.6)[65].

$$Ph_3P + CCl_4 + H_2N{-}\overset{X}{\overset{\|}{P}}R_2 \xrightarrow[-\,[Et_3NH]Cl]{+\,Et_3N} Ph_3P{=}N{-}\overset{X}{\overset{\|}{P}}R_2 + CHCl_3 \quad (52)$$

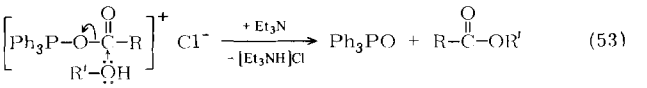
X = O, S; R = OCH_3, OPh, Ph

7. Four-Component Reactions

The tertiary phosphane/CCl_4 reagent can be used not only for intramolecular but also for intermolecular dehydrations. Examples of the latter are the formation of acid anhydrides mentioned above [cf. Section 4.1.3; eqs. (27) and (29)], and condensations of the phosphane/CCl_4/carboxylic acid system to which an alcohol or an amine has been added as a fourth component.

7.1. Esterifications

Ester formation by means of Ph_3P/CCl_4 as a condensing agent has been investigated for the esterification of ethanol and butanol with chloroacetic, butyric, succinic, or benzoic acid. It leads to high yields only when the alcohol is added as the last component after a prereaction of the three-component system (*ca.* 2 h). Under the conditions of a true four-component system, *i.e.* if the alcohol and acid are added simultaneously to the condensing agent, the appreciably poorer yields depend characteristically on the strength of the acid: the acyloxyphosphonium salt assumed as an intermediate may be attacked by the alcohol either on the phosphorus or on the carbonyl carbon; the more electrophilic is the central carbon atom, *i.e.* the stronger the carboxylic acid, the more is ester formation favored.



$$\left[Ph_3P{-}\overset{\overset{O}{\|}}{O{-}C{-}R}\right]^{+} Cl^- \xrightarrow[-\,[Et_3NH]Cl]{+\,Et_3N} Ph_3PO + R{-}\overset{\overset{O}{\|}}{C}{-}OR' \quad (53)$$

$$\left[Ph_3P{-}\overset{\overset{O}{\|}}{O{-}C{-}R}\right]^{+} Cl^- \longrightarrow [Ph_3P{-}O{-}R']^+ Cl^- + R{-}\overset{\overset{O}{\|}}{C}{-}OH \quad (54)$$

$$[Ph_3P{-}O{-}R']^+ Cl^- \longrightarrow Ph_3PO + R'{-}Cl$$

7.2. Acid Amides and Peptides

High yields have been reported for the synthesis of amides as shown in eq. (55)[78].

$$Ph_3P + CCl_4 + RCOOH + 2\ HNR'R'' \longrightarrow R{-}\overset{\overset{O}{\|}}{C}{-}NR'R'' + Ph_3PO + CHCl_3 + [R'R''NH_2]Cl \quad (55)$$

It is particularly interesting that *N*-protected amino acids and amino-acid esters can be linked to form peptides by the two-component phosphane/CCl_4 system[79–83]. After the first successful use of tris(dimethylamino)-, trismorpholino- and tributylphosphane had been reported[79, 81, 82], high yields of peptides, without racemization, were also described for the use of the Ph_3P/CCl_4 system under modified reaction conditions[83]. That the condensation occurs without racemization has been tested so far up to the hexapeptide Z-Leu-Ala-Val-Phe-Gly-ProOBzl[83]. A racemization observed in a few cases could be largely suppressed by addition of 1-hydroxybenzotriazole[83a]. The reaction conditions correspond to a true four-component reaction, in which it is surprising that here the P—N linkage with the amine components plays no part.

It is further of potential importance for some uses of this method that alcoholic groups such as occur in serine, threonine, and tyrosine are not converted into chloride when the condensing agent is used in stoichiometric amounts, so that these groups do not need to be protected. Similarly, glutamine does not need protection since its amide group is not dehydrated to the nitrile[83]. Mechanistic studies show a significant dependence of the reaction rate on the strength of the base added, and it is further clear from these studies that the reaction of eq. (56) producing chloroform is accompanied in the peptide condensation by the B reaction [eq. (57)] proceeding through the dichlorophosphorane formed as an intermediate.

$$Ph_3P + CCl_4 + 2\ Et_3N + Z{-}NH{-}CHR{-}COOH + H_2N{-}CHR{-}COOR{\cdot}HX \longrightarrow Z{-}NH{-}CHR{-}CO{-}NH{-}CHR{-}COOR + Ph_3PO + CHCl_3 + [Et_3NH]Cl + [Et_3NH]X \quad (56)$$

X = Cl, Br, OTos

$$3\ Ph_3P + CCl_4 + 2\ R{-}COOH + 2\ RR'NH + 2\ Et_3N \longrightarrow 2\ R{-}CO{-}NRR' + 2\ Ph_3PO + 2\ [Et_3NH]Cl + [Ph_3P{-}CH_2Cl]Cl \quad (57)$$

The usefulness of the process can, however, be judged only after investigations with still longer peptide chains, and then a decisive factor will be the attempts to find suitable solvent mixtures for the higher polymers.

7.3. Esters, Amidic Esters, and Amides of Phosphinic and Phosphoric Acids

The esterification of mono- and di-esters of phosphoric acid and of phosphinic acids by the use of Ph_3P/CCl_4 can also be carried out as a four-component reaction. Good to very good yields are obtained by the reaction effected as a single-stage process according to eq. (58) if additional triethylamine is added to bind the hydrogen chloride released.

$$Ph_3P + CCl_4 + R_2P(O)OH + R'OH \xrightarrow[-[Et_3NH]Cl]{+Et_3N} R_2P(O)OR' + Ph_3PO + CHCl_3 \quad (58)$$

R = CH_3, OAlkyl; R' = Alkyl

The same is true for the synthesis of phosphinamides and phosphoramidic esters, which can be obtained from phosphinic acids or the mono- or di-esters of phosphoric acid with ammonia or primary or secondary amines together with Ph_3P/CCl_4 as condensing agent[84]; presumably the reaction proceeds by way of the *O*-phosphorylated salt and not of the acid chloride or the anhydride as an intermediate:

$$\left[Ph_3P{-}O{-}\overset{O}{\overset{\|}{P}}R_2\right]^+ Cl^- + 2\ HNR_2' \xrightarrow[-[R'_2NH_2]Cl]{} Ph_3PO + R'_2N{-}\overset{O}{\overset{\|}{P}}R_2 \quad (59)$$

8. Other Two-Component Systems

In the halophosphanes the nucleophilicity of the phosphorus, shown even in the simple replacement of an organyl ligand by chlorine, is so greatly repressed that no reaction occurs with tetrachloromethane in the sense of eqs. (1) and (2)[85]. Admittedly, there is the indication of activation of the phosphorus by a primary dipolar complex in the extremely ready chlorine-fluorine exchange observed in the action of HF on solutions of chlorophosphanes in CCl_4 or $FCCl_3$, which provides a simple synthesis of organylfluorophosphoranes R_nPF_{5-n}[86] or RPF_3H[87].

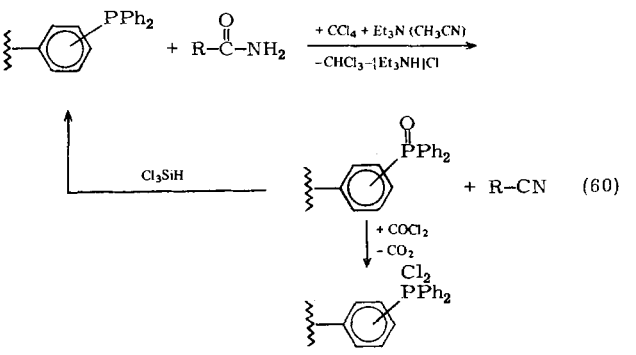
If, however, a primary or secondary amine is added to the chlorophosphane/CCl_4 system, then the replacement of halogen is followed at once by a series of CCl_4-oxidation and P—N linkage reactions. Di-, tri-, and tetraaminophosphonium salts are thus obtained by starting from, respectively, chlorodiorganylphosphanes, dichloroorganylphosphanes, or phosphorus trichloride[88]. Also, diaminodiorganylphosphonium chlorides are formed by the action of amines on diphosphanes and CCl_4[89], and analogously triaminoorganylphosphonium chlorides are the stable products from the three-component cyclophosphane/CCl_4/amine system[90]. This pair of reactions is preceded by fission of the P—P bond by the CCl_4, the resulting chlorine atom and trichloromethyl group adding to the free valences of the phosphorus atoms.

9. Summary and Outlook

The results obtained so far show already that the tertiary phosphane/tetrachloromethane system is a simple and very useful reagent for the synthesis of many important classes of compounds. Of more general importance is its use as chlorinating and dehydrating agent which, for sensitive substrates, is preferable to the aggressive and readily hydrolyzed acid chlorides such as PCl_5, $OPCl_3$, O_2SCl_2, and $OSCl_2$. A great advantage can also be seen in the ability to suit the reaction conditions to a large extent to the demands made by the various donor strengths of the substituents chosen for attachment to the phosphorus. Thus, many reactions that can be carried out with Ph_3P/CCl_4 in the temperature range between 20 and 60 °C require cooling to −60 to −20 °C if they are effected with $[(CH_3)_2N]_3P/CCl_4$. Other variations make it possible to change the halogen in the tetrahalomethane and, as shown in a few isolated examples above, very many bromine derivatives analogous to the chloro compounds mentioned in this report can be obtained by using CBr_4.

It can be expected that a controlled introduction of this reagent will find its greatest successes in mild and selective halogenations and dehydrations. Whether the two-component system, which is primarily a laboratory reagent, will also become suitable for industrial application, is probably a matter of economics. In this connection it remains to find out whether recovery and reactivation of the phosphane oxide is worthwile; possibilities for this are offered by conversion of the oxide by phosgene[91] into the dichlorophosphorane, which is itself an excellent chlorinating and dehydrating agent[92], or by further treatment of the latter with elementary phosphorus to yield, in particular, phosphorus trichloride and triphenylphosphane[93].

Chlorinations and dehydrations on polymers bearing R_2P groups appear to hold considerable promise for the future. Resins[94] suitable for this purpose can be obtained, *e. g.*, from polystyrene crosslinked with divinylbenzene by bromination and subsequent reaction with sodium or lithium diphenylphosphide. Apart from the chlorination of alcohols[95,96] and carboxylic acids[96] the modified procedure is also suitable for numerous intra- and intermolecular eliminations of water as described in Section 5[97].



(60)

A particular advantage of this method is that the solutions of the reaction products are obtained free from phosphane oxide and the $R_2P(O)$ groups of the resin present after the reaction can easily be regenerated. In addition to reduction with trichlorosilane[95,98], they can be transformed by phosgene into the dichlorophosphorane resin[91,99] which can likewise be used for many of the reactions considered in Section 4.

Received: April 1, 1975 [A 90 IE]
German version: Angew. Chem. 87, 863 (1975)
Translated by Express Translation Service, London

[1] *J. I. G. Cadogan* and *R. K. Mackie*, Chem. Soc. Rev. 3, 87 (1974).
[2] *H. Teichmann*, Z. Chem. 14, 216 (1974).

[3] *A. W. Hofmann*, Proc. R. Soc. London *10*, 186 (1859); *11*, 292 (1860).
[4] *A. J. Speziale* and *K. W. Ratts*, J. Am. Chem. Soc. *84*, 857 (1962).
[5] *R. Rabinowitz* and *R. Marcus*, J. Am. Chem. Soc. *84*, 1312 (1962).
[6] *W. Ried* and *H. Appel*, Justus Liebigs Ann. Chem. *679*, 51 (1964).
[7] *R. Appel, F. Knoll, W. Michel, W. Morbach, H.-D. Wihler*, and *H. Veltmann*, Chem. Ber. *109*, 58 (1976).
[8] *H. Hoffmann* and *H. J. Diehr*, Angew. Chem. *76*, 944 (1964); Angew. Chem. internat. Edit. *3*, 737 (1964).
[9] *A. Hantsch* and *H. Hibbert*, Ber. Dtsch. Chem. Ges. *40*, 1508 (1907).
[10] *W. Michel*, Dissertation, Universität Bonn 1974.
[11] *G. Kortüm*: Lehrbuch der Elektrochemie. Verlag Chemie, Weinheim 1966, Chap. VII, 2.
[12] *J. Buchanan* and *S. D. Hamann*, Trans. Faraday Soc. *49*, 1425 (1953).
[13] *C. T. Burris* and *K. J. Laidler*, Trans. Faraday Soc. *51*, 1497 (1955).
[14] *E. Whalley*, Trans. Faraday Soc. *55*, 798 (1959).
[15] *I. M. Downie, J. B. Holms*, and *J. B. Lee*, Chem. Ind. London *1966*, 950.
[16] *J. B. Lee* and *T. J. Nolan*, Can. J. Chem. *44*, 1331 (1966).
[17] *J. B. Lee* and *I. M. Downie*, Tetrahedron *23*, 359 (1967).
[18] *J. Hooz* and *S. S. H. Gilani*, Can. J. Chem. *46*, 86 (1968).
[19] *I. M. Downie, J. B. Lee*, and *M. F. S. Matough*, Chem. Commun. *1968*, 1350.
[20] *B. Castro* and *C. Selve*, Bull. Soc. Chim. Fr. *1971*, 4368.
[21] *R. G. Weiss* and *E. I. Snyder*, Chem. Commun. *1968*, 1358.
[22] *R. G. Weiss* and *E. I. Snyder*, J. Org. Chem. *35*, 1627 (1970).
[22a] *E. I. Snyder*, J. Am. Chem. Soc. *91*, 5118 (1969).
[23] *B. Castro* and *C. Selve*, Bull. Soc. Chim. Fr. *1971*, 2296.
[23a] *R. Boigegrain, B. Castro*, and *C. Selve*, Tetrahedron Lett. *1975*, 2529.
[24] *R. Appel* and *K. Warning*, Chem. Ber. *108*, 6 (1975).
[24a] *I. Tömösközi, L. Gruber*, and *L. Radics*, Tetrahedron Lett. *1975*, 2473.
[25] *R. Appel* and *K. Warning*, Phosphorus *4*, 29 (1974).
[26] *A. J. Burn* and *J. I. G. Cadogan*, J. Chem. Soc. *1963*, 5788.
[27] *H. Teichmann* and *W. Gerhard*, Z. Chem. *14*, 233 (1974).
[28] a) *R. Appel, K. Warning*, and *K. D. Ziehn*, Justus Liebigs Ann. Chem. *1975*, 406; b) *R. D. Miller, M. Schneider*, and *D. L. Dolce*, J. Am. Chem. Soc. *95*, 8469 (1973).
[29] a) *J. B. Lee* and *T. J. Nolan*, Tetrahedron *23*, 2789 (1967); b) *R. Aneja, A. P. Davies*, and *J. A. Knaggs*, J. C. S. Chem. Comm. *1973*, 110; c) *B. Castro, Y. Chapleur*, and *B. Gross*, Bull. Soc. Chim. Fr. *1973*, 11, 3034; d) *R. D. Birkenmeyer*, US-Pat. 3475407 (1969).
[30] *L. B. Hunt, D. F. MacSweeny*, and *R. Ramage*, Tetrahedron *27*, 1491 (1971).
[31] *J. P. H. Verheyden* and *J. G. Moffatt*, J. Org. Chem. *37*, 2289 (1972).
[32] *A. W. Friederang* and *D. S. Tarbell*, J. Org. Chem. *33*, 3797 (1968).
[33] *B. Castro, Y. Chapleur, B. Gross*, and *C. Selve*, Tetrahedron Lett. *1972*, 5001.
[34] *D. Brett, I. M. Downie*, and *J. B. Lee*, J. Org. Chem. *32*, 855 (1967).
[35] *G. Lavielle, J. C. Combret*, and *J. Villiéras*, Bull. Soc. Chim. Fr. *1971*, 2042.
[36] *J. C. Combret, J. Villiéras*, and *G. Lavielle*, Tetrahedron Lett. *1971*, 1035.
[37] *B. Castro, R. Burgada, G. Lavielle*, and *J. Villiéras*, C. R. Acad. Sci. Ser. C *268*, 1067 (1969).
[38] *B. Castro, R. Burgada, G. Lavielle*, and *J. Villiéras*, Bull. Soc. Chim. Fr. *1969*, 2770.
[39] *D. J. Burton* and *J. R. Greenwald*, Tetrahedron Lett. *1967*, 1535.
[40] *N. S. Isaacs* and *D. Kirkpatrick*, J. C. S. Chem. Comm. *1972*, 443.
[40a] *L. Gruber, I. Tömösközi*, and *L. Radics*, Synthesis *1975*, 708.
[41] *N. S. Isaacs* and *D. Kirkpatrick*, Tetrahedron Lett. *1972*, 3869.
[42] *A. N. Thakore, P. Pope*, and *A. C. Oehlschlager*, Tetrahedron *27*, 2617 (1971).
[43] *J. B. Lee*, J. Am. Chem. Soc. *88*, 3440 (1966).
[44] *R. Appel* and *H. Einig*, Z. Anorg. Allg. Chem. *414*, 236 (1975).
[45] *B. Castro* and *J. B. Dormoy*, Bull. Soc. Chim. Fr. *1971*, 3034.
[46] *R. Appel, K. D. Ziehn*, and *K. Warning*, Chem. Ber. *106*, 2093 (1973).
[47] *R. Appel, K. Warning*, and *K. D. Ziehn*, Chem. Ber. *107*, 698 (1974).
[48] *R. Appel, K. Warning*, and *K. D. Ziehn*, Chem. Ber. *106*, 3450 (1973).
[49] *R. Appel, K. Warning*, and *K. D. Ziehn*, German Pat. Appl. 2333110.4 (Le A 15116) (1975), Bayer AG.
[50] *R. Appel* and *K. Warning*, Chem. Ber. *108*, 1437 (1975).
[51] *J. v. Braun, F. Jostes*, and *A. Heymons*, Ber. Dtsch. Chem. Ges. *60*, 92 (1927).
[52] *R. M. Waters, N. Wakabayaski*, and *E. S. Fields*, Org. Prep. Proced. Int. *6*, 53 (1974).
[53] *R. Appel, K. Warning, K. D. Ziehn*, and *A. Gilak*, Chem. Ber. *107*, 2671 (1974).
[54] *R. Appel* and *K. Giesen*, to be published.
[55] *R. Appel* and *K. Giesen*, Chem. Ber., in press.
[56] *E. Yamato* and *S. Sugasawa*, Tetrahedron Lett. *1970*, 4383.
[57] *R. Appel, R. Kleinstück*, and *K. D. Ziehn*, Chem. Ber. *104*, 1030 (1971).
[58] *R. Jaunin* and *W. Arnold*, Helv. Chim. Acta *56*, 2569 (1973).
[59] *R. Appel, R. Kleinstück*, and *K. D. Ziehn*, Chem. Ber. *104*, 2025 (1971).
[60] *R. Appel, R. Kleinstück*, and *K. D. Ziehn*, Angew. Chem. *83*, 143 (1971); Angew. Chem. internat. Edit. *10*, 132 (1971).
[61] *R. Appel, R. Kleinstück*, and *K. D. Ziehn*, Chem. Ber. *104*, 1335 (1971).
[62] *J. Goerdeler* and *C. Lindner*, Tetrahedron Lett. *1972*, 1519.
[63] *R. Appel* and *R. Kleinstück*, Chem. Ber. *107*, 5 (1974).
[64] *J. Okada, K. Jchimura*, and *R. Sudo*, Bull. Chem. Soc. Jpn. *43*, 1185 (1970).
[65] *R. Appel* and *H. Einig*, Chem. Ber. *108*, 919 (1975).
[65a] *T. Ohashi* and *R. Appel*, Bull. Chem. Soc. Jpn. *48*, 1667 (1975).
[65b] *W. Steglich*, to be published.
[66] *R. Appel, R. Kleinstück, K. D. Ziehn*, and *F. Knoll*, Chem. Ber. *103*, 3631 (1970).
[67] *I. N. Zhumovova* and *A. P. Martynyuk*, Zh. Obshch. Khim. *44*, 1, 82 (1974).
[68] *B. Ross* and *K. P. Reetz*, Chem. Ber. *107*, 2720 (1974).
[69] *R. Appel, B. Blaser, R. Kleinstück*, and *K. D. Ziehn*, Chem. Ber. *104*, 1847 (1971).
[70] *R. Appel, B. Blaser*, and *G. Siegemund*, Z. Anorg. Allg. Chem. *363*, 176 (1968).
[71] *R. Appel* and *P. Volz*, Chem. Ber. *108*, 623 (1975).
[72] *R. Appel, R. Kleinstück*, and *K. D. Ziehn*, Chem. Ber. *105*, 2476 (1972).
[73] *R. Appel* and *G. Saleh*, Justus Liebigs Ann. Chem. *766*, 98 (1972).
[74] *R. Appel* and *G. Saleh*, Chem. Ber. *106*, 3455 (1973).
[75] *R. Appel, R. Kleinstück*, and *K. D. Ziehn*, Chem. Ber. *104*, 2250 (1971).
[76] *R. Appel* and *H. Einig*, Z. Naturforsch. *30B*, 134 (1975).
[77] *H. Einig*, Dissertation, Universität Bonn, 1974.
[78] *L. C. Barstow* and *V. J. Haruby*, J. Org. Chem. *36*, 1305 (1971).
[79] *S. Yamada* and *Y. Takeuchi*, Tetrahedron Lett. *1971*, 3595.
[80] *Th. Wieland* and *A. Seeliger*, Chem. Ber. *104*, 3992 (1971).
[81] *Y. Takeuchi* and *S. Yamada*, Chem. Pharm. Bull. *22*, 832 (1974).
[82] *Y. Takeuchi* and *S. Yamada*, Chem. Pharm. Bull. *22*, 841 (1974).
[83] *R. Appel, G. Bäumer*, and *W. Strüver*, Chem. Ber. *108*, 2680 (1975).
[83a] *R. Appel, G. Bäumer*, and *W. Strüver*, Chem. Ber., in press.
[84] *R. Appel* and *H. Einig*, Z. Anorg. Allg. Chem. *414*, 241 (1975).
[85] *U. Warning*, Diplomarbeit, Universität Bonn 1975.
[86] *R. Appel* and *A. Gilak*, Chem. Ber. *107*, 2169 (1974).
[87] *R. Appel* and *A. Gilak*, Chem. Ber. *108*, 2693 (1975).
[88] *H. Teichmann, W. Gerhard*, and *W. Kochmann*, GDR-Pat. 105242 (1973).
[89] *R. Appel* and *R. Milker*, Chem. Ber. *108*, 2349 (1975).
[90] *R. Appel* and *R. Milker*, Z. Anorg. Allg. Chem. *417*, 161 (1975).
[91] *R. Appel* and *W. Heinzelmann*, DBP 1192205 (1966), BASF AG.
[92] *L. Horner, H. Oedinger*, and *H. Hoffmann*, Justus Liebigs Ann. Chem. *626*, 26 (1959).
[93] *G. Wunsch, K. Wintersberger*, and *H. Geierhaas*, DBP 1247310 (1967), BASF AG.
[94] *W. Heitz* and *R. Michels*, Angew. Chem. *84*, 296 (1972); Angew. Chem. internat. Edit. *11*, 298 (1972).
[95] *S. L. Regen* and *D. P. Lee*, J. Org. Chem. *40*, 1669 (1975).
[96] *P. Hodge* and *G. Richardson*, J. C. S. Chem. Comm. *1975*, 622.
[97] *R. Appel* and *R. Milker*, to be published.
[98] *W. Heitz* and *R. Michels*, Justus Liebigs Ann. Chem. *1973*, 227.
[99] *H. M. Relles* and *R. W. Schluenz*, J. Am. Chem. Soc. *96*, 6469 (1974).

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

A New Route to Dialkylstannanediyls (Dialkylstannylenes) and Their Preparative Application[1]

By *Wilhelm P. Neumann* and *Alois Schwarz*[*]

The carbene analogs stannanediyls (stannylenes) R_2Sn bearing saturated alkyl substituents were unknown until recently and have so far only been accessible by thermolysis of distannanes $XR_2Sn—SnR_2X$[2]. We have now found that they can be more readily generated even at room temperature by photolysis of cyclopolystannanes $(R_2Sn)_n$ *(1)*[3]; previous attempts at thermal cleavage of *(1)* were unsuccessful[4].

$$(R_2Sn)_n \xrightarrow{h\nu} R_2\dot{S}n\text{–}(R_2Sn)_{n-2}\text{–}\dot{S}nR_2 \longrightarrow R_2\dot{S}n\text{–}(R_2Sn)_{n-3}\text{–}\dot{S}nR_2 + R_2Sn$$

(1) *(2)*

$$\longrightarrow n\ R_2Sn$$

(3)

R = CH_3, n-C_4H_9

The α,ω-polystannane diradical *(2)* apparently decomposes spontaneously to *n* stannanediyls *(3)* (intermediates can recyclize) which in the absence of other reactants mainly polymerize to cyclostannane and are regenerated on irradiation. However, with suitable reactants, *(3)* generally gives good yields of products and proves to be a versatile reagent. Thus with primary alkyl bromides and chlorides we also obtained ≥80% of insertion product (cf. ref. [2]) and when R′=isobutyl the yields are still 65—67%:

(3) + R′–X ⟶ R′R_2SnX

R′ = CH_3, C_4H_9; CH_2=$CHCH_2$, $C_6H_5CH_2$; X = Cl, Br

(3) can insert into Sn—H, Sn—C, and Sn—Sn bonds:

(3) +
- $R'_3SnH \rightleftharpoons R'_3SnSnR_2H$ (ν_{Sn-H} = 1785 cm^{-1})
- $R'_2SnH_2 \longrightarrow HR'_2SnSnR_2H$ (b.p. 86°C/0.001 torr)
- $R'_4Sn \longrightarrow R'_3SnSnR_2R'$ (b.p. 69°C/0.002 torr)
- $R'_3SnSnR'_3 \longrightarrow R'_3Sn(R_2Sn)SnR'_3$ (b.p. 120°C/10^{-5} torr)

R = n-C_4H_9; R′ = CH_3

With peroxides and disulfides, *(3)* likewise gives high yields (*e.g.* 84—91%) of insertion product. On reaction with dibenzoyl peroxide CO_2 appears only in traces, thus indicating that radical reactions only play a minor role if they are operative at all.

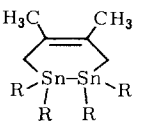
(3) + R′O–OR′ ⟶ $R_2Sn(OR')_2$

R = CH_3, n-C_4H_9; R′ = t-C_4H_9, C_6H_5CO

(3) + R′S–SR′ ⟶ $R_2Sn(SR')_2$

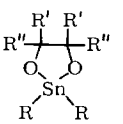
R = CH_3, n-C_4H_9; R′ = C_2H_5, t-C_4H_9, C_6H_5, C_6H_5CO

No reaction has so far been observed with simple alkenes and alkynes, but *(3)* reacts with 2,3-dimethylbutadiene to give a 14% yield of *(4)* which, however, might have been formed from the diradical *(2)*.

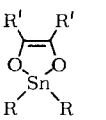


(4), R = CH_3 (m.p. 78°C), n-C_4H_9 (oil)

Carbonyl compounds react more vigorously with *(3)* than with stannyl radicals. Acetaldehyde, benzaldehyde[5], and acetone yield the corresponding 1,3,2-dioxastannolane *(5)*, and benzil and biacetyl the corresponding 1,3,2-dioxastannolene *(6)* [R=*n*-C_4H_9]:



(5a), R′ = CH_3, R″ = H (m.p. 138-141°C)
(5b), R′ = R″ = CH_3 (m.p. 46°C)
(5c), R′ = C_6H_5, R″ = H (m.p. 195-197°C)



(6a), R′ = C_6H_5 (dec. 161°C)
(6b), R′ = CH_3 (dec. 112°C)

All reactions were carried out at 20—24°C in benzene with exclusion of air, the reaction mixture (the cyclostannane *(1)* acting as the source of stannylene together with the substrate) in a Duran glass flask being irradiated externally with daylight lamps. The duration of reaction, 2—76 h, decreases considerably on internal irradiation. The products were identified with the aid of authentic samples, NMR, and IR spectroscopy, and unknown compounds by elemental analysis as well.

Received: August 5, 1975 [Z 305 IE]
German version: Angew. Chem. *87*, 844 (1975)

[1] *A. Schwarz*, Dissertation, Universität Dortmund 1975.
[2] *U. Schröer* and *W. P. Neumann*, Angew. Chem. *87*, 247 (1975); Angew. Chem. internat. Edit. *14*, 246 (1975).
[3] For preparation, see *W. P. Neumann*: Die Organische Chemie des Zinns. Enke, Stuttgart 1967; The Organic Chemistry of Tin. Wiley, London 1970.
[4] *J. Pedain*, Dissertation, Universität Giessen 1965, p. 50.
[5] Experiments by *T. Holtzmann* in this laboratory.

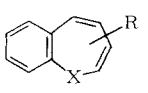
[*] Prof. Dr. W. P. Neumann and Dr. A. Schwarz
Lehrstuhl für Organische Chemie der Universität
46 Dortmund 50, Postfach 500500 (Germany)

The First 1-Benzothiepin 1-Oxides[1]

By *Hans Hofmann* and *Helmut Gaube*[*]

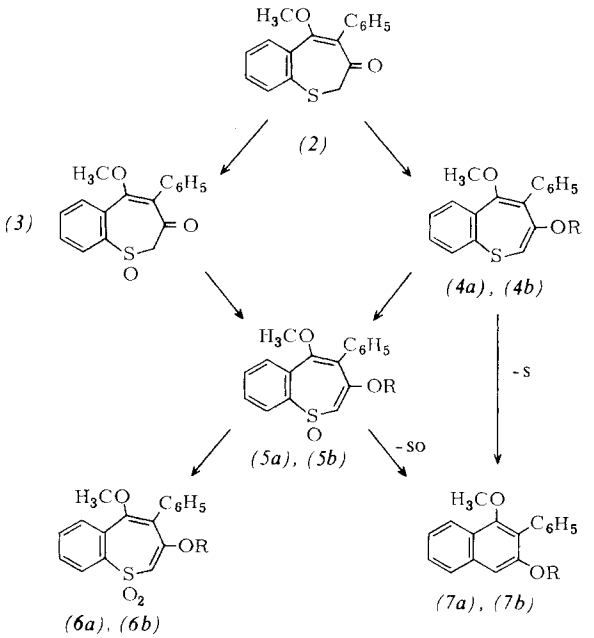
Seven-membered sulfur heterocycles have for some time been the aim of intense preparative effort, which has led

[*] Prof. Dr. H. Hofmann and Dipl.-Chem. H. Gaube
Institut für Organische Chemie der Universität Erlangen-Nürnberg
852 Erlangen, Henkestrasse 42 (Germany)



(1a), X = S
(1b), X = SO
(1c), X = SO_2

to success in the cases of 1-benzothiepin 1,1-dioxides *(1c)*[2], thiepin 1,1-dioxide[3], and 1-benzothiepins *(1a)*[2b, 4]. We have now accomplished the synthesis of 1-benzothiepin 1-oxides *(1b)*.



(a), R = $COCH_3$; *(b)*, R = CH_3

Since it was to be assumed from numerous unsuccessful attempts at preparation that unsubstituted *(1b)* is less stable than benzothiepin *(1a)*, R = H, we first prepared the substituted 1-benzothiepin 1-oxides *(5a)* and *(5b)* both *via* the benzothiepinone 1-oxide *(3)* and by direct oxidation of the benzothiepins *(4a)* and *(4b)*[4a, 4b] (Table 1). Apart from analytical data[5], smooth further oxidation to the 1-benzothiepin 1,1-dioxides *(6a)* and *(6b)*[5] and ^{1}H-NMR data afford structural proof of *(5a)* and *(5b)*.

Table 1. Preparation of *(3)*, *(5a)*, *(5b)*, *(6a)*, and *(6b)*.

Cpd.	Preparation	^{1}H-NMR [a]	Yield [%]	M. p. [°C]
(3)	from *(2)*: with *m*-chloroperbenzoic acid (molar ratio 1:1) in CH_2Cl_2, 12 h at −20 °C [b]		95	132
(5a)	from *(3)*: with Ac_2O/Et_3N/*p*-dimethylaminopyridine [6], 24 h at −30 °C; precipitated from CH_2Cl_2 at −20 °C with light petroleum	3.85	71	72 (dec.)
	from *(4a)*: with *m*-chloroperbenzoic acid (molar ratio 1:1) in CH_2Cl_2, 5 h at −20 °C [b]		89	
(5b)	from *(3)*: with KOtBu/methyl fluorosulfate in THF, 5 h at −120 °C [c]	4.61	86	105
	from *(4b)*: with *m*-chloroperbenzoic acid (molar ratio 1:1) in CH_2Cl_2, 12 h at −20 °C [c]		80	
(6a)	from *(5a)*: as for *(5b)* from *(4b)*	3.37	85	152
	from *(4a)*: with *m*-chloroperbenzoic acid (molar ratio 1:2) in CH_2Cl_2, 12 h at −25 °C		85	
(6b)	from *(5b)*: as for *(5b)* from *(4b)*	3.96	70	142
	from *(4b)*: as for *(6a)* from *(4a)*		81	

[a] 2-H (s); $CDCl_3$, τ values in ppm.
[b] Precipitated with light petroleum.
[c] Crystallized from methanol.

Expectedly, *(5a)* and *(5b)* are thermally less stable than the parent 1-benzothiepins *(4a)* and *(4b)*. On warming in an inert solvent they readily eliminate SO to form the naphthalenes *(7a)* and *(7b)* respectively[4b] without formation of any further reaction product being detectable in the ^{1}H-NMR spectrum. From a comparison of the half-lives for thermal decomposition of *(5a)* and *(5b)* with those of *(4a)* and *(4b)*, respectively, the stability range of 1-benzothiepin 1-oxides *(5)* (in nonpolar solvents) is estimated to lie about 40 to 50 °C lower than that of the corresponding 1-benzothiepins *(4)*. The half-lives are: *(5a)*: 155 ± 6 min (10 °C, $CDCl_3$); *(5b)*: 52 + 2 min (54 °C, $CDCl_3$); *(4a)*: 180 ± 7 min (59 °C, $CDCl_3$)[7]; *(4b)*: 66 ± 2 min (89 °C, CCl_4)[7].

Received: August 25, 1975 [Z 318 IE]
German version: Angew. Chem. *87*, 843 (1975)

CAS Registry numbers:
(2), 57458-93-2; *(3)*, 57458-88-5; *(4a)*, 37014-56-5; *(4b)*, 57458-94-3; *(5a)*, 57458-89-6; *(5b)*, 57458-90-9; *(6a)*, 57458-91-0; *(6b)*, 57458-92-1

[1] Seven-Membered Heterocyclic Compounds, Part 17.—This work was supported by the Fonds der Chemischen Industrie. Part 16: ref. [4b].
[2] a) *V. J. Traynelis* and *R. F. Love*, J. Org. Chem. *26*, 2728 (1961); *29*, 366 (1964); b) *H. Hofmann* and *H. Westernacher*, Angew. Chem. *78*, 980 (1966); Angew. Chem. internat. Edit. *5*, 958 (1966); Chem. Ber. *102*, 205 (1969).
[3] *W. L. Mock*, J. Am. Chem. Soc. *89*, 1281 (1967).
[4] a) *H. Hofmann*, *B. Meyer*, and *P. Hofmann*, Angew. Chem. *84*, 477 (1972); Angew. Chem. internat. Edit. *11*, 423 (1972); b) *H. Hofmann*, *H.-J. Haberstroh*, *B. Appler*, *B. Meyer*, and *H. Herterich*, Chem. Ber. *108*, 3596 (1975); c) *D. N. Reinhoudt* and *C. G. Kouwenhoven*, J. Chem. Soc. Chem. Commun. *1972*, 1232; d) *V. J. Traynelis*, *Y. Yoshikawa*, *J. C. Sih*, and *L. J. Miller*, J. Org. Chem. *38*, 3978 (1973); e) *J. Murata*, *T. Tatsuoka*, and *J. Sugihara*, Angew. Chem. *86*, 161 (1974); Angew. Chem. internat. Edit. *13*, 142 (1974).
[5] Correct elemental analyses were obtained for all new compounds. The mass spectra of *(5a)* and *(5b)* contain $[M-48]^+$ (= $[M-SO]^+$) as the base peak, while the mass spectra of the considerably more stable sulfones *(6a)* and *(6b)* contain the nonfragmented molecular ions.
[6] *W. Steglich* and *G. Höfle*, Angew. Chem. *81*, 1001 (1969); Angew. Chem. internat. Edit. *8*, 981 (1969).
[7] *R. Heidrich*, Diplomarbeit, Universität Erlangen-Nürnberg 1975.

Conversion of 1,2-Diols into Aldehydes Induced by Photolysis of Alkylcobaloximes: A Model System for Dioldehydrase[**]

By *Bernard T. Golding*, *Terence J. Kemp*, *Enrico Nocchi*, and *William P. Watson*[*]

5'-Deoxy-5'-adenosylcobalamin (AdoCbl) acts as a coenzyme for the conversion of certain 1,2-diols into aldehydes catalyzed by the dioldehydrase of *Aerobacter aerogenes*[1]. In these reactions enzymatically-induced homolysis of the cobalt-carbon bond of AdoCbl is followed by attack of the

[*] Dr. B. T. Golding [+], Dr. T. J. Kemp, Dr. E. Nocchi, and Dr. W. P. Watson
Department of Molecular Sciences, University of Warwick
Coventry CV4 7AL (England)
[+] To whom correspondence should be addressed.

[**] Financial support was given by the Science Research Council (to *W. P. W.*) and by the Academia Nazionale dei Lincei (to *E. N.* under the auspices of the Royal Society European Exchange Scheme).—We acknowledge excellent technical assistance from *L. C. Carr* and *G. Noon*.

resulting 5'-deoxy-5'-adenosyl radical on the substrate (SH) giving 5'-deoxyadenosine and the radical S'. The latter is somehow transformed to radical P' which abstracts a hydrogen atom from 5'-deoxyadenosine, thereby regenerating the 5'-deoxy-5'-adenosyl radical and producing a 1,1-diol (PH), from which product aldehyde arises[2].

We have pointed out[3] similar reactions which ensue following attack of hydroxyl radicals on 1,2-diols[4], *e.g.*:

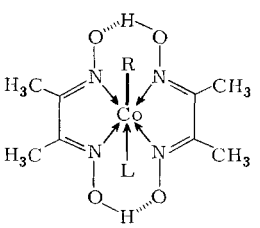
$$HOCH_2CH_2OH \xrightarrow{\cdot OH} HOCH_2\dot{C}HOH \longrightarrow H_2O + \cdot CH_2CHO \quad (a)$$

An even more compelling model system would achieve the nonenzymatic formation of an aldehyde from a 1,2-diol with the help of an alkyl radical R' derived from an alkylcobalt compound like AdoCbl:

$$R^1CHOHCH_2OH \xrightarrow{R} R^1CHOH\dot{C}HOH \longrightarrow H_2O + R^1\dot{C}HCHO \xrightarrow[\text{source}]{\text{H-atom}} R^1CH_2CHO \quad (b)$$

We now report our experiments in the pH range 2—3, which apparently demonstrate transformations of the type in eq. (b).

A de-aerated solution of methyl(aquo)cobaloxime *(1)*[5] (4 mM) in aqueous KCl/HCl buffer (pH 2.0) containing 1,2-ethanediol (1.0 M) was photolyzed [$\lambda = 380 \pm 15$ nm, charge-transfer band of *(1)*]. The disappearance of *(1)* followed the classical form [$\varphi(-1) = 0.14 \pm 0.01$] giving Co^{2+}_{aq}, free ligands, and acetaldehyde [isolated as its 2,4-dinitrophenylhydrazone: yield $\approx 10\%$ (estimated by NMR spectroscopy); 5% isolated]. No acetaldehyde was produced in reaction mixtures kept in darkness for the duration of photolyses (45 min)[6]. The yield of acetaldehyde given is based on cobaloxime and is 250× lower when related to 1,2-ethanediol. This is evidently due to the low probability of intermolecular attack of methyl radicals on 1,2-ethanediol and/or to the lack of an efficient chain process emanating from the radical $HOCH_2\dot{C}HOH$. As the concentration of 1,2-ethanediol increases, so does that of acetaldehyde, presumably due to the increasing efficiency of the capture of methyl radicals with production of the radical $HOCH_2\dot{C}HOH$ and hence of acetaldehyde (cf. eq. (a) and refs. [4a, 4c]).



(1), R = CH_3, L = H_2O
(2), R = $(CH_2)_3CHOHCH_2OH$,
L =

4,5-Dihydroxypentyl(pyridine)cobaloxime *(2)*[5] contains both a 1,2-diol and potential alkyl radical; hydrogen atom transfer between radical and diol can then be an intramolecular process. Photolysis ($\lambda = 380 \pm 15$ nm) of a de-aerated solution of *(2)* [3.5 mM] in 0.1 M aqueous acetic acid (pH 3.0) gave pentanal [isolated as dinitrophenylhydrazone in 3.5 ± 0.3% yield (three experiments)]. Control experiments performed in the dark [storing the following compounds in 0.1 M acetic acid: *(2)* (3.5 mM); 1,2-pentanediol (3.5 mM); 1,2-pentanediol (2.8 mM) and cobalt(II) acetate (4 mM)] gave no detectable pentanal[6]. Photolysis ($\lambda = 380 \pm 15$ nm) of a de-aerated solution containing biacetylglyoxime (7 mM), cobalt(II) acetate (3.5 mM), and 1,2-pentanediol (3.5 mM) in 0.1 M acetic acid also gave no pentanal[6]. When *(2)* was photolyzed in 0.1 M acetic acid in the presence of oxygen, only a trace of pentanal was obtained ($\lesssim 0.5$% yield). The main product derived from the 4,5-dihydroxypentyl group of *(2)* in anaerobic photolyses was 1,2-pentanediol (≈ 50% yield).

We propose that pentanal arises as follows in the anaerobic photolysis of *(2)*: Photoinduced homolysis of the Co—C bond of *(2)* gives the 4,5-dihydroxypentyl radical which mainly becomes 1,2-pentanediol, but partly undergoes a specific hydrogen transfer (favored by a six-membered cyclic transition state[7]) to generate the radical $n\text{-}C_3H_7CHOH\dot{C}HOH$; acid-catalyzed rearrangement[3, 4a] of this radical can give the radical $n\text{-}C_3H_7\dot{C}HCHO$ which produces pentanal after a hydrogen atom abstraction (from a source to be determined).

Although enzymatic reactions involving dioldehydrase and AdoCbl are not photochemically induced[8], we submit that the clean, rapid photohomolysis of alkylcobalt compounds justifies the use of photolyses in model experiments. We predict that the 4,5-dihydroxypentyl radical plays a similar role to the 5'-deoxy-5'-adenosyl radical in the enzymatic system, by performing a *selective* hydrogen atom abstraction on a 1,2-diol[9].

Received: August 13, 1975;
in abbreviated form: September 2, 1975 [Z 312 IE]
German version: Angew. Chem. *87*, 841 (1975)

CAS Registry numbers:
Methyl(aquo)cobaloxime, 25360-55-8; 1,2-ethanediol, 107-21-1; acetaldehyde, 75-07-0; 4,5-dihydroxypentyl(pyridine)cobaloxime, 57031-36-4; pentanal, 110-62-3

[1] Cf. *H. A. Barker*, Annu. Rev. Biochem. *41*, 55 (1972).
[2] *T. H. Finlay, J. Valinsky, K. Sato*, and *R. H. Abeles*, J. Biol. Chem. *247*, 4197 (1972).
[3] *B. T. Golding* and *L. Radom*, J. Chem. Soc. Chem. Commun. *1973*, 939.
[4] a) *B. C. Gilbert, J. P. Larkin*, and *R. O. C. Norman*, J. Chem. Soc. Perkin II *1972*, 794; b) *K. M. Bansal, M. Grätzel, A. Henglein*, and *E. Janata*, J. Phys. Chem. *77*, 16 (1973); c) *C. Walling* and *R. A. Johnson*, J. Am. Chem. Soc. *97*, 2405 (1975).
[5] Alkyl(base)cobaloximes are bis(biacetyldioximato)cobalt complexes with a σ-alkyl group and a Lewis base as axial ligands, used as models for alkylcobalamins [cf. *G. N. Schrauzer*, Acc. Chem. Res. *1*, 97 (1968)]. Syntheses of *(1)* and *(2)*: *B. T. Golding et al.*, to be published.
[6] In the control experiments mentioned, ≥0.2% yield (based on cobaloxime) of acetaldehyde or pentanal would have been detected.
[7] *J. W. Wilt* in *J. K. Kochi*: Free Radicals. Wiley-Interscience, New York 1973, Vol. 1, Chap. 8, p. 380.
[8] See, however, *T. Yamane, S. Shimizu*, and *S. Fukui*, Biochim. Biophys. Acta *110*, 616 (1965).
[9] 1,4-Hydrogen transfer in the 4,5-dihydroxypentyl radical giving the radical $n\text{-}C_3H_7\dot{C}OHCH_2OH$, followed by acid-catalyzed rearrangement[4a], would yield 2-pentanone which was not detected after photolysis of *(2)*.

Thermal Cycloaddition between 3,6-Diphenyl-*s*-tetrazine and 9-Oxabicyclo[6.1.0]nona-2,4,6-triene; Construction of the Oxonino[4,5-*d*]pyridazine Frame[**]

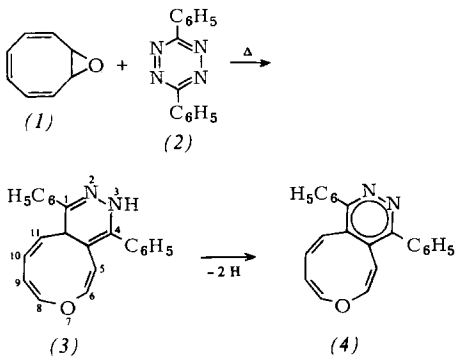
By *A. G. Anastassiou* and *S. J. Girgenti*[*]

In an attempt to extend the scope of the pericyclic synthesis of novel π systems[1] to molecules containing more than one heteroatom we examined the synthetic potential of diphenyltetrazine *(2)*[2] as a pericyclic trap of properly structured molecules. In this report we briefly describe the use of *(2)* in the first successful thermally activated cycloadditive trapping of 9-oxabicyclo[6.1.0]nona-2,4,6-triene *(1)* to produce an oxa-

[*] Prof. Dr. A. G. Anastassiou and S. J. Girgenti
Department of Chemistry, Syracuse University,
Syracuse, New York 13210 (USA)

[**] We thank the National Science Foundation (GP-38553X) and the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.—We should also like to express our appreciation to Mr. *L. McCandless* for the determination of the 100 MHz spectra.

diazabicyclo[7.4.0]tridecane skeleton and the subsequent synthetic application of this process to the construction of the novel oxoninopyridazine frame.



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

Lengthy (*ca.* 2 days) exposure of *(2)* to excess *(1)* in 1,4-dioxane at 105 °C produces cycloadduct *(3)* as an air-sensitive yellow powder in 27% yield[3] based on recovered (*ca.* 50%) *(2)*. Our choice of structure *(3)* derives chiefly from the appearance of two mutually coupled ($J = 6.0$ Hz) doublets in the NMR spectrum [100 MHz, [D_6]acetone; $\tau = 3.96$ and 4.60 (H^5, H^6)] which serves to implicate the presence of a magnetically isolated ethylene.

Mild oxidative treatment of *(3)* with *o*-chloranil produces, in 60% yield, the novel 1,4-diphenyloxonino[4,5-*d*]pyridazine *(4)*[4] [white crystals, m.p. 147.5—148 °C; NMR (100 MHz; $CDCl_3$): $\tau = 3.54$ (d, H^6 or H^5, $J_{6,5} = 6$ Hz), 3.75 (d, H^8, $J_{8,9} = 7.5$ Hz), 3.95 (pseudo d, $H^{10} + H^{11}$), 4.15 (d, H^5 or H^6, $J_{5,6} = 6.0$ Hz), 4.86 (dt, H^9, $J_{8,9} = 7.5$ Hz, $J_{9,10} = J_{9,11} = 2.5$ Hz); λ_{max} (CH_3CN) = 262 nm (ε 20700)].

Compound *(4)* represents the first example of a monoannelated oxonin and judging from the chemical shifts of key protons H^8 and H^9 and also from the magnitude of $J_{8,9}$, all of which are virtually identical to their counterparts in the spectrum of the parent molecule oxonin[5], it is safe to conclude that the oxonin segment of this bicycle *(4)* does not sustain a ring current and hence that it must be regarded as an unexceptional polyene.

Received: September 8, 1975 [Z 313 IE]
German version: Angew. Chem. *87*, 842 (1975)

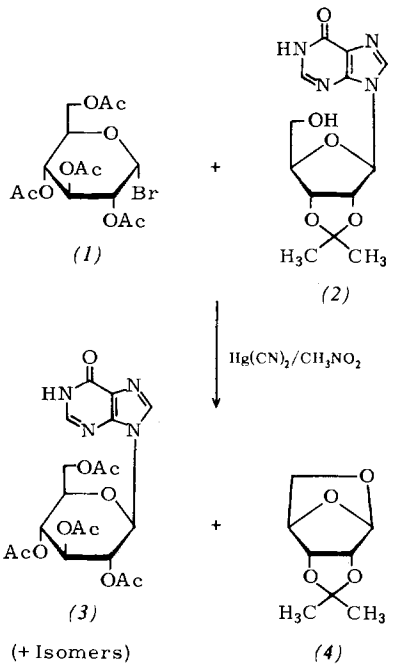
CAS Registry numbers:
(1), 4011-20-5; *(2)*, 6830-78-0; *(3)*, 57015-09-5; *(4)*, 57015-10-8

[1] *A. G. Anastassiou*, Pure Appl. Chem., in press.
[2] For use of symmetrical tetrazines in cycloadditions see, for example, *J. Sauer* and *G. Heinrichs*, Tetrahedron Lett. *1966*, 4979; *P. L. Watson* and *R. N. Warrener*, Aust. J. Chem. *26*, 1725 (1973), and references cited therein.
[3] Separation of the mixture into its individual components was accomplished by column chromatography a *ca.* −15 °C.
[4] The elemental composition of this substance was established by C,H,N combustion analysis.
[5] *A. G. Anastassiou* in *T. Nozoe*, *R. Breslow*, *K. Hafner*, *S. Ito*, and *I. Murata*: Topics in Nonbenzenoid Aromatic Chemistry. Hirokawa Publishing Company, Tokyo 1973, pp. 1 ff.

Ribose-Glucose Exchange in Purine Nucleosides[1]

By *Frieder W. Lichtenthaler* and *Katsuhiko Kitahara*[*]

Transfer of the sugar moiety of a nucleoside to another nucleobase has repeatedly been observed and constitutes the integral part of a synthesis of purine ribosides from pyrimidine ribosides and purines[2]. We here report the first example of the counterpart of this reaction, *i. e.* the transfer of a nucleobase from one sugar (ribose) to another (glucose), that should be of similar preparative importance.



Mercuric cyanide catalyzed reaction of acetobromoglucose *(1)* with 2′,3′-*O*-isopropylidene-inosine *(2)* in nitromethane leads not to the expected 5′-*O*-glycosylated disaccharide nucleosides but to a mixture of peracetylglucosylhypoxanthines due to excision of the ribose portion in the form of its 1,5-anhydro derivative *(4)*. The product distribution within this mixture depends on the reaction conditions.

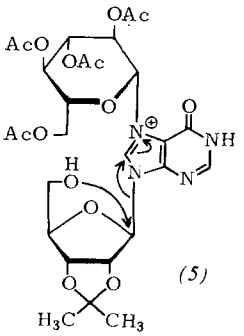
At 70 °C conversion is complete within 1 h, affording, alongside 69% of *(4)*[3], 66% of a crystalline mixture consisting of *(3)* and its N^7-isomer which was separated by chromatography[4]: 39% of N^7-nucleoside [m.p. 242—244 °C, $[\alpha]_D^{25} = -5.0°$ ($c = 1$, $CHCl_3$), $H^{1'}$ in $CDCl_3$ at $\delta = 6.29$ as 9 Hz-d; λ_{max} (C_2H_5OH) = 254 nm ($\varepsilon = 10400$) and 216 (5800)] and 20% of 9-peracetylglucosyl hypoxanthine *(3)* [m.p. 256—258 °C, $[\alpha]_D^{25} = -29.5°$ ($c = 1$, $CHCl_3$), 9 Hz-d for H^1 at $\delta = 5.93$; λ_{max} (C_2H_5OH) = 244 nm ($\varepsilon = 11000$)].

At 40 °C, the reaction is considerably slower (5 days) and gives a different *N*-glucosylation pattern as shown by the isolation[4] of *(3)* (10%), the N^9-isomer (12%), and a crystalline mixture[5] of the N^1- and N^3-nucleosides (7%), alongside 54% of anhydrosugar *(4)*. The β configuration of each of the isomeric nucleosides readily followed from their $J_{1',2'}$ values (9 Hz), whilst the site of glycosylation in the hypoxanthine moiety was deduced from the chemical shifts of the anomeric protons ($\delta \approx 6.2$ for N^7- and N^1-glucosides as compared to $\delta \approx 6.6$ for the N^9- and N^3-isomers), from the absence of an amide-NH signal around $\delta = 13.3$ in the N^1/N^3-nucleosides, and from the fair agreement of the other physical data of *(3)* and the N^7-isomer with those reported previously[6].

In this sugar interchange reaction, $Hg(CN)_2$ may be replaced by $HgCl_2$ or $HgBr_2$, yet with increasing formation of bis-glucosylated hypoxanthines alongside *(4)* and *(5)* and its N^7-isomer, which was not unexpected in view of the course of the $HgBr_2$-induced glucosylation of hypoxanthine with *(1)*[6]. The variability of the *ribo*-nucleoside component is exemplified by the formation of *(4)* and a mixture of isomeric peracetylglucosylpurines on reaction of *(1)* with the 2′,3′-*O*-isopropylidene derivates of N^1-benzyl-inosine[7] and xanthosine, as well as—in clearly slower reactions—of N^6-benzoyladenosine,

[*] Prof. Dr. F. W. Lichtenthaler and Dr. K. Kitahara
Institut für Organische Chemie der Technischen Hochschule
61 Darmstadt, Petersenstrasse 15 (Germany)

N^2-acetylguanosine, and adenosine. With the corresponding pyrimidine nucleosides, *i.e.* 2',3'-*O*-isopropylidene-uridine, the sugar exchange cannot be induced under these conditions, a mixture of 5'-*O*- and N^3-glucosylated products being formed instead.



(5)

These results, together with the experimental finding that excision of the anhydrosugar *(4)* from *(2)* cannot be performed with $Hg(CN)_2$/nitromethane alone, *i.e.* that the reaction is dependent on the availability of the glycosyl bromide or, more appropriately, of the respective 1,2-acetoxonium ion formed therefrom by the catalyst, strongly suggests diglycosylpurines as intermediates in this reaction. More likely than the formation of N^1,N^9- or N^3,N^9-bisglycosylated products appears to be the electrophilic attack of the tetraacetylglucosyl cation at N^7[8] to give the quaternary salt intermediate *(5)*, followed by ejection of the ribose moiety, the driving force undoubtedly being intramolecular stabilization of the initially formed ribosyl carboxonium ion to form the anhydrosugar (4). The N^7-nucleoside formed in this way would then undergo N→N glucosyl shifts that are well documented in the literature[9] and thus give rise to the isomeric mixtures observed.

Received: July 28, 1975 [Z 288 IE]
German version: Angew. Chem. 87, 839 (1975)
Publication delayed at authors' request

CAS Registry numbers:
(1), 572-09-8; *(2)*, 2140-11-6; *(3)*, 3444-10-8; *(3)* N^7-isomer, 18883-86-8; *(4)*, 51246-99-2; *(5)*, 56391-16-3; *(6)*, 56391-17-4

[1] Nucleosides, Part 32. This work was generously supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.— Part 31: *F. W. Lichtenthaler* and *T. Kulikowski*, J. Org. Chem., in press.
[2] *B. Shimizu* and *M. Miyaki*, Tetrahedron Lett. *1968*, 855; *M. Miyaki, A. Saito*, and *B. Shimizu*, Chem. Pharm. Bull. *18*, 2459 (1970).
[3] Melting point, rotation, and NMR data were identical with those of a sample prepared according to *P. A. Levene* and *E. T. Stiller* [J. Biol. Chem. *102*, 187 (1933)].
[4] Separation was performed on an alumina column by elution of *(4)* with benzene/ether (1:1) and of *(3)* and its isomers with chloroform/methanol (10:1); alternatively, elution from silica gel with 6:1 chloroform/methanol could be employed followed by fractional crystallization from methanol/ethyl acetate.
[5] This product of $[\alpha]_D^{25} = -20°$ ($c = 1$, $CHCl_3$) showed two melting points (143—144 °C and 224—226 °C), two 9 Hz doublets for the respective anomeric protons at $\delta = 6.22$ and 5.88, and no amide-NH signal around $\delta = 13.3$.
[6] *H. Yamasaki* and *T. Hashizume*, Agric Biol. Chem. Jap. *32*, 1362 (1968).
[7] Obtained in 71% yield on treatment (10 h, 25 °C) of *(2)* with benzyl bromide/Ag_2CO_3 in nitromethane; m.p. 158—159 °C; $[\alpha]_D^{22} = -87°$ ($c = 1$, $CHCl_3$).
[8] On attack of the tetraacetylglucosyl cation at N^1—in analogy to the $Hg(CN)_2$-induced reaction of N^1-benzyl-2',3'-*O*-isopropylidene-inosine with *(1)*—N^1,N^7- and N^1,N^9-diglucosylhypoxanthines would be expected in sizable quantities, which, however, are only observed in the $HgCl_2$-catalyzed reaction. A corresponding N^3-attack of the glucosyl cation with formation of an uncharged N^3,N^9-diglycosyl intermediate is considerably impeded due to steric hindrance exerted by the N^9-ribosyl moiety.
[9] *L. Goodman* in *P. O. P. Tso*: Basic Principles in Nucleic Acid Chemistry, Academic Press, New York 1974, pp. 190ff.

Unusual Cycloaddition of Tetracyanoethylene to Dispiro[2.0.2.4]deca-7,9-diene[**]

By *Dieter Kaufmann, Armin de Meijere, Brian Hingerty*, and *Wolfram Saenger*[*]

Dispiro[2.0.2.4]deca-7,9-diene *(1)*[1] contains both a 1,3-diene system and a bishomo-1,3-diene system, *viz.* the bicyclopropyl unit. While numerous dienophiles undergo normal reaction with addition to the 1,3-diene unit, tetracyanoethylene (TCNE) is an exception.

On reaction of *(1)* with TCNE in benzene at 10 °C a pale brown almost insoluble solid precipitates after 15 min. However, when an equimolar amount of *(1)* is added dropwise to a solution of TCNE in tetrahydrofuran (THF) at 0 °C, the mixture merely turns dark green. Removal of the solvent leaves a highly viscous dark green residue which affords white crystals (m. p. 157—158 °C, yield 34 %) when chromatographed on silica gel (elution with methylene chloride).

The complex ^{1}H-NMR spectrum merely indicates that this product contains no cyclopropyl groups but does possess a phenylene group. According to its high resolution mass spectrum and elemental analysis it is a 1:1:2 adduct of *(1)*, TCNE, and THF; its structure was elucidated by X-ray analysis.

The prismatic crystals have space group $P2_1/c$ with $a = 10.920$, $b = 16.985$, $c = 12.624$ Å, $\beta = 102.8°$. A total of 3384 reflections[2] were recorded (automated STOE four-circle diffractometer, $Cu_{K\alpha}$, Ni filter); the structure was solved by direct methods[3]. The structure *(4)* could be deduced directly from the calculated Fourier synthesis (Fig. 1). Refinement of the atomic coordinates and anisotropic temperature factors by the full matrix technique gave a convergence factor of $R = 0.048$ after inclusion of the hydrogen atoms.

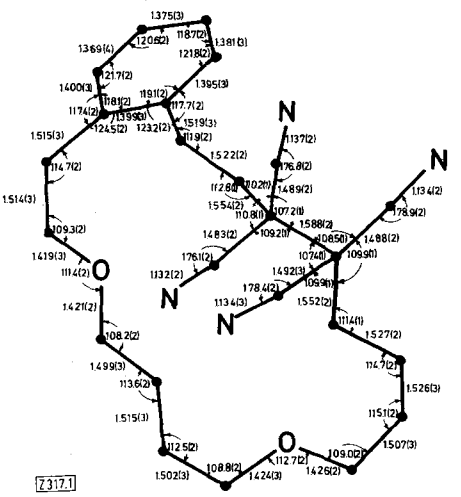


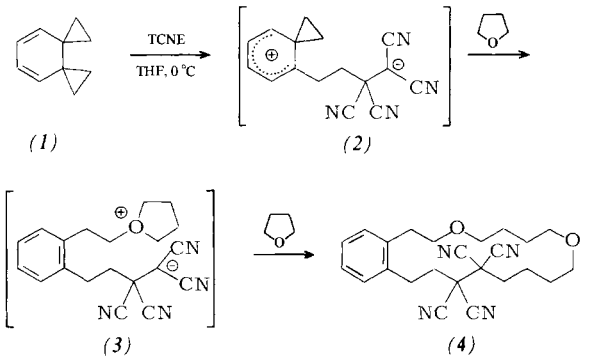
Fig. 1. Bond lengths [Å] and angles [°] in *(4)*[4].

Thus the adduct is a 15,16-benzo-1,6-dioxa-15-cyclooctadecene-11,11,12,12-tetracarbonitrile *(4)*. The mode of formation of *(4)* can be readily interpreted in terms of the stabilized zwitterionic intermediate *(2)*[5] formed by electrophilic attack of TCNE on *(1)*[6]. The species *(2)* does not cyclize to

[*] Dr. D. Kaufmann and Prof. Dr. A. de Meijere [+]
Organisch-Chemisches Institut der Universität
34 Göttingen, Tammannstrasse 2 (Germany)
Dr. B. Hingerty and Priv.-Doz. Dr. W. Saenger
Max-Planck-Institut für experimentelle Medizin
34 Göttingen, Hermann-Rein-Strasse 3 (Germany)
[+] To whom correspondence should be addressed.

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

give a benzocyclooctene derivative, but suffers nucleophilic attack by solvent THF to form the new zwitterion *(3)* which is transformed into the 18-membered macrocycle *(4)* by further reaction with THF.



It should prove possible to increase the yield by use of the dilution principle. It is conceivable that this type of reaction can be applied to a number of appropriately substituted cyclopropane derivatives in the presence of THF or other cyclic ethers to afford different macrocycles.

Received: September 9, 1975 [Z 317 IE]
German version: Angew. Chem. 87, 842 (1975)

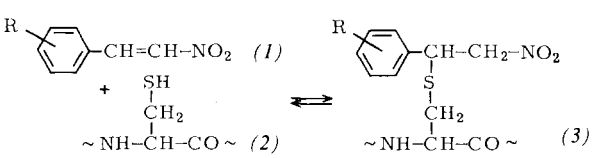
CAS Registry numbers:
(1), 30353-70-9; *(4)*, 57459-03-7; TCNE, 670-54-2; THF, 109-99-9

[1] *A. de Meijere*, Chem. Ber. *107*, 1702 (1974).
[2] The reflections were corrected for geometric factors and absorption effects. Cf. *A. C. T. North, D. C. Phillips*, and *F. S. Matthews*, Acta Crystallogr. *A 24*, 351 (1968).
[3] *P. Main, M. M. Woolfson*, and *P. Germain*: MULTAN, a Multi Solution Tangent Formula Refinement Program. University of York, York 1971.
[4] Assignment of the C,N,O atoms by difference Fourier syntheses. Verified by agreement of bond lengths and angles in the C—O—C and C—C≡N groups with values reported in the literature.
[5] Cycloadditions of TCNE to phenylcyclopropanes and vinylcyclopropanes which are formulated *via* intermediate zwitterions and afford five-, four-, and seven-membered rings, are known reactions: a) *Th. Martini* and *J. A. Kampmeier*, Angew. Chem. *82*, 216 (1970); Angew. Chem. internat. Edit. *9*, 236 (1970); b) *F. Effenberger* and *W. Podszun*, Angew. Chem. *81*, 1046 (1969); Angew. Chem. internat. Edit. *8*, 976 (1969); c) *S. Nishida, I. Moritani, E. Tsuda*, and *T. Teraji*, Chem. Commun. *1969*, 781; d) *S. Sarel, A. Felzenstein*, and *J. Yovell*, J. Chem. Soc. Chem. Commun. *1974*, 753.
[6] Formation of *(2)* is probably initiated by electron transfer from *(1)* to TCNE. Detection of the radical ion intermediates has yet to be accomplished.

2-Nitro-1-phenylethyl: A New Protecting and Chiroptical Reporter Group for Cysteine Peptides

By *Günther Jung, Hassanein Fouad*, and *Gerhard Heusel*[*]

The colored β-nitrostyrenes *(1)* readily obtainable from benzaldehydes and nitroalkanes add to the thiol group of cysteine, cysteine derivatives, and cysteine peptides *(2)* under mild conditions. The resulting sulfides *(3)* can be employed for the synthesis of cysteine peptides. This was proved by two new glutathione syntheses with *N-tert*-butoxycarbonyl-*S*-(2-nitro-1-phenylethyl)-L-cysteine (Boc-Cys(Npe)-OH).



The Npe (2-nitro-1-phenylethyl) group in *(3)*, R = H, is stable towards reagents used for acidic removal of the *tert*-butoxycarbonyl and benzyloxycarbonyl amino protecting groups. The thiol group of *(3)* can be liberated without loss of methyl and benzyl ester groups under mild alkaline conditions. Glutathione and cysteine form sulfides *(3)* with 3,4-dimethoxy-β-nitrostyrene in good yields when the reaction is conducted in methanol/water with *N*-methylmorpholine catalysis at pH 7—8. Under these conditions free amino groups do not react with β-nitrostyrenes. Both addition and deblocking can readily be followed by means of pronounced absorption maxima at 300—500 nm. The rate of addition and the stability of the addition products can be modified within wide limits by substituents on the benzene ring.

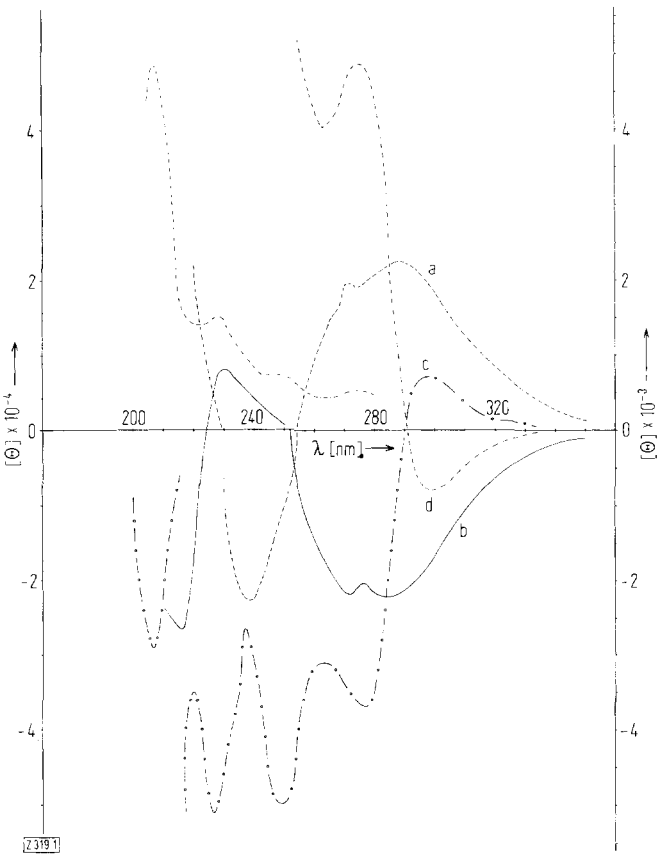


Fig. 1. Circular dichroism of the diastereomeric adducts of *N*-acetyl-L-cysteine to β-nitrostyrene (a, b, 25 °C, 5×10^{-3} M in 95% ethanol) and of L-cysteine (c) and L-glutathione (d) to 3,4-dimethoxy-β-nitrostyrene (25 °C, 2×10^{-3} M in 0.1 N HCl). The left-hand ordinate refers to the short wavelength curves, and the right-hand one to the long wavelength region.

The adducts *(3)* are suitable for chiroptical studies since a new center of asymmetry is generated during addition. All the adducts are characterized by favorably located Cotton effects of high molar ellipticity in the range of the phenyl and nitro chromophores. The CD spectra of the diastereomeric adducts of *N*-acetyl-L-cysteine to β-nitrostyrene, which can be resolved by crystallization, show almost exact mirror image Cotton effects in the long wave region (Fig. 1). Studies on analogous adducts indicate a frequently surprisingly high degree of stereoselectivity of addition. Thus, for example, addition of 3,4-dimethoxy-β-nitrostyrene to L-glutathione or to *N*-acetyl-L-cysteine leads exclusively to products having opposite chirality compared with that of the L-cysteine adduct (Fig. 1). Hence chiroptical monitoring of the reaction of β-nitrostyrenes with the SH groups of enzymes should permit

[*] Prof. Dr. G. Jung, Dipl.-Chem. H. Fouad, and Dipl.-Chem. G. Heusel
Chemisches Institut der Universität
74 Tübingen, Auf der Morgenstelle (Germany)

conclusions to be drawn about the topology of the environment of reactive thiol groups. The scope of the above addition can be widened considerably since lipophilic, hydrophilic, colored, or polymer-bound β-nitrostyrenes are readily accessible *via* suitably substituted aldehydes and could also find application in the isolation and chromatography of cysteine peptides.

N-tert-Butoxycarbonyl-S-(2-nitro-1-phenylethyl)-L-cysteine

N-Methylmorpholine (10 ml) is added to a stirred solution of *N-tert*-butoxycarbonyl-L-cysteine[1] (0.1 mol) and β-nitrostyrene (0.1 mol) in anhydrous, N_2-saturated ethanol (100 ml). The colorless *N*-methylmorpholinium salt of the adduct precipitates within 2 min. After 10 min the mixture is cooled to 0 °C, filtered, and the precipitate washed with ether (yield 70 %; m.p. 131—133 °C). The *S*- and *N*-protected acid can be liberated by ethyl acetate extraction of an acidified aqueous solution of the salt and recrystallized from ethyl acetate/light petroleum; m.p. 74—77 °C; $R_f = 0.85$ ($CHCl_3/CH_3OH/CH_3COOH/H_2O$ 60:45:6:24).

Received: September 12, 1975;
in shortened form: September 22, 1975 [Z 319 IE]
German version: Angew. Chem. 87, 876 (1975)

CAS Registry numbers:
(1), 102-96-5; L-glutathione, 70-18-8; *N*-acetyl-L-cysteine, 616-91-1

[1] *H. Zahn* and *K. Hammerström*, Chem. Ber. *102*, 1048 (1969).

Selective Acidic Cleavage of the *tert*-Butoxycarbonyl Group[1]

By *Helmut Vorbrüggen* and *Konrad Krolikiewicz*[*]

Selective acidic cleavage of the *tert*-butoxycarbonyl (BOC) group in the presence of the benzyloxycarbonyl group (Z) and especially *tert*-butyl esters is difficult and often leads to complications[2].

We recently observed during synthesis of a nucleoside that BOC groups are cleaved by $(CH_3)_3SiClO_4$[3]. Hence we have treated the peptides *(1)*—*(4)*[4], which contain other protecting groups besides the BOC group, in benzene, CH_2Cl_2, or benzene/acetonitrile at 24 °C with equivalent amounts of $(CH_3)_3SiClO_4$[5] in benzene. Cleavage of the BOC group occurred immediately, leading to rapid precipitation of the crystalline or oily peptide perchlorates. According to TLC[6] only one major product was present alongside traces of starting material after 5 min at 24 °C. The ^{1}H-NMR spectra of the precipitated perchlorates in [D_5]pyridine confirmed quantitative removal of the BOC group leaving the Z group in *(3)* and the benzyl and *tert*-butyl esters in *(4)* intact (Table 1).

Table 1. Selective removal of the *tert*-butoxycarbonyl group by $(CH_3)_3SiClO_4$.

Peptide	Solvent	Product	Yield [%]
(1) BOC-Ala-Phe-OCH_3	C_6H_6	H-Ala-Phe-OCH_3 ·$HClO_4$	87 [a]
(2) BOC-Val-Leu-OCH_3	C_6H_6	H-Val-Leu-OCH_3 ·$HClO_4$	≈ 100
(3) Z-Lys-(BOC)Arg-(NO_2)OCH_3	C_6H_6/CH_3CN 1:1	Z-Lys-Arg(NO_2)-OCH_3·$HClO_4$ [b]	≈ 100
(4) BOC-Gly-Ile-Val-Glu(OtBu)-OBZL	C_6H_6/CH_3CN 1:1	H-Gly-Ile-Val-Glu(OtBu)-OBZL ·$HClO_4$ [c]	≈ 100

[a] After recrystallization from CH_3OH m.p. 189—191 °C.
[b] ^{1}H-NMR: Z group δ = 5.25 ppm (q, J = 13 Hz).
[c] ^{1}H-NMR: —O—C(CH_3)$_3$ δ = 1.40 ppm (s); O—CH_2—C_6H_5 δ = 5.30 ppm (s).

[*] Dr. H. Vorbrüggen and K. Krolikiewicz
Research Laboratories of Schering AG, Berlin/Bergkamen
1 Berlin 65, Postfach 650311 (Germany)

It would be interesting to apply this new acidic cleavage at lower temperatures to larger tryptophan-containing peptides as well as to other protecting groups like the BPOC and the NPS group[7].

Procedure:

To BOC-Gly-Ile-Val-Glu(OtBu)-OBZL *(4)* (165.7 mg, 0.25 mmol) in benzene/acetonitrile (1:1, 4 ml) at 24 °C is added $(CH_3)_3SiClO_4$ (0.25 mmol) in benzene (1.67 ml of a standard solution). The mixture immediately becomes turbid and forms a gel. Only traces of *(4)* are left after 5 min according to TLC[6]. From ethanol/H_2O an amorphous perchlorate (167 mg) is obtained, which was homogeneous according to TLC[6] and ^{1}H-NMR.

Received: September 25, 1975 [Z 320 IE]
German version: Angew. Chem. 87, 877 (1975)

CAS Registry numbers:
(1), 2280-66-2; *(2)*, 15215-73-3; *(3)*, 23931-83-1;
(4), 57458-98-7; H-Ala-Phe-OCH_3·$HClO_4$, 57458-99-8;
H-Ala-Leu-OCH_3·$HClO_4$, 57459-00-4;
Z-Lys-Arg(NO_2)-OCH_3·$HClO_4$, 57459-02-6;
H-Gly-Ile-Val-Glu(OtBu)-OBZL·$HClO_4$, 57474-15-4;
$(CH_3)_3SiClO_4$, 18204-79-0

[1] Reactions with Silyl Esters of Strong Acids, Part 2.—Part 1: *H. Vorbrüggen* and *K. Krolikiewicz*, Angew. Chem. *87*, 417 (1975); Angew. Chem. internat. Edit. *14*, 421 (1975).
[2] Compare, *e.g.*, *E. Wünsch* in Houben-Weyl: Methoden der organischen Chemie. Thieme, Stuttgart 1974, Vol. XV/1, pp. 126ff. *H. Kinoshita* and *H. Kotake*, Chem. Lett. *1974*, 631.
[3] *H. Vorbrüggen* and *K. Krolikiewicz*, Angew. Chem. *87*, 251 (1975); Angew. Chem. internat. Edit. *14*, 255 (1975).
[4] We thank Dr. *K. Lübke* and Miss *I. Beetz* for the peptides.
[5] *C. Eaborn*, J. Chem. Soc. *1955*, 2517; *U. Wannagat* and *W. Liehr*, Angew. Chem. *69*, 783 (1957); $(CH_3)_3SiSO_3CF_3$ [*H. C. Marsmann* and *H.-G. Horn*, Z. Naturforsch. *27b*, 1448 (1972)] reacts analogously.
[6] *n*-BuOH:AcOH:5% NH_3 (65:30:15) on SiO_2-G plates, E. Merck, Darmstadt.
[7] *P. Sieber* and *B. Iselin*, Helv. Chim. Acta *51*, 614, 622 (1968); *W. Kessler* and *B. Iselin*, *ibid.* *49*, 1330 (1966).

Secoanthraquinones from Emodin[1][**]

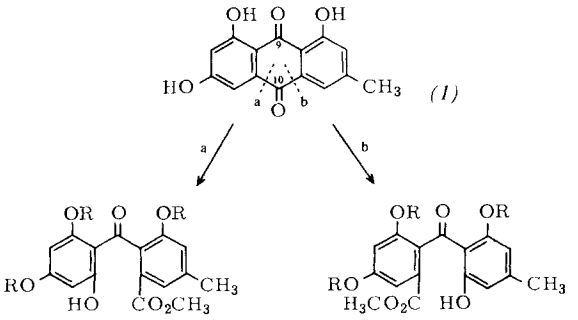
By *Burchard Franck* and *Bernd Berger-Lohr*[*]

Emodin *(1)*, itself made up of eight molecules of acetic acid, is a key substance for the biosynthesis of numerous biologically active metabolites of molds[2, 3]. Some of these mold constituents arise by oxidative ring opening of the anthraquinone skeleton[1, 3, 4]. In analogy with these novel biosynthetic reactions we have now accomplished the *in vitro* conversion of emodin *(1)* into "secoanthraquinones" of types *(2)* and *(3)*[3] in high yields.

During the *in vivo* "oxygenolysis"[1] of emodin *(1)* the bonds a and b on each side of C-10 are cleaved. Of the resulting benzophenones, *(2a)* and *(3a)*, the former affords mycotoxins of the ergochrome group, *e.g.* secalonic acid A[3], by intramolecular phenol oxidation, and subsequent transformations, while the latter is converted into the natural products sulochrin[4] and dihydrogeodin[1], by methylation and chlorination, and into the antibiotic geodin[1] by oxidative condensation.

[*] Prof. Dr. B. Franck and Dipl.-Chem. B. Berger-Lohr
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)

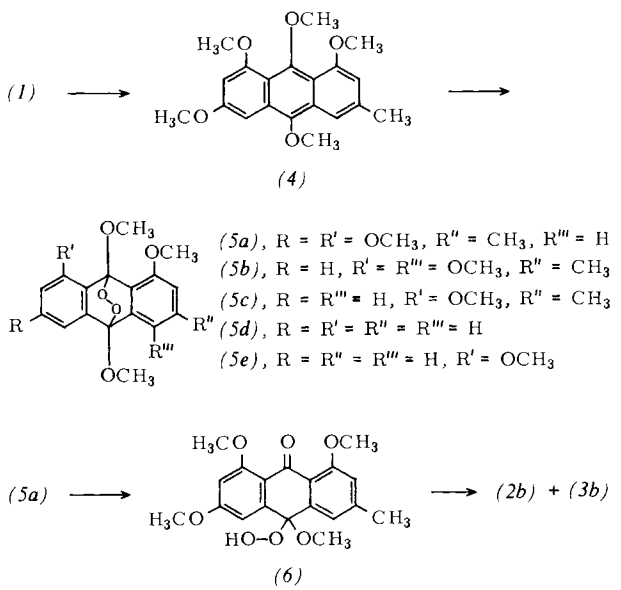
[**] This work was supported by the Landesamt für Forschung des Landes Nordrhein-Westfalen.



(2a), R = H
(2b), R = CH_3

(3a), R = H
(3b), R = CH_3

[4+2]-Cycloaddition of the pale yellow leucopenta(methyl ether) (4)[5] (obtainable from emodin (1)), which also serves as a sensitizer (m.p. 126 °C), with singlet oxygen (O_2, $\lambda > 350$ nm, +10 °C in ether, 25 min) led to a 73% yield of the endoperoxide (5a)[5]; colorless prisms, m.p. 174 °C (dec.); mass spectrum: *m/e* 374 (1.3%, $M^{\oplus}$), 342 (100%, $M^{\oplus} - O_2$); UV (ether): λ_{max} 297, 281, 231 nm. Partial ketal hydrolysis (0.2 N aq. HCl/dioxane 1:4, 2 h, 20 °C) of (5a) afforded the hydroperoxide (6)[5] as starting material for the ring-opening acid-catalyzed rearrangement; 88% yield, pale yellow prisms of m.p. 182 °C (dec.); mass spectrum: *m/e* 360 (5%, $M^{\oplus}$), 327 (18, $M^{\oplus} - OOH$); UV (ethanol): λ_{max} 343, 293 nm; ^{1}H-NMR ($CDCl_3$): δ 8.70 (s, 1H, OOH).



(5a), R = R' = OCH_3, R'' = CH_3, R''' = H
(5b), R = H, R' = R''' = OCH_3, R'' = CH_3
(5c), R = R''' = H, R' = OCH_3, R'' = CH_3
(5d), R = R' = R'' = R''' = H
(5e), R = R'' = R''' = H, R' = OCH_3

(6)

Rearrangement of the hydroperoxide (6) (conc. H_2SO_4/acetone, 3 h, 20 °C) proceeded in 50% yield (rearrangement of the endoperoxide (5a) *via* the intermediate (6) in 70% yield) to give a crystalline 3:4 mixture of the isomeric secoanthraquinones (2b) and (3b). After ester hydrolysis the components were separated by chromatography (PLC: silica gel, $CHCl_3/CH_3OH = 19:1$) and again esterified (CH_2N_2). (2b), m.p. 162 °C and (3b), m.p. 157 °C, were identified by their ^{1}H-NMR spectra[5].

Like (5a), the endoperoxides (5b) and (5c) could be obtained in yields of up to 80% from natural hydroxyanthraquinones, and (5d) and (5e) from synthetic ones, and transformed into secoanthraquinones[5]. Hence promising pathways open up for facile syntheses of natural products.

Received: September 29, 1975 [Z 321a IE]
German version: Angew. Chem. 87, 845 (1975)

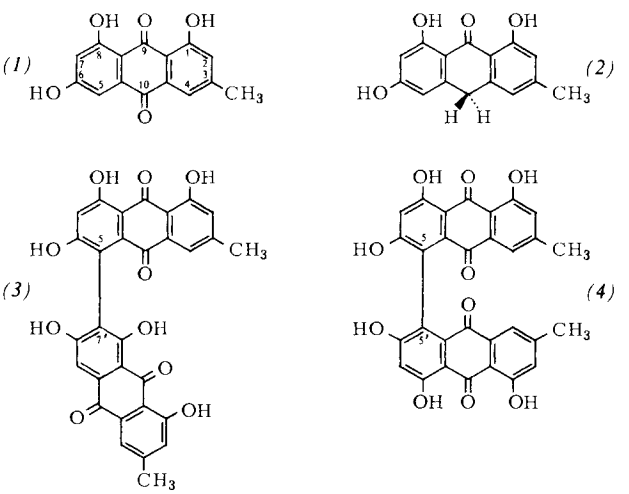
CAS Registry numbers:
(1), 518-82-1; (2a), 57459-04-8; (2b), 57459-05-9; (3a), 57459-06-0; (3b), 57459-07-1; (4), 57459-08-2; (5a), 57459-09-3; (5b), 57459-10-6; (5c), 57459-11-7; (5d), 57459-12-8; (5e), 57459-13-9; (6), 57459-14-0

[1] Constituents of Fungi, Part 26.—Part 25: *H. Fujimoto, H. Flasch,* and *B. Franck,* Chem. Ber. *108,* 1224 (1975).
[2] *R. H. Thomson:* Naturally Occurring Quinones. Academic Press, London 1971, pp. 1 and 367; *W. B. Turner:* Fungal Metabolites. Academic Press, London 1971, p. 74.
[3] *B. Franck, F. Hüper, D. Gröger,* and *D. Erge,* Chem. Ber. *101,* 1954 (1968); *B. Franck* and *H. Flasch,* Fortschr. Chem. Org. Naturst. *30,* 151 (1973).
[4] *S. Gatenbeck* and *L. Malmström,* Acta Chem. Scand. *23,* 3493 (1969).
[5] All compounds prepared for the first time were characterized by elemental analysis and spectroscopic data.

Biomimetic Synthesis of Skyrin[1][**]

By *Burchard Franck, Rabi Chahin, Hans-Georg Eckert, Rainer Langenberg,* and *Volker Radtke*[*]

Skyrin (4), the main pigment of the toxic rice fungus *Penicillium islandicum,* is a potential[2] and in some cases proven[3] biosynthetic precursor for almost 40 structurally related mycotoxins[4, 5] from molds and lichens. As demonstrated by labeling experiments[3, 6], it can arise from emodin (1) in the fungal cell, probably *via* a condensation proceeding by the mechanism of phenol oxidation. We now report the first biomimetic synthesis of skyrin (4) from emodin (1) and emodinanthrone (2) by chemical oxidation.



Oxidation of emodin (1) with $K_3[Fe(CN)_6]$ in the molar ratio 1:4 (0.06 N NaOH, 2 h, 20 °C) initially gave a 30% yield[7] of amorphous 5,7'-bisemodinyl (3) as the sole isolable oxidation product; the compound does not melt below 360 °C; mass spectrum: *m/e* 538 (15%, M^+); UV (CH_3OH): λ_{max} 445, 288, 254, 220 nm; IR (KBr): 1680, 1630 (C=O) cm^{-1}. It was identified as the crystalline hexamethyl (m.p. 285—287 °C) and hexaacetyl derivative (m.p. 153 °C) and by analysis of ^{1}H-NMR spectra and pK_a measurements (80% aq. dimethylformamide)[8, 9].

In order to establish by isotopic dilution analysis whether the desired skyrin (4) might nevertheless have been formed, the oxidation was repeated with biosynthetically prepared[11] [U-^{14}C]emodin (1). Admixture of inactive skyrin (4) to the

[*] Prof. Dr. B. Franck, Dr. R. Chahin, Dr. H.-G. Eckert, Dipl.-Chem. R. Langenberg, and Dr. V. Radtke
Organisch-Chemisches Institut der Universität
44 Münster, Orléans-Ring 23 (Germany)

[**] This work was supported by the Landesamt für Forschung des Landes Nordrhein-Westfalen.

oxidation mixture, re-isolation and repeated thorough chromatographic purification to constant radioactivity (a) silica gel G impregnated with tartaric acid, $CHCl_3$ +2% CH_3OH; b) acetylated polyamide 6-Ac (*ex* Macherey, Nagel & Co.), 80% aq. CH_3OH) afforded radioactive skyrin *(4)*. Its ^{14}C content showed that [U-^{14}C]emodin *(1)* was transformed in 0.28% yield into skyrin *(4)* on oxidation, thus proving formation of skyrin by *in vitro* phenol oxidation.

Formation of 5,7'-bisemodinyl *(3)* as the major product of emodin oxidation reveals some steric hindrance of position 5 of emodin by the n orbitals of the carbonyl oxygen at C-10 which are coplanar with the ring skeleton; this hindrance should be lower in emodinanthrone *(2)*. Accordingly, when compound *(2)*, which is readily accessible from emodin *(1)*, was subjected to oxidation by $K_3[Fe(CN)_6]$ a 1.2% yield of skyrin *(4)* (m.p. 360°C, dec., also characterized as the hexa(methyl ether) could be isolated, together with *(3)* (1.0%) and higher condensed products after chromatographic workup (PLC, see above)[8].

These results show that skyrin *(4)* is formed from emodin *(1)* by phenol oxidation, and in 4.3-fold higher yield from emodinanthrone *(2)*. A condensation mechanism of this kind can therefore also be considered for the biosynthesis of skyrin.

Former unsuccessful attempts to prepare skyrin by oxidation of emodin[10] were construed as a reason for assuming an alternative non-oxidative mechanism for the biosynthesis of skyrin *(4)* from emodin *(1)*[4].

Received: September 29, 1975 [Z 321b IE]
German version: Angew. Chem. *87*, 846 (1975)

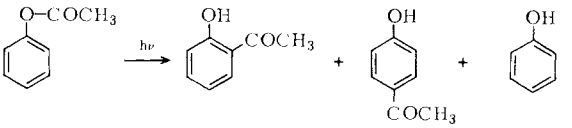
CAS Registry numbers:
(1), 518-82-1; *(2)*, 491-60-1; *(3)*, 57458-95-4; *(3)*-hexamethyl deriv., 57458-96-5; *(3)*-hexaacetyl deriv., 57458-97-6; *(4)*, 602-06-2

[1] Constituents of Fungi, Part 27.—Part 26: *B. Franck* and *B. Berger-Lohr*, Angew. Chem. *87*, 845 (1975); Angew. Chem. internat. Edit. *14*, 818 (1975).
[2] *W. B. Turner*: Fungal Metabolites. Academic Press, London 1971, p. 74.
[3] *H. Backhaus*, Dissertation, Universität Münster 1974; *M. Rolf*, Dissertation, Universität Münster 1974.
[4] *N. Takeda, S. Seo, Y. Ogihara, U. Sankawa, I. Iitaka, I. Kitagawa*, and *S. Shibata*, Tetrahedron *29*, 3703 (1973).
[5] *B. Franck* and *H. Flasch*, Fortschr. Chem. Org. Naturst. *30*, 151 (1973).
[6] *U. Sankawa, Y. Ebizuka*, and *S. Shibata*, Tetrahedron Lett. *1973*, 2125.
[7] Systematic investigations showed $K_3[Fe(CN)_6]$ to be superior to the following oxidizing agents with regard to formation of bisemodinyls: $VOCl_3$, DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), $Ce(SO_4)_2$, MnO_2, $FeCl_3$, CrO_3.
[8] The compounds described were characterized by elemental analysis and spectroscopic data.
[9] According to IR and UV spectra, compound *(3)* is identical with a product obtained by *Ikekawa* [10] in 5% yield by autoxidation of emodin *(1)*. The structure of a 5,4'-bisemodinyl assumed by that author can now be ruled out in favor of *(3)* on the basis of the presently available spectroscopic data.
[10] *T. Ikekawa*, Chem. Pharm. Bull. *11*, 749 (1963).
[11] *D. Gröger, D. Erge, B. Franck, U. Ohnsorge, H. Flasch*, and *F. Hüper*, Chem. Ber. *101*, 1970 (1968).

Selective Photochemical Fries Rearrangement of Phenyl Acetate in the Presence of β-Cyclodextrin

By *Masaaki Ohara* and *Kugako Watanabe*[*]

The Fries rearrangement of phenyl esters, *e.g. (1)*, affords a mixture of *o*- and *p*-hydroxy ketones, *e.g. (2)* and *(3)*. In addition, solvolysis gives phenol *(4)*. This rearrangement can also be carried out photochemically[1].



(1) *(2)* *(3)* *(4)*

We attempted to obtain one of the positionally isomeric rearrangement products preferentially by joint irradiation of phenyl acetate *(1)* and β-cyclodextrin. β-Cyclodextrin, a cyclic oligosaccharide made up of seven D-glucose units, can form inclusion complexes; this technique has been used on several occasions to induce a stereoselective course of an organic reaction[2].

Table 1. Influence of β-cyclodextrin on the course of the photochemical Fries rearrangement of phenyl acetate *(1)* (reaction conditions as given in procedure).

Reaction mixture (molar ratio)	Conversion [%]	Relative yields [%] *o*-Hydroxyacetophenone *(2)*	*p*-Hydroxyacetophenone *(3)*	Phenol *(4)*	*para*:*ortho*
(1)	12	25.7	25.7	48.6	1:1
β-Cyclodextrin:*(1)* (0.45:1)	41	11.2	69.0	19.8	6.2:1
Methyl α-D-glucopyranoside:*(1)* (3.1:1)	25.2	32.4	32.6	35.0	1:1

We have now found that the photochemical Fries rearrangement of phenyl acetate *(1)* in the presence of β-cyclodextrin in an aqueous medium does indeed follow a stereoselective course. The experimental results are summarized in Table 1. Only the three reaction products listed were detected. The content of tarry products was negligible. The isomers *(2)* and *(3)* are stable under the reaction conditions.

As seen from Table 1, *p*-hydroxyacetophenone *(3)* is preferentially formed in the presence of β-cyclodextrin, the formation of phenol falling from *ca.* 50 to *ca.* 20%. Moreover, the conversion increased about 3.5-fold. A control experiment showed that methyl α-D-glucopyranoside, which corresponds to a structural unit of β-cyclodextrin, has hardly any influence on the ratio of positional isomers.

Procedure:

A mixture of *(1)* (3 ml, 23.6 mmol) and β-cyclodextrin (12 g, 10.6 mmol) in H_2O (300 ml) was irradiated with UV light (100 W Hg high pressure lamp) for 38 h at 30°C with continuous passage of N_2. The reaction mixture was then extracted several times with ether. The dried ether extract was evaporated in a vacuum and analyzed by gas chromatography.

Received: September 22, 1975 [Z 330 IE]
German version: Angew. Chem. *87*, 880 (1975)

[*] Prof. Dr. M. Ohara [+] and M. Pharm. Sci. K. Watanabe
Faculty of Pharmaceutical Sciences, Josai University
Sakado, Saitama (Japan)
[+] To whom correspondence should be addressed.

[1] *H. Kobsa*, J. Org. Chem. *27*, 2293 (1962); *J. C. Anderson* and *C. B. Reese*, J. Chem. Soc. *1963*, 1781.
[2] *F. Cramer* and *H. Hettler*, Naturwissenschaften *54*, 625 (1967); *R. Breslow* and *P. Campbell*, Bioorg. Chem. *1*, 140 (1971).

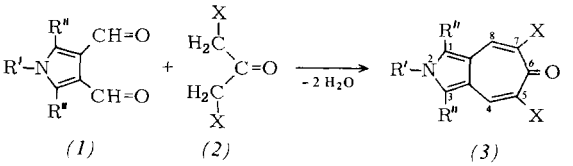
Synthesis of 2*H*-Cyclohepta[*c*]pyrrol-6-ones. A Route to 2-Azaazulenes[1]

By *Richard Kreher*, *Günter Vogt*, and *Marie-Luise Schultz*[*]

To study the spectroscopic properties and chemical behavior of carbocyclically annelated 1*H*- and 2*H*-pyrroles[2] as a function of the topology of the π system we have synthesized the 2*H*-cyclohepta[*c*]pyrrol-6-one *(3)* and a 2-azaazulene *(5)*.

The α-substituted heterocyclic dialdehydes *(1)* required for the synthesis are accessible from 2,5-dimethyl- and 1,2,5-trimethylpyrrole by formylation with dimethylformamide/phosphorus oxide chloride. Cyclizing-condensation with 1,3-bifunctional CH-acidic compounds *(2)* proved suitable for union of the troponoid system[3].

In the case of the dialkyl acetonedicarboxylates *(2)*, X = CO_2CH_3 and $CO_2C_2H_5$, twofold elimination of water occurs even in the presence of diethylamine. The limit of the range of application is reached in the case of dialkyl ketones *(2)*, X = phenyl and methyl, which are condensable with 1,2,5-trimethylpyrrol-3,4-dicarbaldehyde *(1b)* under forcing conditions in the presence of morpholine/potassium hydroxide. The low reactivity of the *N*-unsubstituted dialdehyde *(1a)* may primarily be due to its deprotonation to a resonance-stabilized anion.



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

(a), R' = H, R'' = CH_3
(b), R' = R'' = CH_3

Table 1. Prepared 2*H*-cyclohepta[*c*]pyrrol-6-ones *(3)*.

(3a), X = CO_2CH_3, yield 86 %, m. p. 292—294 °C (ethanol).—X = $CO_2C_2H_5$, yield 90 %, m. p. 255—258 °C (ethanol).—X = C_6H_5, yield 13 %, m. p. 311 °C (dec) (DMF).

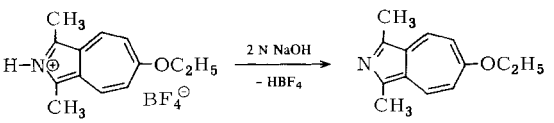
(3a), X = H, conc. HCl, 48—60 h under reflux, yield 88 %, m. p. 284—286 °C (isopropanol).—^{1}H-NMR (trifluoroacetic acid): τ = 1.3—1.5 (d, H^4, H^8), 2.7—2.9 (d, H^5, H^7), 7.1 (s, $2CH_3$).

(3b), X = CO_2CH_3, yield 89 %, m. p. 227—231 °C (ethanol).—X = $CO_2C_2H_5$, yield 92 %, m. p. 185—189 °C (ethanol).—X = C_6H_5, yield 45 %, m. p. 207—212 °C (dec) (ethyl acetate/CCl_4).—X = CH_3, yield 72 %, m. p. 207—212 °C (ethyl acetate)

(3b), X = H, solvolysis and decarboxylation, conc. HCl, 48—60 h under reflux, yield 88 %, m. p. 194—197 °C (ethanol/isopropanol).—^{1}H-NMR ($CDCl_3$): τ = 2.67—2.90 (d, H^4, H^8), 3.64—3.87 (d, H^5, H^7), 6.47 (s, NCH_3), 7.66 (s, $2CH_3$).

The 7*H*-cyclohepta[*c*]pyrrol-6-ones *(3)* behave like cyclic conjugated vinylogous carboxamides and do not react as carbonyl-homologous isoindoles under the usual conditions with activated dienophiles such as diethyl acetylenedicarboxylate or 1-diethylamino-1-propyne.

For the synthesis of substituted 2-azaazulenes *(5)*, 1,3-dimethyl-2*H*-cyclohepta[*c*]pyrrol-6-one *(3a)*, X = H, is obtained from the condensation product *(3a)*, X = CO_2CH_3 or $CO_2C_2H_5$, by hydrolysis and decarboxylation in acid medium. Selective alkylation of the vinylogous amide at the carbonyl oxygen with triethyloxonium tetrafluoroborate leads to the intensely violet salt *(4)*, which after basic hydrolysis and chromatographic workup, affords the 6-ethoxy-1,3-dimethyl-2-azaazulene *(5)*[4].



(4) *(5)*

Table 2. 6-Ethoxy-1,3-dimethyl-2-azaazulene *(5)*.

Yield 15 %, m. p. 123—124 °C (pet. ether).—Mol. wt. 201 (mass spec.).—UV (methanol): λ_{max} = 242 (log ε = 3.96), 303 (4.81), 340 (3.66), 350 (3.61), 585 nm (2.85).—^{1}H-NMR ($CDCl_3$): τ = 1.96—2.14 (d, H^4, H^8) and 3.54—3.72 (d, H^5, and H^7, *J* = 11 Hz), 5.65—6.05 and 8.42—8.63 (q and t, OCH_2CH_3), 7.62 (s, $2CH_3$).

The azulenoid hetarenes *(5)* as well as the isomeric 1-, 3a-, and 5-azaazulenes[5] are readily accessible in this way.

Received: August 19, 1975 [Z 311 IE]
in abridged form: September 17, 1975
German version: Angew. Chem. *87*, 840 (1975)

CAS Registry numbers:
(1a), 56139-74-3; *(1b)*, 31618-55-0; *(2)*, X = CO_2CH_3, 1830-54-2; *(2)*, X = H, 67-64-1; *(2)*, X = C_6H_5, 102-04-5; *(2)*, X = CH_3, 96-22-0; *(2)*, X = $CO_2C_2H_5$, 105-50-0; *(3a)*, X = CO_2CH_3, 57015-24-4; *(3a)*, X = $CO_2C_2H_5$, 57015-25-5; *(3a)*, X = C_6H_5, 57015-26-6; *(3a)*, X = H, 57015-27-7; *(3b)*, X = CO_2CH_3, 57015-28-8; *(3b)*, X = $CO_2C_2H_5$, 57015-29-9; *(3b)*, X = C_6H_5, 57015-30-2; *(3b)*, X = CH_3, 57015-31-3; *(3b)*, X = H, 57015-32-4; *(4)*, 57031-27-3; *(5)*, 57015-33-5

[1] Structure and Reactivity of Isoannelated Heterocyclic Systems with 4*n*π- and (4*n* + 2) π-electrons, Part 4.—This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.—Part 3: *R. Kreher* and *W. Köhler*, Angew. Chem. *87*, 288 (1975); Angew. Chem. internat. Edit. *14*, 264 (1975).

[2] *R. Kreher* and *G. Vogt*, Angew. Chem. *82*, 958 (1970); Angew. Chem. internat. Edit. *9*, 955 (1970); *R. Kreher*, *H. Hennige*, and *H. Möller*, Allg. Prakt. Chem. *23*, 82 (1972) (to be considered as Part 1).

[3] Applications of the synthetic principle: *A. V. El'tsov*, *A. A. Ginesina*, and *L. N. Kivokurtseva*, Tetrahedron Lett. *1968*, 735; *J. Duflos*, *D. Letouzé*, *G. Queguiner*, and *P. Pastour*, Tetrahedron Lett. *1973*, 3453.

[4] Applications of the reaction principle: *K. Hafner*, *K. H. Vöpel*, *G. Ploss*, and *C. König*, Liebigs Ann. Chem. *661*, 52 (1963), for the synthesis of azulenes from fulvenotropones.

[5] a) *T. Nozoe*, *S. Seto*, *S. Matsumura*, and *T. Terasawa*, Chem. Ind. (London) *1954*, 1357; b) *W. Flitsch*, *B. Müter*, and *U. Wolf*, Chem. Ber. *106*, 1993 (1973); c) *K. Hafner* and *M. Kreuder*, Angew. Chem. *73*, 657 (1961).

[*] Prof. Dr. R. Kreher, Dr. G. Vogt, and Dipl.-Chem. M.-L. Schultz
Institut für Organische Chemie der Technischen Hochschule
61 Darmstadt, Petersenstrasse 15 (Germany)

Simple Synthesis of Dicyclopropylidenemethane[**]

By *Richard Kopp* and *Michael Hanack*[*]

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

In order to generate vinyl cations[1] of type *(1)* we required large amounts of dicyclopropylidenemethane *(2)* and therefore sought a new and simple entry to this hydrocarbon.

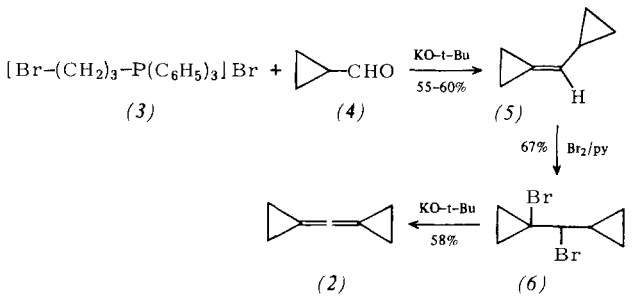
(1) *(2)*

[*] Prof. Dr. M. Hanack and Dipl.-Chem. R. Kopp
Institut für Organische Chemie der Universität
74 Tübingen 1, Auf der Morgenstelle 18 (Germany)

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

Compound *(2)* was first prepared by *Fitjer* and *Conia* by a ten-step synthesis, starting from methyl cyclopropyl ketone, and isolated pure by gas chromatography[2].

The hydrocarbon is now more readily accessible by our new synthetic pathway: 3-bromopropyltriphenylphosphonium bromide *(3)*[3] is reacted with cyclopropanecarbaldehyde *(4)*[4] in dimethyl sulfoxide (DMSO) in the presence of two equivalents of potassium *tert*-butoxide to give cyclopropylmethylenecyclopropane *(5)*[5]. Compound *(5)* can be brominated in pentane at −17 °C in the presence of pyridine to form the dibromide *(6)*. On treatment with a 10-fold excess of potassium *tert*-butoxide in tetrahydrofuran, *(6)* eliminated HBr to give dicyclopropylidenemethane *(2)* which is almost pure on analysis by gas chromatography. *(2)* is stored in pentane solution and isolated as required by distillation and gas chromatography. Dicyclopropylidenemethane polymerizes very readily when pure or in concentrated solution.



Cyclopropylmethylenecyclopropane (5)

A solution of KO-t-Bu (79 g, 0.71 mol) in anhydrous DMSO (750 ml) is added dropwise to finely powdered *(3)* (165 g, 0.355 mol) under N_2. Ice-bath cooling is adjusted such that the DMSO just remains liquid. Stirring is continued for 40 min at room temperature and a solution of *(4)* (22.6 g, 0.322 mol) in DMSO (100 ml) is then added, whereupon the solution gradually turns dark. After stirring at room temperature for 6 h and at *ca.* 75 °C for 3 h the reaction mixture is added to *ca.* 4 l of an ice-cold saturated aqueous solution of common salt. Extraction with pentane (800 ml), washing of the extract with saturated, aqueous salt solution, and drying is followed by distillative removal of the pentane over a Vigreux column and vacuum fractionation of the residue. B. p. 46—48 °C/50 torr; yield 55—60 %[5].

Cyclopropylbromomethyl-1-bromocyclopropane (6)

A solution of bromine in pentane (*ca.* 20 vol % Br_2) is added dropwise to a solution of *(5)* (3 g) and pyridine (0.2 g) in pentane (300 ml) at −17 °C until a persisting brown color appears. The reaction mixture is shaken with an ice-cold aqueous sodium sulfite/common salt solution and then dried. After 10 min the pentane is drawn off at 0 °C under water pump vacuum. The resulting dibromide *(6)*[5] (*ca.* 80 % solution) can be reacted without further purification; yiels 67%.

Dicyclopropylidenemethane (2)

A solution of *(6)* (5.4 g, 21.3 mmol) in THF (50 ml) is slowly added dropwise to a solution of KO-t-Bu (23.9 g, 213 mmol) in anhydrous THF (300 ml) at −17 °C under N_2. The reaction mixture is warmed to 50 °C and stirring continued for 7 h. It is then poured onto *ca.* 800 ml of ice-cold saturated common salt solution and extracted (under N_2) with pentane (600 ml). The pentane phase is washed with ice-cold saturated aqueous common salt solution and dried over sodium sulfate. A yield of 58 % is established by comparison with the gas chromatogram of an added standard (*o*-xylene). Compound *(2)* can readily be isolated from the concentrated pentane solution by preparative gas chromatography on a 3 m glass column packed with 15 % SGR SE 30 on Voraport 30 (60—80 mesh) at 100 °C. ^{1}H-NMR (CCl_4): δ = 1.5 ppm (s). IR (CCl_4): 813, 863, 916, 1043, 1125, 1248, 1412, 2100, 2950 cm^{-1}.

Received: September 19, 1975 [Z 322 IE]
German version: Angew. Chem. 87, 874 (1975)

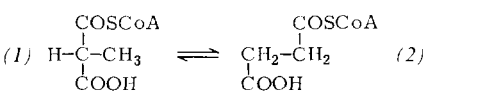
[1] *H. U. Siehl, J. C. Carnahan jr., L. Eckes,* and *M. Hanack,* Angew. Chem. *86,* 677 (1974); Angew. Chem. internat. Edit. *13,* 675 (1974).
[2] *L. Fitjer* and *J. M. Conia,* Angew. Chem. *85,* 832 (1973); Angew. Chem. internat. Edit. *12,* 761 (1973).
[3] *K. Utimoto, M. Tamura,* and *K. Sisido,* Tetrahedron *29,* 1169 (1973).
[4] *L. B. Young* and *W. S. Trahanovsky,* J. Org. Chem. *32,* 2349 (1967); *J. P. Barnier, J. M. Denis, J. Salaün,* and *J. M. Conia,* Tetrahedron *30,* 1392 (1974).
[5] *M. Hanack, T. Bässler, W. Eymann, W. E. Heyd,* and *R. Kopp,* J. Am. Chem. Soc. *96,* 6686 (1974).

Nonenzymatic Model Reaction for the Coenzyme B_{12}-Catalyzed Rearrangement of Methylmalonyl-CoA into Succinyl-CoA[**]

By *Gisela Bidlingmaier, Helmut Flohr, Uwe M. Kempe, Traute Krebs,* and *János Rétey*[*]

The coenzyme B_{12}-dependent enzymatic reactions have to this day defied explanation in terms of a chemically plausible mechanism. Notably, the biochemical findings[1] contradict attempted explanations based on the organometallic chemistry of cobalt complexes as models[2].

An example of coenzyme B_{12}-dependent reactions is the reversible conversion of methylmalonyl-CoA *(1)* into succinyl-CoA *(2)*, which occurs both in bacteria and in animals.



Experiments with ^{14}C-labeled substrates showed that the COSCoA group shifts from C-2 onto the methyl C atom of methylmalonyl-CoA *(1)* during the enzymatic reaction[3]. Whereas this shift proceeds intramolecularly[4], the migration of the H atom in the opposite direction is apparently intermolecular[5], the cobalt-bound methylene group of coenzyme B_{12} serving as the acceptor-donor site for the migrating H atom[6].

While searching for model reactions we found that the photochemical decomposition of 2,2-diethoxycarbonylpropyl-(pyridinato)cobaloxime *(3)* affords not only diethyl dimethylmalonate *(4)* but also diethyl methylsuccinate *(5)*.

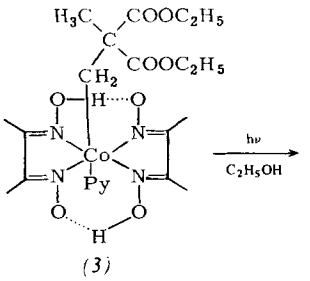
The products were characterized both by gas chromatography and by the identity of their fragmentation pattern in the mass spectrometer with that of authentic samples. Irradiation of *(3)* in anhydrous ethanol gave good yields (maximum of 80 % of the volatile products) of *(5)* in some cases; however, the experiments became reproducible only on addition of small amounts of acetic acid. Addition of pyridine suppressed the rearrangement.

Numerous studies confirm[7] that irradiation of alkylcobalt complexes leads to homolysis of the cobalt-carbon bond. In

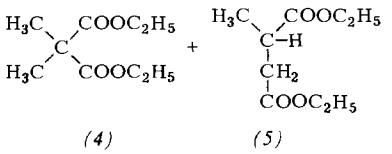
[*] G. Bidlingmaier, Dipl.-Chem. H. Flohr, Dr. U. M. Kempe, T. Krebs, and Prof. Dr. J. Rétey
Lehrstuhl für Biochemie im Institut für Organische Chemie der Universität
75 Karlsruhe, Richard-Willstätter-Allee (Germany)

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

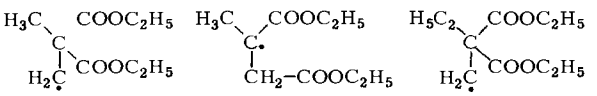
principle, the resulting alkyl radical *(6)* could spontaneously rearrange into radical *(7)*. However, if the homologous radical *(8)* is generated by decarbonylation of the corresponding aldehyde no rearrangement takes place[8].



(3)



(4) *(5)*



(6) *(7)* *(8)*

Regardless of the role the central cobalt atom and its *trans* ligand (pyridine) play in the rearrangement of *(3)*, an analogy with the coenzyme B_{12}-dependent transformation of methylmalonyl-CoA *(1)* into succinyl-CoA *(2)* appears compelling. Further characterization of the model reaction will show whether the analogy can be pursued to greater depths.

After having obtained the present results, we learned that *Dowd et al.*[9] have observed a similar rearrangement in a system different from ours[11].

2,2-Diethoxycarbonylpropyl(pyridinato)cobaloxime (3)

To a solution of $CoCl_2 \cdot 6H_2O$ (1 mmol) and biacetyldioxime (2 mmol) in anhydrous ethanol (99.85 %) are added potassium hydroxide (2 mmol) and pyridine (1 mmol), both in the form of 1 M alcoholic solutions. After stirring for 15 min at 25 °C the solution is purged with argon and cooled to −10 °C. Potassium hydroxide (1 mmol) and $NaBH_4$ (2 mmol) are then added under argon in the dark, the argon replaced by hydrogen, and the mixture allowed to react for 1 h at −10 °C. After warming to 25 °C, diethyl 2-bromomethyl-2-methylpropanedioate[10] (5 mmol) is added to the stirred reaction mixture. The black solution turns light orange. After 15 min the solvent is removed under vacuum, the residue taken up in dichloromethane, and filtered under nitrogen. Chromatography on silica gel with ethyl acetate as eluant affords 393 mg (0.71 mmol) *(3)*. (Beautiful orange-red needles from methanol/water + one drop of pyridine.) NMR (100 MHz, $CDCl_3$): δ = 1.18 t (6H); 1.30 s (3H); 2.00 s (2H); 2.12 s (12H); 4.09 double sextet (4H); 7.32 m (2H); 7.75 t (1H); 8.56 d (2H). Compound *(3)* gave a correct elemental analysis.

Example of photochemical reaction of (3)

Compound *(3)* (4 mg, 7.2 μmol) is dissolved in anhydrous ethanol (1 ml) containing 1 % of acetic acid with half-an-hour's stirring in the dark under argon. The solution is maintained at 15—20 °C during 90 minutes' irradiation with a high pressure mercury lamp (125 watt, Philips) at a distance of 8 cm. After removal of solvent under vacuum, the residue is extracted with pentane and the extract analyzed by gas chromatography and mass spectrometry. The residue which cannot be extracted with pentane contains still unreacted *(3)* in most cases.

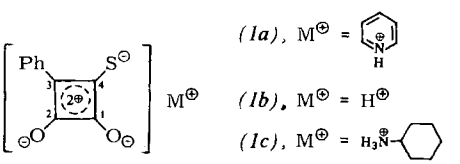
Received: October 2, 1975 [Z 328 IE]
German version: Angew. Chem. 87, 877 (1975)

[1] For a review, see *W. Friedrich* in *R. Ammon* and *W. Dirscherl:* Vitamin B_{12} und verwandte Corrinoide. Thieme, Stuttgart 1975.
[2] *G. N. Schrauzer*, Acc. Chem. Res. *1*, 97 (1968); *G. N. Schrauzer* and *J. W. Sibert*, J. Am. Chem. Soc. *92*, 1022 (1970).
[3] *H. Eggerer, P. Overath, F. Lynen*, and *E. R. Stadtman*, J. Am. Chem. Soc. *82*, 2643 (1960).
[4] *R. W. Kellermeyer* and *H. G. Wood*, Biochemistry *1*, 1124 (1962); *E. F. Phares, M. V. Long*, and *S. F. Carson*, Biochem. Biophys. Res. Commun. *8*, 142 (1962).
[5] *R. H. Abeles* and *B. Zagalak*, J. Biol. Chem. *241*, 1245 (1966); *P. A. Frey, M. K. Essenberg*, and *R. H. Abeles, ibid. 242*, 5369 (1967).
[6] *J. Rétey* and *D. Arigoni*, Experientia *22*, 783 (1966); *G. J. Cardinale* and *R. H. Abeles*, Biochim. Biophys. Acta *132*, 517 (1967).
[7] For a review, see *D. G. Brown*, Progr. Inorg. Chem. *18*, 207 (1973).
[8] *S. N. Lewis, J. J. Miller*, and *S. Winstein*, J. Org. Chem. *37*, 1478 (1972).
[9] *P. Dowd, M. Shapiro*, and *K. Kang*, J. Am. Chem. Soc. *97*, 4754 (1975). It is not clear from this publication whether it is the acrylyl or the tetrahydropyranyloxycarbonyl which migrates.
[10] Prepared from diethyl methylmalonate and dibromomethane with 1 mol of base.
[11] *Note added in proof* (Nov. 13, 1975): The cobalamin complex corresponding to *(3)* is so unstable that it decomposes in the dark at pH 7 within a few hours, affording *(4)* and *(5)*.

Nucleophilic Attack on the 3-Phenyl-4-sulfidocyclobutenediylium-1,2-diolate Anion[**]

By *Arthur H. Schmidt, Walter Ried, Peter Pustoslemsek*, and *Walter Schuckmann*[*]

The 4-sulfidocyclobutenediylium-1,2-diolates *(1a)* and *(1b)*[1] belong to a new class[1, 2] of four-membered carbocycles displaying 2π-electron delocalization, in which oxygen and sulfur bear the negative charge in the anion. As expressed in formula *(1)* the anion possesses electrophilic character; it should therefore react with nucleophilic reagents.



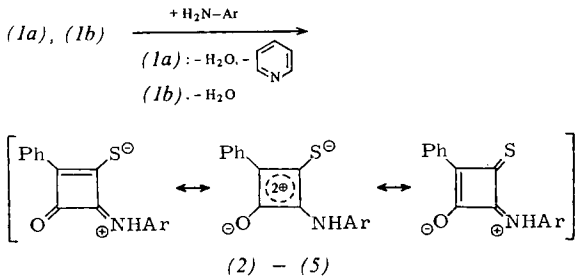
(1)

(1a), $M^{\oplus}$ =
(1b), $M^{\oplus} = H^{\oplus}$
(1c), $M^{\oplus}$ =

Surprisingly, however, heating of *(1b)* with aliphatic amines merely affords ammonium salts such as *(1c)*, thus underlining the pronounced acidity[1] of *(1b)*. In contrast, reaction of equimolar solutions of *(1a)* or *(1b)* with primary aromatic amines (THF; ethanol) leads to deeply colored condensation products *(2)*—*(5)*, even when the reaction is performed in an ice-cold medium. Thus the electrophilic character of system *(1)* is confirmed and atom C-4 is ruled out as the point of attack by nucleophiles. The IR spectrum of *(4)* (Table 1) suggests a delocalized bond system[3] as a structural component of the novel class of compounds. Apart from the expected absorptions, the ^{1}H-NMR spectra of *(2)* and *(5)* contain the broad signal due to a single proton at low field

[*] Dr. A. H. Schmidt [+], Prof. Dr. W. Ried, and Dipl.-Chem. P. Pustoslemsek
Institut für Organische Chemie der Universität
6 Frankfurt/Main, Theodor-Stern-Kai 7 (Germany)
Dr. W. Schuckmann
Institut für Kristallographie der Universität
6 Frankfurt/Main, Senckenberganlage 30 (Germany)
[+] To whom correspondence should be addressed.

[**] Reactions with Cyclobutenediones, Part 43.—Part 42: *W. Ried, H. Knorr*, and *U. Knorr*, Chem. Ber., in press.



(2) – (5)

hydrogen carbonate and can be regenerated unchanged by cautious acidification. If (2) is added to cyclohexylamine and the ice-cold solution treated with dilute sulfuric acid then (1c) is obtained. This suggests the intermediacy of the salt (6) and emphasizes its ease of hydrolysis.

The action of diazomethane on (2) affords the thioether (7). Cautious hydrolysis permits its degradation to (8)[1]. Treatment of a solution of (2) in THF with an aqueous solution of $HgCl_2$ immediately precipitates the mercury salt (9) which fulfils the conditions necessary for inner chelate

Table 1. Properties of 2-arylamino-4-phenyl-3-sulfidocyclobutenediylium-1-olates (2)—(5) [4] and of compounds (7) and (9). Satisfactory elemental analyses are available for all compounds.

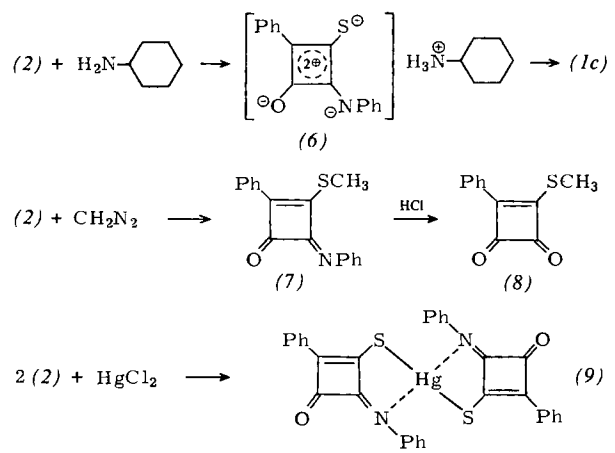
Cpd. Ph = C_6H_5	Ar	M.p. [°C] solvent, color	IR [cm^{-1}] [a]	^{1}H-NMR [δ, ppm]
(2)	C_6H_5	212—215 ethanol, red	3165—2850 br, 1780 w, 1735 s, 1705 sh, 1650 w, 1590 w	9.9—10.3 [b]
(3)	2-Br—C_6H_4	178—180 benzene, dark red	1725 s, 1700 w, 1620 s, 1570 s, 1550 m	
(4)	4-CH_3—C_6H_4	206 acetonitrile, red	3180—2700 br, 1720 w, 1700 s, 1625 sh, 1610 s, br, 1570 m	
(5)	4-OCH_3—C_6H_4	200—202 benzene, red	3190—2680 br, 1720 w, 1700 s, 1620 s, br, 1585 sh, 1570 m	11.6—12.0 [b]
(7)		129 ethanol, yellow	3060 w, 2970 w, 2820 w, 1740 s, 1655 m	7.88—7.69 (2 H, m) 6.94—7.50 (8 H, m) 3.09 (3 H, s) [c]
(9)		350 (dec.) —, yellow	3060 w, 1750 s, 1655 m, 1500 m	

[a] s = strong, m = medium, w = weak, sh = shoulder, b = broad.
[b] 60 MHz, [D_6]-DMSO, acidic H.
[c] 100 MHz, $CDCl_3$.

which undergoes ready exchange with D_2O. The mass spectrum of (2) is not very characteristic.

Since the spectroscopic data of the condensation products were insufficient to permit a distinction between the structures (2)—(5) and the 2-substituted isomers, compound (3) was subjected to X-ray structure analysis[5]. The result confirmed the structures (2)—(5) and hence C-1 as the site of nucleophilic attack on the 3-phenyl-4-sulfidocyclobutenediylium-1,2-diolate anion. The molecular diagram[5] of (3) reveals furthermore that the four-membered ring system is planar and that the four substituents lie in the same plane. Accordingly, the linkages between the four different substituents and the four-membered ring system are formed by double bonds and partial double bonds.

Compounds (2)—(5) are characterized by their high acidity. They are readily soluble in a 10% solution of sodium



formation between the lone pairs of the nitrogen and the mercury atom. Hydrolysis of (2) with concentrated hydrochloric acid leads to (1b) (see Table 1 for properties of the new compounds).

Received: September 12, 1975;
revised: October 15, 1975 [Z 329 IE]
German version: Angew. Chem. 87, 879 (1975)

[1] A. H. Schmidt, W. Ried, P. Pustoslemsek, and H. Dietschmann, Angew. Chem. 84, 110 (1972); Angew. Chem. internat. Edit. 11, 142 (1972).
[2] a) D. Coucouvanis, F. Hollander, R. West, and D. Eggerding, J. Am. Chem. Soc. 96, 3006 (1974); b) G. Seitz, H. Morck, K. Mann, and R. Schmiedel, Chem.-Ztg. 98, 459 (1974); c) G. Seitz, K. Mann, R. Schmiedel, and R. Matusch, ibid. 99, 90 (1975).
[3] W. Ried, A. H. Schmidt, G. Isenbruck, and F. Bätz, Chem. Ber. 105, 325 (1972).
[4] Of the three resonance formulas of compounds (2)—(5) we employ the central one for purposes of description and designation.
[5] W. Schuckmann, P. Pustoslemsek, W. Ried, and A. H. Schmidt, to be published.

Simple Synthesis of 1-Halobicyclooctanes[**][***]

By *Wolfgang Kraus* and *Hans-Dieter Gräf*[*]

Dedicated to Professor Eugen Müller on the occasion of his 70th birthday

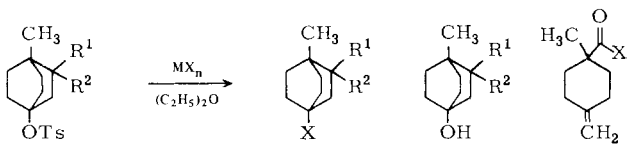
We have found that 1-halobicycloalkanes are formed in very good yield from corresponding bridgehead tosylates on

[*] Prof. Dr. W. Kraus and Dr. H.-D. Gräf
Chemisches Institut der Universität Tübingen
Present address:
Lehrstuhl für Organische Chemie der Universität Hohenheim
7 Stuttgart 70, Emil-Wolff-Strasse 14 (Germany)

[**] Part of Doctoral Dissertation of H.-D. Gräf, Universität Tübingen 1975.

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

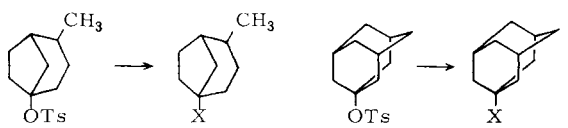
treatment with anhydrous metal halides in diethyl ether. No reaction occurs in more strongly solvating solvents such as THF, dioxane, glyme, or HMPT. In order to prepare the 1-chloro compounds the tosylates are reacted with $FeCl_3$ or $TiCl_4$ in boiling diethyl ether, the 1-bromo and 1-iodo compounds being obtained with $MgBr_2$ and MgI_2 respectively.



(1), $R^1 = R^2 = H$ — *(2)* — —

(3), $R^1 = H$, $R^2 = C_6H_5$ — *(4)* + *(5)* —

(6), R^1, $R^2 = O$ — *(7)* + *(8)* + *(9)*



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

(a), X = Cl; *(b)*, X = Br; *(c)*, X = I

in Table 1; the bromides and iodides are prepared by adding the tosylate to a freshly prepared solution of $MgBr_2$[3] or MgI_2[4], respectively, in ether. The mixture is refluxed with exclusion of moisture, cooled, and poured into ice-water. After separation of the ethereal phase the aqueous phase is extracted twice with ether. The combined ethereal phases are washed with water and dried over sodium sulfate. After the ether has been distilled off the residue is chromatographed over silica gel with pentane, and with pentane/ether (0—50%) in the case of ketones.

Received: October 2, 1975;
revised: October 29, 1975 [Z 333 IE]
German version: Angew. Chem. *87*, 878 (1975)

[1] *J. W. McKinley, R. E. Pincock*, and *W. B. Scott*, J. Am. Chem. Soc. *95*, 2030 (1973); *Z. Suzuki* and *K. Morita*, J. Org. Chem. *32*, 31 (1967); Bull. Chem. Soc. Japan *41*, 1724 (1968); cf. *H. E. Zimmerman* and *R. D. McKelvey*, J. Am. Chem. Soc. *93*, 36 (1971); *J. Kopecký* and *J. Šmejkal*, Tetrahedron Lett. *1967*, 1931, 3889; *J. Kopecký*, *J. Smejkal*, and *M. Hudlický*, Chem. Ind. (London) *1969*, 271, and references cited therein.

[2] Cf. *J. Gore, P. Place*, and *M. L. Roumestant*, J. Chem. Soc. Chem. Commun. *1973*, 821.

[3] *D. Seyferth, H. P. Hofmann, R. Burton*, and *J. F. Helling*, Inorg. Chem. *1*, 227 (1962).

[4] *K. Nützel* in Houben-Weyl-Müller: Methoden der Organischen Chemie. 4th Edit. Thieme, Stuttgart 1973, Vol. 13/2a, p. 174.

Table 1. Reaction of the bridgehead tosylates *(1)*, *(3)*, *(6)*, *(10)*, and *(12)* with anhydrous metal halides MX_n in refluxing diethyl ether.

Tosylate	MX_n	MX_n:Tosylate	Reaction time [h]	Products	Yield [%]	M. p. [°C] B. p. [°C/torr]
(1)	$FeCl_3$	4:1	8	*(2a)*	70	75—75.5
(1)	$TiCl_4$	4:1	5	*(2a)*	74	
(1)	$MgBr_2$	1.3:1	1	*(2b)*	83	90.5
(1)	MgI_2	1.3:1	1	*(2c)*	74	71—71.5
(3)	$FeCl_3$	4:1	3	*(4a)*	90	94/0.2
				(5)	2	
(3)	$TiCl_4$	4:1	1	*(4a)*	91	
				(5)	6	
(3)	$MgBr_2$	1.3:1	1	*(4b)*	91	124—127/0.5
				(5)	7	
(3)	MgI_2	1.3:1	1	*(4c)*	69	59
				(5)	5	
(6)	$TiCl_4$	8:1	60	*(7a)*	80	63.5—64
				(8)	18	
				(9a)	trace	[a]
(6)	$MgBr_2$	2.6:1	8	*(7b)*	82	75—75.5
				(8)	3	
				(9b)	15	[a]
(6)	MgI_2	2.6:1	8	*(7c)*	79	68.5
				(8)	3	
				(9c)	18	[a]
(10)	$TiCl_4$	6:1	3	*(11a)*	92	68—70/11
(10)	$MgBr_2$	6:1	3	*(11b)*	90	82—83/11
(10)	MgI_2	6:1	3	*(11c)*	81	45/0.25
(12)	$TiCl_4$	1.3:1	0.25	*(13a)*	95	163—164
(12)	$MgBr_2$	1.3:1	0.25	*(13b)*	90	119
(12)	MgI_2	1.3:1	0.25	*(13c)*	89	151—152

[a] Identified as carboxylic acid.

In contrast to previously described syntheses of 1-halodicyclo[2.2.2]octanes[1] this method can also be applied to systems containing functional groups (see Table 1).

Tosylates *(3)* and *(6)*, which contain substituents having a negative inductive effect attached to C-3, also give small amounts of the parent alcohols *(5)* and *(8)*, respectively. It may therefore be assumed that the reactions proceed *via* bridgehead cations formed according to a S_N1 mechanism[2].

Procedure:

The tosylate (5.4 mmol) is dissolved in anhydrous ether (40 ml) and treated with the amount of $TiCl_4$ or $FeCl_3$ given

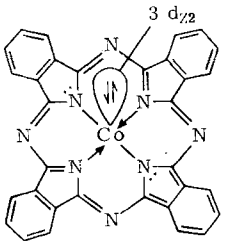
Phthalocyaninecobalt(I) Salts, "Supernucleophilic" Vitamin B_{12} Models Stable in Neutral Medium[**]

By *Heiner Eckert* and *Ivar Ugi*[*]

Salts of the phthalocyaninemetal anion $[PcM]^{\ominus}$ such as $Li_2[PcFe]\cdot 5.5\ THF$[1] and $Li[PcCo]\cdot 4.5\ THF$, with a central

[*] Dipl.-Chem. H. Eckert and Prof. Dr. I. Ugi
Laboratorium für Organische Chemie der Technischen Universität
8 München 2, Arcisstrasse 21 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—We thank Dr. *D. Lenoir* for kindly helping with the conductometric investigations.



$[PcCo^I]^{\ominus}$

atom in low oxidation state and having d^8 configuration with $2a_{1g}$ orbital formed predominantly from a $3d_{z^2}$ orbital, undergo substitution reactions with alkyl halides in THF to give stable organometalphthalocyanines[2]

$$PcCo^{II} \xrightarrow{+e^{\ominus}} [PcCo^I]^{\ominus} \xrightarrow{+R-X} PcCo^{III}-R + X^{\ominus}$$

We have recently found that Li[PcCo]·4.5 THF, which is very sensitive toward oxygen and water, yet completely stable in their absence, forms stable neutral solutions in alcohols (ethanol, methanol) and has "supernucleophilic" properties therein which had not been observed in previous investigations in THF.

Anionic complexes with formal negative charges, strongly nucleophilic transition metal central atoms, and high relative nucleophilicities ($n_{CH_3I} > ca.$ 10; cf. Table 2) are referred to as "supernucleophiles"[3]. The relative nucleophilicity is calculated from the rate constant k_2 of the methylation reaction (Tables 1 and 2).

Table 1. Conductometrically determined kinetic data of the following 2nd order reactions:

$$Li[PcCo^I]\cdot 4.5\,THF + CH_3I \xrightarrow{k_2} PcCo^{III}-CH_3 + LiI + 4.5\,THF \quad (1)$$

$$Li[PcCo^I]\cdot 4.5\,THF + n\text{-}C_4H_9Br \xrightarrow{k_2} PcCo^{III}\text{-}n\text{-}C_4H_9 + LiBr + 4.5\,THF \quad (2)$$

in methanol at 25 °C.

		Reaction with CH_3I	Reaction with n-C_4H_9Br
Rate constant k_2 [l mol^{-1} s^{-1}]	at 0 °C	0.37	—
	at 25 °C	7.4	2.9×10^{-3}
Activation enthalpy $\Delta H^{\neq}$ [kcal/mol]		18.7	—
Activation entropy $\Delta S^{\neq}$ [cal K^{-1} mol^{-1}]		7.0	—

Table 2. Relative nucleophilicity n_{CH_3I} (according to *Pearson* [4]) for reactions of the type

$$CH_3I + Y^{\ominus} \xrightarrow{k_Y} CH_3Y + I^{\ominus}$$

n_{CH_3I} is defined as $\log (k_Y/k_{CH_3OH})$. k_Y is the 2nd order rate constant for the methylation of nucleophile Y with CH_3I in CH_3OH at 25 °C (for $[PcCo]^{\ominus}$, $k_Y = k_2$); k_{CH_3OH}, the corresponding constant for the solvolysis of CH_3I in CH_3OH, is 1.3×10^{-10} l mol^{-1} s^{-1}.

Nucleophile	n_{CH_3I}	Ref.
CH_3OH	0.00	[4]
$Cl^{\ominus}$	4.37	[4]
$Br^{\ominus}$	5.79	[4]
$CN^{\ominus}$	6.70	[4]
$I^{\ominus}$	7.42	[4]
$S_2O_3^{\ominus}$	8.95	[4]
$C_6H_5S^{\ominus}$	9.92	[4]
$[PcCo]^{\ominus}$ [a]	10.8	
Cobaloximes$_s$ [a]	10.5—14.3 [b]	[3, 5]
Vitamin B_{12s} [a]	14.4 [b]	[3]

[a] Contains Co^I.
[b] Determined at 30 °C.

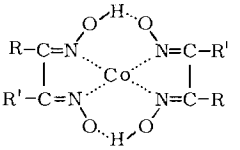
$[PcCo^I]^{\ominus}$ is prepared by reduction of $PcCo^{II}$ with benzophenonedilithium or naphthalenesodium in THF at 20 °C[2]. The blue $PcCo^{II}$ is practically insoluble in all common solvents, while $Li[PcCo^I]$ and $Na[PcCo^I]$ are readily soluble in methanol, ethanol, isopropanol, acetonitrile, DMSO, DMF, and dioxane. In cold THF and cold dioxane they are only sparingly soluble and can be recrystallized from these solvents.

In contrast to the cobaloximes derivatives and vitamin B_{12s}, which contain Co^I and are only stable in alkaline medium, the $[PcCo^I]$ ion is also stable in neutral, protonic solution.

Received: September 12, 1974 [Z 188 IE]
revised: January 21, 1975
German version: Angew. Chem. 87, 847 (1975)
Publication delayed at authors' request

CAS Registry numbers:
$Li[PcCo^I]$, 14516-90-6; CH_3I, 74-88-4; n-C_4H_9Br, 109-65-9; $PcCo^{III}$—n-C_4H_9, 54774-62-8

[1] Pc = phthalocyanine, THF = tetrahydrofuran.
[2] *R. Taube, H. Drevs,* and *T. Duc-Hiep,* Z. Chem. *9,* 115 (1969).
[3] *G. N. Schrauzer* and *E. Deutsch,* J. Amer. Chem. Soc. *91,* 3341 (1969).
[4] *R. G. Pearson, H. Sobel,* and *J. Songstad,* J. Amer. Chem. Soc. *90,* 319 (1968).
[5] The cobalt(II) complexes of the type



R, R' = H, Alkyl, Aryl

were named cobaloximes by *Schrauzer* [3]. The relative nucleophilicity of the cobaloximes with Co^I (also referred to as cobaloximes$_s$) is strongly dependent on the type of substituents R and R', particularly on their inductive effect. Thus n_{CH_3I} for bis(glyoxaldioximato)cobalt(I) is 10.5 and for bis(butanedionedioximato)cobalt(I) 13.3 (both complexes have tri-*n*-butylphosphane as axial ligands).

Formation of Cyclopolyphosphazenes in an "Anomalous Kirsanov Reaction"

By *Christopher Glidewell*[*]

The Kirsanov reaction[1] between primary amines and dihalophosphoranes generally produces either imidophosphoranes ($m = 1$) or 1,3,2λ^5,4λ^5-diazadiphosphetidines ($m = 2$):

$$RNH_2 + X_2PR'_3 \rightarrow 2HX + \frac{1}{m}(RNPR'_3)_m \quad (1)$$

For X = R' = Cl, the reaction is generally carried out either by refluxing PCl_5 with the amine or its hydrochloride in an inert solvent, or by heating PCl_5 with the amine (if solid) or its hydrochloride in the absence of a solvent.

Thus when $R = C_6H_5CH_2$, treatment of PCl_5 with either benzylamine or benzylammonium chloride in refluxing carbon tetrachloride yields $(C_6H_5CH_2NPCl_3)_2$ *(1)*, identified by its mass spectrum and its NMR spectra [^{1}H-NMR (from TMS): $\delta = 7.18$ (C_6H_5), 4.58 (t, CH_2) ppm, ^3J (*HCNP*) = 30 Hz; ^{31}P-NMR (from 85% H_3PO_4): $\delta = +75.04$ ppm]. However, when $[C_6H_5CH_2NH_3]Cl$ and PCl_5 are heated *alone* at *ca.* 150 °C, no diazadiphosphetidine *(1)* is produced: instead the sole products are now benzyl chloride and the cyclopoly-λ^5-phosphazenes $(NPCl_2)_3$ *(2)* and $(NPCl_2)_4$ *(3)*, characterized by their mass[2] and NMR spectra [*(2)*: $\delta_P = -19.78$ (-19 ± 1[3]) ppm; *(3)*: $\delta_P = +3.04$ ($+4.6 \rightarrow +7.0$[3]) ppm:

[*] Dr. C. Glidewell
Chemistry Department, University of St. Andrews
St. Andrews KY 16 9ST (Great Britain)

$$[C_6H_5CH_2NH_3]Cl + PCl_5 \rightarrow 3HCl + C_6H_5CH_2Cl + \frac{1}{n}(NPCl_2)_n \quad (2)$$

$n = 3, 4$

The product *(1)* isolated after the "normal Kirsanov reaction" decomposes to the same products on heating under similar conditions:

$$(RNPCl_3)_m \rightarrow m\,RCl + \frac{m}{n}(NPCl_2)_n \quad (3)$$

e.g. (1): $R = C_6H_5CH_2$; $m = 2$; $n = 3, 4$

The results of heating other $(RNPCl_3)_m$ compounds under similar conditions are shown below:

R	m	Reaction *(3)*
CH_3	2	–
C_2H_5	2	+
C_3H_7	2	+
$(CH_3)_2CH$	1	+
C_4H_9	2	+
$CH_3(C_2H_5)CH$	1	+
$(CH_3)_3C$	1	+
$C_6H_5CH_2$	2	+
C_6H_{11}	1	–
p-$CH_3C_6H_4$	1	–
p-$O_2NC_6H_4$	1	–
p-$CH_3OC_6H_4$	1	–
$C_6H_5SO_2$	1	–
p-$CH_3C_6H_4SO_2$	1	–
Cl_3PNSO_2	1	–

No correlation exists between the formation of $(NPCl_2)_n$ and the value of m.

For the monomeric acyl compounds $RC(O)NPCl_3$, where $R = CH_3$ or C_6H_5, the pyrolysis takes a different course, yielding only the nitrile and phosphoryl chloride:

$$RC(O)NPCl_3 \rightarrow RCN + OPCl_3 \quad (4)$$

Procedure:

Compounds $(RNPCl_3)_m$ were prepared by refluxing equimolar mixtures of $[RNH_3]Cl$ and PCl_5 in CCl_4 until evolution of HCl had ceased. Reactions in the absence of a solvent were carried out under dry nitrogen. For pyrolyses, 1-g samples were heated in closed systems (initial pressure 1 atm N_2, 147 °C, 6 h). After cooling, any volatiles were removed and involatiles were recrystallized from CCl_4 or light petroleum.—All products were identified by mass spectrometry and NMR spectroscopy.

Received: July 24, 1975 [Z 304 IE]
German version: Angew. Chem. *87*, 875 (1975)

[1] *A. V. Kirsanov*, Zh. Obshch. Khim. *22*, 88 (1952).
[2] *C. E. Brion* and *N. L. Paddock*, J. Chem. Soc. *A 1968*, 388.
[3] *V. Mark*, *C. Dungan*, *M. Crutchfield*, and *J. R. Van Wazer*, Top. in Phosphorus Chem. *5*, 227 (1961).

ABSTRACTS

Reviews

Abstracts of selected progress reports and review articles

van der Waals molecules, considered by *G. E. Ewing*, are weakly bound complexes held together by intermolecular forces. Thus gaseous argon cooled to its boiling point contains a few per cent of Ar_2. Similarly, not only do we know $(N_2)_2$, $(O_2)_2$, $(H_2)_2$, *etc.*, but also "mixed" van der Waals molecules such as H_2—Ar and Cl—H—Ar. Moreover, the study of these species should disclose details of the intermolecular potential energy surface. [Structure and Properties of van der Waals Molecules. Acc. Chem. Res. *8*, 185—192 (1975); 49 references]

[Rd 804 IE—L]

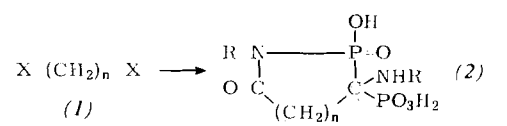
Protein mobility in membranes is the subject of a report by *R. J. Cherry*. Most experiments indicate a relatively free lateral mobility and rotation about an axis perpendicular to the plane of the membrane. The rates are independent of the inhibitors of the metabolism, but are influenced by temperature and interactions with other membrane components. It is hoped to describe these, as yet only qualitatively interpretable phenomena much better with more modern techniques. [Protein Mobility in Membranes. FEBS Lett. *55*, 1—7 (1975); 67 references]

[Rd 814 IE—R]

Patents

Abstracts of selected "Deutsche Offenlegungsschriften" (DOS), *i. e.* provisionally published specifications as filed with the German Patent Office

Cyclic aminophosphonic acids of formula *(2)* can be obtained by reaction of dicarboxylic acid derivatives *(1)* with phosphorus trihalides or phosphorous acid and phosphorus trihalides with subsequent hydrolysis of the reaction products. Owing to their ability to complex alkaline-earth-metal ions, the acids *(2)* and their salts are suitable for many industrial applications. They also show therapeutic effects in certain diseases asso-

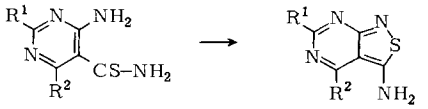


$n = 1$ to 4; X = CN, $CONH_2$, CONHalkyl (C_1—C_4); R = H or alkyl (C_1—C_4)

ciated with the deposition or dissolution of difficultly soluble calcium salts and could therefore be used as pharmaceutical active principles. [DOS 2343195; Henkel & Cie. GmbH, Düsseldorf (Germany)]

[PR 300 IE—D]

3-Aminoisothiazolo[3,4-*d*]pyrimidines *(2)* that can be used as diazo components are formed by oxidation of the thioamides

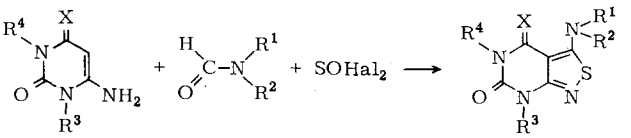


(1) *(2)*

R^1 = H, alkyl, cycloalkyl, aryl, aralkyl, disubstituted amino, or substituted mercapto group; R^2 = H or methyl

(1). [DOS 2354685; BASF AG, Ludwigshafen (Germany)] [PR 296—K IE]

3-Aminoisothiazolo[3,4-*d*]pyrimidines *(4)* are obtained from aminopyrimidine derivatives *(1)*, formamides *(2)*, and thionyl halides *(3)*. Compounds *(4)* have strong inhibitory action



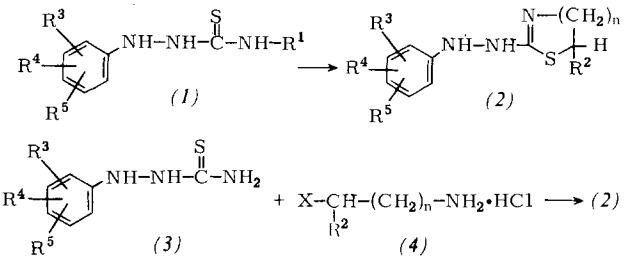
(1) *(2)* *(3)* *(4)*

R^1, R^2, R^3 = alkyl, aryl or aralkyl groups; R^4 = H or alkyl; X = O or NH; Hal = Cl or Br

against cAMP-phosphodiesterase and are suitable as anti-inflammatory agents and sedatives. [DOS 2453212; Takeda Chem. Ind., Osaka (Japan)]

[PR 297—K IE]

2-(Phenylhydrazino)thiazoline and -thiazine derivatives *(2)* are obtained either from the thiosemicarbazides *(1)* by ring closure or from the thiosemicarbazides *(3)* by reaction with



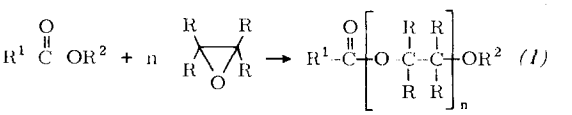
(1) *(2)* *(3)* *(4)*

R^1 = —$(CH_2)_n$—CHR^2—OH or —$(CH_2)_n$—CHR^2-halogen; R^2 = H or CH_3; R^3, R^4, R^5 = H, halogen, NO_2, CF_3, OH, alkyl, or alkoxyl; n = 1 or 2; X = halogen

halo amines *(4)*. Compounds *(2)* have hypnotic properties. [DOS 2457309; Egyt Gyogyszervegyeszeti Gyar, Budapest (Hungary)]

[PR 298—K IE]

Mono- or polyalkylene glycol ethers *(1)* with one *O*-acyl group are formed directly from alkylene oxides and alkyl esters of carboxylic acids in the presence of catalysts from the series



(1)

R^1 = H or (substituted) hydrocarbon residue (C_1—C_{20}); R^2 = (substituted) hydrocarbon residue (C_1—C_{20}); R = same or different (substituted) hydrocarbon residues (C_1—C_{10}) or H

of halides or organometallic compounds of zinc, aluminum, titanium, tin, or iron, if necessary with the addition of cocatalysts. [DOS 2454616; Nisso Petrochemical Industries Co., Ltd., Tokyo (Japan)]

[PR 299 IE—D]

BOOK REVIEWS

Topics in Carbon-13 NMR Spectroscopy. Vol. 1. Edited by *G. C. Levy*. John Wiley & Sons, Ltd., New York 1974. 1st Edit., x, 292 pp., numerous figures and tables, bound, £ 9.45.

With increasing volume of primary chemical literature good secondary literature becomes ever more important as a bridge for the "consumer". The development of carbon-13 NMR-spectroscopy, which has become so rapid owing to the development of the Fourier transformation technique since 1970, therefore justifies the foundation of a new series of "Topics in...". Eight competent authors have now treated aspects of ^{13}C-NMR spectroscopy that had previously been presented only briefly, and the book consequently is more like a monograph than a reference work. The choice of the themes is skilful and will appeal to a wide circle of readers. *R. Ditchfield* and *P. D. Ellis* report in detail on the state of theoretical calculations of chemical shifts (52 pp.), and *G. Maciel* provides a critical treatment of the philosophy of empirical interpretation of substituent effects (25 pp.). In reviews, complete in themselves, *J. R. Lyerla, Jr.* and *G. C. Levy* write on spin relaxation (70 pp., theory, experiment, and application), and *J. Schaefer* on the spectra of synthetic polymers (58 pp.), discussing in particular the dynamic experiments. The book is concluded by *F. A. L. Anet* with views on the uses and disadvantages of high field strengths (19 pp.) and by *J. B. Stothers* with a review (57 pp.) of ^{13}C-NMR studies of reaction mechanisms (labeling with ^2H and ^{13}C, dynamic effects) and reactive intermediates (carbocations, carbanions, CIDNP). The book contains approximately 500 references, mainly from the years 1971 to 1973 (1971: 80, 1972: 116, 1973: 95; 1974: 11), and a subject index. Later volumes, which will be welcomed after this successful and self-consistent beginning, should be supplemented by an author index.

Harald Günther [NB 287 IE]

Specialist Periodical Reports. Reaction Kinetics. Vol. 1. Senior Reporter: *P. G. Ashmore*. The Chemical Society, London, 1975. 1st Edit., xi, 396 pp., bound, £ 13.50.

In recent years the number of publications on kinetics and reaction mechanisms has ranged between 4000 and 5000 a year. With such a wealth of material the series on Reaction Kinetics introduced by the Chemical Society within the framework of its Specialist Periodical Reports provides a necessary and important aid for the specialist in this area in his task of keeping in mind the important developments over the whole field, and provides access for workers in neighboring fields to the most recent literature of interesting specialist subjects.

The first volume contains a review chapter entitled "Chemical Kinetics—Retrospect and Prospects" by *S. W. Benson*, and in seven further chapters a selection of reports on new

developments, mainly in the field of gas-phase reactions. According to *Benson*, gas-phase reactions were and are the most valuable area for understanding the molecular reaction step, and their investigation forms the "most advanced front in fundamental kinetic research". This concept seems to have determined the selection of contributions to the first volume of this series.

Chapters 2 to 5—"Reactions of Atoms in Ground and Electronically Excited States" *(R. J. Donovan* and *H. M. Gillespie)*, "Unimolecular Reactions" *(P. J. Robinson)*, "A Critical Survey of Rate Constants for Reactions in Gas-phase Hydrocarbon Oxidation" *(R. W. Walker)*, and "Kinetic Studies in Silicon Chemistry" *(I. M. T. Davidson)*—contain a critical selection of reaction data, the main emphasis being placed on the discussion of currently relevant methods for the determination of rate constants and activation data. This part of the book is largely oriented toward organic physical chemistry. In subsequent chapters 6 to 8—"Network Effects in the Dissociation and Recombination of a Diatomic Gas" *(H. O. Pritchard)*, "Recent Advances in the Analysis of Kinetic Data" *(A. Jones)*, and "Kinetics of Oscillating Reactions" *(B. F. Gray)*—there are collections of investigations on the treatment of elementary reactions.

Each chapter contains detailed references, usually from between the end of the sixties and the end of 1973, the total number being about 1200. For the older literature the reader is given references to reviews and monographs. All parts of the present first volume in the series provide a splendid up-to-date source of information. In subsequent volumes, which are scheduled to be published every 2 years, the specialist fields of kinetics in liquid and solid phases will be reported.

Josef Barthel [NB 285 IE]

Chemical and Biochemical Applications of Lasers. Vol. 1. Edited by *C. B. Moore*. Academic Press, New York—London 1974. 1st Edit., 398 pp., numerous figures, bound, £ 14.15.

This is the first volume of a new series offering a wide readership review articles on the uses of lasers in chemistry, biochemistry, and physical chemistry. The series is intended, as the editor writes in the preface, to encourage the application of lasers in new areas of these specialist fields.

The book begins with an article by *S. R. Leone* and *C. B. Moore* treating the physical basis of lasers and the most important nonlinear optical effects, together with a review of laser types and their properties. This gives the reader, including the nonspecialist, a clear idea of what sources of laser light are available as an experimental tool. Numerous and well chosen references make it possible to gain further details from the original publication.

The subsequent ten articles, all by thoroughly competent authors, treat applications of lasers to the spectroscopy and kinetics of simple molecules and biochemical systems. The articles are prefaced by readily intelligible introductions particularly useful to the nonspecialist. Each article ends with interesting glimpses into probable developments.

The book can be recommended to all interested readers who wish to obtain an insight into the manifold applications of lasers. Furthermore, the collections of data and references will be essential to all workers dealing with laser applications.

Reviews that treat the application of a special experimental tool very easily give the reader a one-sided picture of a specialist field. This danger will also become evident to the reader of some of the articles in the present book. Nevertheless, we can expect that it will be possible in subsequent volumes to maintain the generally high level of contributions to this first volume.

E. H. Fink [NB 288 IE]

Recent Books

The following books have been received by the editor. Detailed reviews will not be published in all cases because of the limited space available under this heading in the journal.

Annual Reports of the Progress of Chemistry, Vol. 71, 1974. Section B: Organic Chemistry. By *M. F. Ansell* and *P. G. Sammes*. The Chemical Society, London 1975. xviii, 594 pp., bound, £ 10.00.

The Organic Chemistry of Nickel. By *P. W. Jolly* and *G. Wilke*. Vol. II: Organic Synthesis. From the series "Organometallic Chemistry". Edited by *P. M. Maitlis, F. G. A. Stone*, and *R. West*. Academic Press, New York 1975. ix, 400 pp., bound, $ 48.00.

Chemical Infrared Fourier Transform Spectroscopy. By *P. R. Griffiths*. Vol. 43 of the series "Chemical Analysis". Edited by *P. J. Elving, J. D. Winefordner*, and *I. M. Kolthoff*. John Wiley & Sons, New York 1975. x, 340 pp., bound, £ 13.50.

Flame Retardancy of Polymeric Materials, Vol. 3. Edited by *W. C. Kuryla* and *A. J. Papa*. Marcel Dekker, Inc., New York 1975. ix, 364 pp., bound, $ 29.75.

The Alkaloids, Vol. 5. Senior Reporter: *J. E. Saxton*. The Chemical Society, London 1975. x, 303 pp., bound, £ 17.50.—A volume in the series "Specialist Periodical Reports".

Sulfur Dioxide Removal from Waste Gases. By *A. V. Slack* and *G. A. Hollinden*. Volume 21 of the series "Pollution Technology Reviews". Noyes Data Corporation, Park Ridge 1975. 2nd Edit., xii, 294 pp., bound, $ 36.00.

Annual Reports of the Progress of Chemistry, Vol. 71, 1974. Section A: Physical and Inorganic Chemistry. By *R. P. Bell* and *D. W. A. Sharpe*. The Chemical Society, London 1975. xv, 370 pp., bound, £ 9.00.

Saturated Heterocyclic Chemistry, Vol. 3. Senior Reporter: *M. F. Ansell*. The Chemical Society, London 1975. ix, 301 pp., bound, £ 13.00.—A volume in the series "Specialist Periodical Reports".

Quantitative Analysis by Gas Chromatography. By *J. Novák*. Vol. 5 of the series "Chromatographic Science Series". Marcel Dekker, Inc., New York 1975. ix, 218 pp., bound, $ 16.75.

Turbulence in Mixing Operations. Theory and Application to Mixing and Reaction. Edited by *R. S. Brodkey*. Academic Press, New York 1975. xi, 339 pp., bound, $ 19.50.

Handbook of Moisture Determination and Control. Principles, Techniques, Applications. Vol. 4. By *A. Pande*. Marcel Dekker, Inc., New York 1975. xiii, 1184 pp., bound, $ 33.50.

Reviews in Macromolecular Chemistry, Vol. 13. Edited by *G. B. Butler, K. F. O'Driscoll*, and *M. Shen*. Marcel Dekker, Inc., New York 1975. xiii, 355 pp., bound, $ 29.50.

Interfacial Phenomena in Metals and Alloys. By *L. E. Murr*. Addison-Wesley Publishing Company, Reading, Mass. 1975. xiv, 376 pp., bound, $ 24.50/paper, $ 14.50.

Excited States in Organic Chemistry. By *J. A. Barltrop* and *J. D. Coyle*. John Wiley & Sons, London 1975. xii, 376 pp., bound, £ 15.00.

The Chemistry of Amidines and Imidates. Edited by *S. Patai*. From the series "The Chemistry of Functional Groups". Edited by *S. Patai*. John Wiley & Sons, London 1975. xiii, 677 pp., bound, £ 22.00.

Annual Reports in Organic Synthesis—1974. Edited by *L. S. Hegedus* and *S. R. Wilson*. Academic Press, New York 1975. xiv, 397 pp., paper, $ 14.00.

Emulsion Polymerisation. Theory and Practice. By *D. C. Blackley*. Applied Science Publishers Ltd., London 1975. ix, 566 pp., bound, £ 16.00.

Surface and Defect Properties of Solids, Vol. 4. Senior Reporters: *M. W. Roberts* and *J. M. Thomas*. The Chemical Society, London 1975. ix, 255 pp., bound, £ 14.00.—A volume in the series "Specialist Periodical Reports".

Concepts of Inorganic Photochemistry. Edited by *A. W. Adamson* and *P. D. Fleischauer*. John Wiley & Sons, London 1975. xiii, 439 pp., bound, £ 13.30.

Lepton and Hadron Structure. Edited by *A. Zichichi*. Vol. 12 of the series "Subnuclear Series". Academic Press, New York 1975. x, 951 pp., bound, $ 49.00.

Advances in Liquid Crystals, Vol. 1. Edited by *G. H. Brown*. Academic Press, New York 1975. xi, 320 pp., bound, $ 31.50.

Guidebook to Stereochemistry. By *F. D. Gunstone*. Longman, London 1975. xii, 112 pp., paper, £ 2.95.

Advances in Quantum Electronics, Vol. 3. Edited by *D. W. Goodwin*. Academic Press, New York 1975. xii, 473 pp., bound, $ 46.00.

Laws of Hadronic Matter. Edited by *A. Zichichi*. Vol. 11 of the series "Subnuclear Series". Academic Press, New York 1975. 920 pp., bound, $ 49.00.

Patent Law of the United Kingdom. Texts, Commentary and Notes on Practice by The Chartered Institute of Patent Agents. (Revised Edition of The Patent Acts 1949—1961.) Sweet & Maxwell, London 1975. xii, 420 pp., bound, £ 15.00.

Organophosphorus Stereochemistry. Edited by *W. E. McEwen* and *K. D. Berlin*. From the series "Benchmark Papers in Organic Chemistry". Edited by *C. A. VanderWerf*. Halsted Press, a Division of John Wiley & Sons, London 1975. Part I: Origins and P(III and IV) Compounds. xviii, 387 pp., bound, £ 16.20. Part II: P(V) Compounds. xv, 319 pp., bound, £ 15.20.

NMR—Basic Principles and Progress/Grundlagen und Fortschritte. Edited by *P. Diehl*, *E. Fluck*, and *R. Kosfeld*. Vol. 9: Lyotropic Liquid Crystals. By *C. L. Khetrapal*, *A. C. Kunwar*, *A. S. Tracey*, and *P. Diehl*. Springer-Verlag, Berlin 1975. iv, 85 pp., bound, DM 38.—.

Organic Sulphur Chemistry. Structure, Mechanism and Synthesis. Edited by *C. J. M. Stirling*. Butterworths, London 1975. 495 pp., bound, £ 14.00.

Physical Chemistry. An Advanced Treatise. Edited by *H. Eyring*, *D. Henderson*, and *W. Jost*. Vol. VIB: Kinetics of Gas Reactions. Academic Press, New York 1975. xxii, 1030 pp., bound, $ 49.50.

Mass Spectrometry of Metal Compounds. Edited by *J. Charalambous*. Butterworths, London 1975. 297 pp., bound, £ 15.00.

Russian-English. Chemical and Polytechnical Dictionary. By *L. Ignatiev Callaham*. John Wiley & Sons, London 1975. xxviii, 852 pp., bound, £ 18.95.

Encyclopedia of the Alkaloids. By *J. S. Glasby*. Plenum Press, New York 1975. Vol. 1 (A—H): 734 pp.; Vol. 2 (I—Z): pp. 735—1423. Bound, together $ 103.00.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1975. – Printed in Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG Wissenschaft GmbH, Frankfurt/Main 1, Grosser Hirschgraben 17/21, from whom conditions of payment can be obtained on request.

Editorial office: Boschstrasse 12, D-6940 Weinheim, Germany, Telephone 14036, Telex 465516 vchwh d.

Editor: *H. Grünewald* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany
and Academic Press Inc. (President *Charles Hutt*), 111 Fifth Avenue, New York 3, N.Y., USA, and 24-28 Oval Road, London NW1, England.

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *H. Both*). D-6940 Weinheim, Pappelallee 3, P.O. Box 1260/1280 Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

AUTHOR INDEX

G.E. = Reference to Volume *87* (1975) of the German Edition of Angewandte Chemie. References are given for Review Articles, Short Communications, and Conference Reports only.

"G.E. –" indicates an Abstract or a Book Review.

ABDEL-RAHMAN, M. O. 486 [G.E. 487]
Abrahamson, E. W. 503
Adelman, R. C. 717
Ahrens, W. 550 [G.E. 589]
Albanbauer, J. 766, 767 [G.E. 816, 816]
Albini, A. 182 [G.E. 206]
Alzérreca, A. 172 [G.E. 194]
Amann, A. 755, 756 [G.E. 773, 775]
Ambühl, J. 369 [G.E. 380]
Anastassiou, A. G. 814 [G.E. 842]
Ansmann, A. 364 [G.E. 345]
Antonini, E. 72
Appel, R. 768, 769, 801 [G.E. 810, 810, 863]
Arbuzov, B. A. 71
Ashmore, P. G. 828
Augustin, G. 262 [G.E. 286]
Aumann, D. C. 117 [G.E. 77]
Aurich, H. G. 551 [G.E. 590]
Auwärter, M. 207 [G.E. 227]

BAARDMAN, F. 709 [G.E. 740]
Babsch, H. 753 [G.E. 772]
Bachhuber, H. 177 [G.E. 202]
Backes, J. 553 [G.E. 587]
Baier, H. 710 [G.E. 743]
Ballard, J. 577
Bardakos, V. 560 [G.E. 551]
Barrett, J. 74
Bartholmei, P. 64 [G.E. 39]
Bartholomé, E. 73, 268, 578
Bartmann, W. 337 [G.E. 143]
Bartoň, K. 771
Baumann, K. 440
Bayer, E. 493 [G.E. 484]
Bayer, H. 177, 178 [G.E. 202, 203]
Beck, F. 441
Becker, H.-D. 761 [G.E. 782]
Becker, H. J. 184 [G.E. 196]
Beckey, H. D. 403 [G.E. 425]
Bell, R. P. 440
Berger, S. 144 [G.E. 152]
Berger-Lohr, B. 818 [G.E. 845]
Bergmeyer, H. U. 268
Bernal, I. 353 [G.E. 379]
Berndt, A. 69, 70, 366, 550 [G.E. 72, 73, 285, 589]
Bersuker, I. B. 438
Berth, P. 94 [G.E. 115]
Bestmann, H. J. 53, 634 [G.E. 34, 630]
Betz, A. 374
Bidlingmaier, G. 822 [G.E. 877]
Bieber, L. 428 [G.E. 422]
Bieberbach, A. 562 [G.E. 550]
Biedermann, H.-G. 639 [G.E. 634]
Biekert, E. 73, 268, 578
Bieniek, D. 181 [G.E. 201]
Binger, P. 371, 706 [G.E. 383, 715]
bin Samsudin, M. W. 552 [G.E. 540]
Birnie, D. G. 577
Bitter, W. 56 [G.E. 34]
Black, D. St. C. 649
Blumer, M. 507 [G.E. 527]
Boche, G. 562 [G.E. 550]
Bock, H. 173 [G.E. 197]
Bock, R. 269
Boekelheide, V. 107 [G.E. 138]
Boldt, P. 64 [G.E. 39]
Bonačič-Koutecký, V. 575 [G.E. 599]
Born, L. 602 [G.E. 639]
Bornatsch, W. 420 [G.E. 412]
Boyd, R. N. 191
Bracher, G. 563 [G.E. 547]
Brandt, W. 643 [G.E. 671]
Brauer, D. J. 185 [G.E. 205]
Braun, H. 755, 756 [G.E. 773, 775]
Breitmaier, E. 144 [G.E. 152]
Breuninger, M. 347, 348 [G.E. 349, 350]
Brossmer, R. 715 [G.E. 747]
Brown, E. V. 717
Bruckmann, P. 575 [G.E. 599]
Brunner, H. 353 [G.E. 379]
Buch, V. 566 [G.E. 592]
Buckingham, J. 441
Buncel, E. 717
Burger, K. 766, 767 [G.E. 816, 816]
Bürgi, H.-B. 460 [G.E. 461]
Burnett, G. M. 579
Bürstinghaus, R. 57 [G.E. 37]

CALLOT, H. J. 567 [G.E. 545]
Cameron, J. D. 166 [G.E. 208]
Caulton, K. G. 503
Cava, N. P. 717
Chahin, R. 819 [G.E. 846]
Chappell, J. B. 503
Cherry, R. J. 827
Chevrier, B. 567 [G.E. 545]
Christensen, H. N. 374
Christl, M. 765 [G.E. 815]
Chukovskaya, E. C. 71
Cleland, W. W. 769
Cohen, M. D. 386 [G.E. 439]
Conia, J. M. 373, 473 [G.E. —, 505]
Connert, J. 427 [G.E. 421]
Cooper, W. Ch. 652
Cradock, S. 167 [G.E. 207]
Crass, G. 762 [G.E. 812]
Criegee, R. 745 [G.E. 765]
Crozier, R. F. 649

DANEN, W. C. 783 [G.E. 823]
Dannenberg, J. J. 641 [G.E. 632]
Daub, J. 487 [G.E. 489]
Dauben, W. G. 438
Davis, V. C. 649
Däweritz, A. 346 [G.E. 360]
de Meijere, A. 816 [G.E. 842]
Dempsey, B. 190
Dietrich, K. 358 [G.E. 384]
Dimroth, K. 111, 112, 112 [G.E. 135, 135, 136]
Dörhöfer, K. 422 [G.E. 416]
Dorlars, A. 665 [G.E. 693]
Dötz, K. H. 644 [G.E. 672]
Downie, I. M. 370 [G.E. 357]
Dreher, H. 416 [G.E. 447]
Dumont, W. 350, 700 [G.E. 347, 709]
du Mont, W.-W. 368 [G.E. 354]
Dürckheimer, W. 721 [G.E. 751]
Dürr, H. 646, 647 [G.E. 674, 674]
Dvorko, G. F. 431 [G.E. 453]
Dyllick-Brenzinger, R. 491 [G.E. 520]

EADY, C. R. 278 [G.E. 300]
Eberson, L. 440
Ebsworth, E. A. V. 167 [G.E. 207]
Eckert, H. 825 [G.E. 847]
Eckert, H.-G. 819 [G.E. 846]
Eckstein, F. 160 [G.E. 179]
Eder, U. 417 [G.E. 413]
Effenberger, F. 62 [G.E. 71]
Eggersdorfer, M. 766 [G.E. 816]
Eigenmann, K. 647 [G.E. 635]
ElGomati, T. 59 [G.E. 66]
Elschenbroich, Chr. 174 [G.E. 198]
Elter, G. 709 [G.E. 741]
Enders, D. 15 [G.E. 1]
Engelhardt, U. 554 [G.E. 541]
Erdmann, V. A. 113
Ertl, G. 504
Eschenfelder, V. 715 [G.E. 747]
Essenbreis, H. 427 [G.E. 421]
Esser, F. 579
Ewers, U. 354 [G.E. 356]
Ewing, G. E. 827

FAROOQ, S. 647 [G.E. 635]
Fehlhammer, W. P. 369, 757 [G.E. 290, 776]
Finlayson, B. J. 1 [G.E. 18]
Fischer, E. O. 345, 346, 760 [G.E. 359, 360, 781]
Fischer, P. 487 [G.E. 489]
Fischler, I. 54 [G.E. 35]
Fitjer, L. 360 [G.E. 381]
Flick, W. 363 [G.E. 355]
Flint, C. D. 113
Flitsch, W. 63 [G.E. 38]
Flohr, H. 822 [G.E. 877]
Florkin, M. 190, 719
Foag, W. 767 [G.E. 816]
Ford, P. C. 114
Form, M. 250 [G.E. 245]
Fouad, H. 817 [G.E. 876]
Franck, B. 423, 424, 818, 819 [G.E. 418, 419, 845, 846]
Frank, A. 572, 705, 760 [G.E. 597, 714, 781]
Franz, K.-D. 249 [G.E. 244]
Fraser-Reid, B. 769
Freidlina, R. Kh. 71
Freund, F. 568 [G.E. 593]
Fricke, H. 440
Fritz, H. 253 [G.E. 249]
Fritz, H.-G. 180 [G.E. 174]
Fuchs, J. 644 [G.E. 634]
Fuhr, H. 105 [G.E. 132]
Fuhrhop, J.-H. 361, 363, 435 [G.E. 387, 388, 456]
Full, R. 262 [G.E. 286]
Füllgrabe, H.-J. 359 [G.E. 382]

GAINSFORD, G. J. 495 [G.E. 523]
Gallenkamp, B. 348, 347 [G.E. 349, 350]
Galloy, J. 53 [G.E. 33]
Gärtner, B. 110 [G.E. 137]
Gaube, H. 812 [G.E. 843]
Gentsch, H. 568 [G.E. 593]
Gerhards, E. 65 [G.E. 70]
Gerhardt, W. 265 [G.E. 289]
Ghosez, L. 569 [G.E. 552]
Gilbert, A. 552 [G.E. 540]
Gillette, J. R. 577
Girgenti, S. J. 814 [G.E. 842]
Girodeau, J.-M. 764 [G.E. 813]
Glässel, W. 629 [G.E. 667]
Glemser, O. 186, 709 [G.E. 208, 741]
Glidewell, C. 826 [G.E. 875]
Golding, B. T. 495, 813 [G.E. 523, 841]
Gompper, R. 704 [G.E. 711]
Gornall, A. G. 577
Goto, T. 504
Gotthardt, H. 422 [G.E. 416]
Gräf, H.-D. 824 [G.E. 878]
Gray, R. 107 [G.E. 138]
Greenwood, N. N. 115
Greving, B. 713 [G.E. 745]
Grieco, P. A. 437
Griesbaum, K. 716 [G.E. 748]
Gros, F. 188
Grushka, E. 772
Grütze, J. 559 [G.E. 543]
Guilliard, W. 64 [G.E. 69]
Gundermann, K.-D. 560 [G.E. 546]
Günther, H. 354 [G.E. 356]
Gurke, K. 63 [G.E. 38]
Gusel'nikov, L. E. 373

HAFFER, G. 417 [G.E. 413]
Hagedorn, I. 486 [G.E. 486]
Hagemann, H. 698 [G.E. 707]
Hahn, K. 551 [G.E. 590]
Halbritter, K. 86 [G.E. 124]
Halstenberg, M. 768, 769 [G.E. 810, 810]
Hanack, M. 821 [G.E. 874]
Hanson, R. W. 577
Hara, O. 170 [G.E. 170]

Hartl, H. 554, 644 [G.E. 541, 634]
Hartmann, W. 698 [G.E. 708]
Hartter, P. 429 [G.E. 448]
Hasegawa, K. 636 [G.E. 668]
Hashimoto, H. 106 [G.E. 111]
Hasselmann, D. 257 [G.E. 252]
Hauptmann, H. 498 [G.E. 490]
Heaney, H. 370 [G.E. 357]
Heibl, C. 248 [G.E. 171]
Heine, H.-G. 698 [G.E. 708]
Heinrich, S. 710 [G.E. 743]
Hellmann, H. 73, 268, 578
Hemmerich, P. 110 [G.E. 137]
Henrici-Olivé, G. 104 [G.E. 110]
Herberhold, M. 351, 700 [G.E. 351, 710]
Herberich, G. E. 184 [G.E. 196]
Herlt, A. J. 495 [G.E. 523]
Herrmann, W. A. 353, 355 [G.E. 379, 358]
Hertenstein, U. 179 [G.E. 195]
Hesbain-Frisque, A. M. 569 [G.E. 552]
Hess, B. 72
Heuschmann, M. 486 [G.E. 487]
Heusel, G. 817 [G.E. 876]
Hiberty, P. 575 [G.E. 599]
Hildenbrand, K. 54 [G.E. 35]
Hillard III, R. L. 712 [G.E. 744]
Hingerty, B. 816 [G.E. 842]
Hintze, R. E. 114
Ho, T. L. 438
Hodges, D. R. 504
Hoefs, J. 75 [G.E. 104]
Hoffmann, R. W. 553 [G.E. 587]
Höfle, G. 58 [G.E. 64]
Hofmann, H. 812 [G.E. 843]
Hohler, W. 486 [G.E. 486]
Hohner, G. 497 [G.E. 522]
Holm, R. 602 [G.E. 639]
Holzinger, W. 760 [G.E. 781]
Honig, B. 503
Honymus, G. 261 [G.E. 291]
Hoornaert, C. 569 [G.E. 552]
Hopf, H. 501 [G.E. 492]
Hoppe, D. 424, 426 [G.E. 449, 450]
Hoppe, I. 765 [G.E. 814]
Horner, M. 556 [G.E. 548]
Hosmane, N. S. 167 [G.E. 207]
Höver, H. 115
Hubbell, W. L. 503
Hucho, F. 591 [G.E. 614]
Huisgen, R. 499 [G.E. 491]
Hummel, D. O. 267
Hünig, S. 179, 556 [G.E. 195, 548]
Hunkler, D. 347, 348 [G.E. 349, 350]
Hunnius, W.-D. 644 [G.E. 634]
Hutmacher, H.-M. 180 [G.E. 174]
Huttner, G. 352, 433, 434, 571, 572, 705, 760 [G.E. 353, 454, 455, 596, 597, 714, 781]

IPPEN, J. 566 [G.E. 592]
Isaacs, N. S. 652
Itahara, T. 356 [G.E. 386]
Itô, S. 504
Ivanov, D. 438

JAENICKE, L. 354 [G.E. 356]
Jaenicke, O. 278 [G.E. 300]
Jagendorf, A. T. 770
Jakobi, G. 94 [G.E. 115]
Jarre, W. 181 [G.E. 201]
Jeffrey, A. 190
Jenner, G. 137 [G.E. 186]
Jödden, K. 570 [G.E. 594]
Joesten, M. D. 651
Jonas, K. 752 [G.E. 809]
Jorgensen, W. L. 191
Jung, G. 429, 817 [G.E. 448, 876]
Jutz, Ch. 418 [G.E. 415]
Jutzi, P. 232 [G.E. 269]

KAGABU, S. 252 [G.E. 248]
Kaiser, C. 253 [G.E. 249]
Kaldor, G. 649
Kalinowski, H.-O. 762 [G.E. 812]
Karg, J. 64 [G.E. 69]
Karplus, M. 503
Karsch, H. H. 637 [G.E. 630]
Karstens, T. 176 [G.E. 200]
Kato, T. 188
Kauffmann, Th. 713, 714 [G.E. 745, 746]
Kaufmann, D. 816 [G.E. 842]
Kaupp, G. 491 [G.E. 520]
Kayama, Y. 418 [G.E. 414]
Kayane, Y. 170 [G.E. 170]
Keese, R. 528 [G.E. 568]
Keller, R. 632, 633 [G.E. 626, 627]
Kemp, G. 370 [G.E. 357]
Kemp, T. J. 813 [G.E. 841]
Kempe, U. W. 822 [G.E. 877]
Kerek, F. 109 [G.E. 133]
Keul, H. 716 [G.E. 748]
Kimura, A. 170 [G.E. 170]
Kindl, H. 772
King, J. F. 438
Kirch, M. 555 [G.E. 542]
Kisch, H. 182 [G.E. 206]
Kitahara, K. 815 [G.E. 839]
Kitahara, Y. 418 [G.E. 414]
Klabunde, K. J. 287 [G.E. 309]
Klehr, M. 247 [G.E. 173]
Klein, H.-F. 637 [G.E. 630]
Klein, W. 651
Kleine, W. 760 [G.E. 781]
Kleiner, D. 80 [G.E. 97]
Kleinschmidt, E. 571 [G.E. 595]
Kliger, D. S. 503
Klyne, W. 441
Knolle, J. 758 [G.E. 777]
Köbrich, G. 708 [G.E. 715]
Koerner von Gustorf, E. A. 54, 278 [G.E. 35, 300]
Köhler, W. 264 [G.E. 288]
Kohlschütter, H. W. 193 [G.E. 213]
Kondo, K. 103 [G.E. 109]
König, J. 713 [G.E. 745]
Köniğer-Ahlborn, E. 573, 574 [G.E. 598, 599]
Kopp, H.-P. 638 [G.E. 631]
Kopp, R. 821 [G.E. 874]
Kornblum, N. 734 [G.E. 797]
Korte, F. 181 [G.E. 201]
Koshland Jr., D. E. 187
Koutecký, J. 575 [G.E. 599]
Kouwenhoven, A. P. 709 [G.E. 740]
Krauch, C. H. 94 [G.E. 115]
Kraus, W. 824 [G.E. 878]
Krauss, D. 427 [G.E. 421]
Krebs, B. 261, 436 [G.E. 284, 451]
Krebs, T. 822 [G.E. 877]
Kreher, R. 264, 265, 821 [G.E. 288, 289, 840]
Kricheldorf, H. R. 502 [G.E. 517]
Kricka, L. J. 71
Krief, A. 350, 700 [G.E. 347, 709]
Krolikiewicz, K. 255, 421, 818 [G.E. 251, 417, 877]
Kroner, J. 178 [G.E. 203]
Krüger, C. 185, 262 [G.E. 205, 286]
Krumbholz, E. 553 [G.E. 588]
Kuball, H.-G. 176 [G.E. 200]
Kübel, B. 58 [G.E. 64]
Kühle, E. 698 [G.E. 707]
Külps, H.-J. 709 [G.E. 741]
Kummer, D. 699 [G.E. 742]
Kündig, E. P. 292 [G.E. 314]
Küppers, J. 504

L'ABBÉ, G. 775 [G.E. 831]
Lachmann, H. 429 [G.E. 448]
Lackner, H. 375 [G.E. 400]
Lakshmikantham, M. V. 718
Lane, C. F. 503
Langenberg, R. 819 [G.E. 846]
La Placa, S. J. 353 [G.E. 379]
Lauer, G. 172 [G.E. 194]
Laurent, H. 65 [G.E. 70]
Lechner, M. 765 [G.E. 815]
Ledwitch, A. 71
Leforestier, C. 575 [G.E. 599]
Lehn, J.-M. 555, 764 [G.E. 542, 813]
Leinberger, P. 762 [G.E. 811]
Lenoir, D. 59 [G.E. 66]
Le Perchec, P. 373
Levy, G. C. 828
Ley, H. 73, 268, 578
Ley, K. 770
Lichtenthaler, F. W. 815 [G.E. 839]
Liew, C. C. 577
Lindner, E. 256, 416 [G.E. 251, 447]
Linke, K.-H. 643 [G.E. 671]
Löbering, H.-G. 418 [G.E. 415]
Łopusiński, A. 108 [G.E. 134]
Lorenz, H. 572, 705 [G.E. 597, 714]
Lorenz, I.-P. 256 [G.E. 251]
Lückoff, M. 112 [G.E. 135]
Lucy, J. A. 72
Lukas, J. H. 709 [G.E. 740]
Lüke, H.-W. 427 [G.E. 420]
Lüttke, W. 52 [G.E. 63]
Lyle, L. R. 72

MACKAY, K. M. 167 [G.E. 207]
Mahjour, S. 644 [G.E. 634]
Mahnke, H. 314 [G.E. 337]
Maier, G. 172, 648 [G.E. 194, 675]
Manchester, K. L. 113
Märkl, G. 710 [G.E. 743]
Markley, J. L. 502
Marsili, M. 434 [G.E. 455]
Matsumoto, M. 94 [G.E. 109]
Matsuura, T. 356 [G.E. 386]
Mattes, R. 436 [G.E. 452]
Matusch, R. 260 [G.E. 283]
Mauser, H. 719
Mayer, H. 651
Mayr, A. 369, 757 [G.E. 290, 776]
Mayr, H. 499, 500 [G.E. 491, 491]
McGivan, J. D. 503
McGlinchey, M. J. 195 [G.E. 215]
McMeeking, J. 371 [G.E. 383]
McMurry, J. E. 266
Maier, Hans 374
Meier, Herbert 32, 103 [G.E. 52, 109]
Meller, A. 359 [G.E. 382]
Menger, E. L. 503
Mensch, S. 704 [G.E. 711]
Menzel, P. 62 [G.E. 71]
Mews, R. 186, 640 [G.E. 208, 669]
Meyer, R. 629 [G.E. 624]
Michalski, J. 108 [G.E. 134]
Min, B. K. 649
Minisci, F. 717
Mitschker, A. 713 [G.E. 745]
Miyazaki, H. 418 [G.E. 414]
Mödlhammer, U. 501 [G.E. 492]
Moore, C. B. 829
Mori, F. 103 [G.E. 109]
Morrison, R. T. 191
Moskovits, M. 292 [G.E. 314]
Moule, D. C. 503
Muke, B. 714 [G.E. 746]
Müller, A. 266, 573, 574 [G.E. —, 598, 599]
Müller, C. 172 [G.E. 194]
Müller, E. 653
Müller, H.-D. 571, 572, 705 [G.E. 596, 597, 714]
Müller, J. 760 [G.E. 781]
Müller, W. 357 [G.E. 385]
Murai, S. 636 [G.E. 668]
Murata, I. 170, 711 [G.E. 170, 742]
Musso, H. 180, 358 [G.E. 174, 384]

NAKANISHI, K. 504
Nakasuji, K. 170 [G.E. 170]
Nakazawa, T. 170, 711 [G.E. 170, 742]
Nametkin, N. S. 373
Natori, S. 504
Neef, G. 417 [G.E. 413]
Neidlein, R. 762 [G.E. 811]
Neugebauer, D. 352, [G.E. 353]
Neugebauer, F. A. 783 [G.E. 823]
Neumann, W. P. 246, 812 [G.E. 247, 844]
Neumüller, O.-A. 651
Niecke, E. 56, 261, 363 [G.E. 34, 284, 355]
Niedermayer, R. 212 [G.E. 233]
Niederprüm, H. 614 [G.E. 652]
Nielsen, F. H. 72
Nierhaus, K. H. 113
Nishinaga, A. 356 [G.E. 386]
Nishiwaki, T. 266
Nocchi, E. 813 [G.E. 841]
Nógrádi, M. 168 [G.E. 168]
Noll, W. 602 [G.E. 639]
Nozoe, S. 504
Nürnberg, H. W. 771

ODA, M. 418 [G.E. 414]
Oehlmann, L. 698 [G.E. 707]
Oei, H. A. 634 [G.E. 629]
Öfele, K. 639 [G.E. 634]

Offermanns, H. 330 [G.E. 372]
Ohara, M. 820 [G.E. 880]
Olgemöller, B. 369 [G.E. 290]
Olivé, S. 104 [G.E. 110]
Ollerich, D. A. 72
Ollis, W. D. 168, 169 [G.E. 168, 169]
O'Neill, P. 430 [G.E. 417]
Orfanides, N. 427 [G.E. 421]
Orlopp, A. 251 [G.E. 246]
Ostoja Starzewski, K.-H. A. 173 [G.E. 197]
Otter, R. 714 [G.E. 746]
Ottnad, M. 429 [G.E. 448]
Ovchinnikov, Yu. A. 113
Ozin, G. A. 292 [G.E. 314]

PALMER, G. A. 374
Panayotov, I. 438
Paquette, L. A. 496, 769 [G.E. 488, —]
Parikh, V. M. 191
Parker, C. W. 72
Parker, G. 185 [G.E. 205]
Parmantier, M. 53 [G.E. 33]
Parshall, G. W. 649
Pass, G. 771
Paulsen, H. 558 [G.E. 547]
Perrin, D. D. 190
Peter, W. 642 [G.E. 670]
Petersen, J. D. 114
Petz, W. 367 [G.E. 288]
Pimentel, G. C. 199 [G.E. 220]
Pitts, Jr., J. N. 1 [G.E. 18]
Pohl, H. H. 111 [G.E. 135]
Pohl, S. 261 [G.E. 284]
Pongs, O. 113
Ponomareva, E. A. 431 [G.E. 453]
Pook, K.-H. 702 [G.E. 712]
Pregosin, P. S. 369, 563 [G.E. 380, 547]
Preuss, R. 357 [G.E. 385]
Price, J. A. 169 [G.E. 169]
Prinzbach, H. 252, 253, 347, 348, 630, 632, 633, 753 [G.E. 248, 249, 349, 350, 625, 626, 627, 772]
Pryor, W. A. 439
Puppe, L. 620 [G.E. 659]
Pustoslemsek, P. 823 [G.E. 879]

QUAST, H. 428, 486 [G.E. 422, 487]
Quinkert, G. 851 [G.E. 790]

RADTKE, V. 819 [G.E. 846]
Rautenstrauch, V. 259 [G.E. 254]
Razavi, A. 351, 352 [G.E. 351, 353]
Regitz, M. 222 [G.E. 259]
Reichardt, C. 86 [G.E. 124]
Reichelt, W. 218 [G.E. 239]
Reimschuessel, H. K. 43 [G.E. 43]
Renth, E.-O. 361 [G.E. 379]
Reshef, L. 577
Rétey, J. 822 [G.E. 877]
Reuther, W. 256 [G.E. 251]
Richardson, J. P. 445 [G.E. 497]
Richter, K. 345 [G.E. 359]
Richter, W. 183 [G.E. 204]
Rickwood, D. 577
Ried, W. 823 [G.E. 879]
Rigo, P. 72
Ritter, G. 645 [G.E. 673]
Robson, M. J. 473 [G.E. 505]
Roesky, H. W. 258, 498 [G.E. 254, 521]
Röhr, A. 493 [G.E. 486]
Röllgen, F. W. 561 [G.E. 544]
Rösner, M. 708 [G.E. 715]
Roth, G. S. 577
Roth, W. R. 758 [G.E. 777]
Rowold, A. 423 [G.E. 418]
Ruge, B. 761 [G.E. 782]

SAENGER, W. 816 [G.E. 842]
Saier, H.-D. 457 [G.E. 476]
Salem, L. 191, 438, 575 [G.E. —, —, 599]
Sandmeier, D. 53, 634 [G.E. 34, 630]
Sargeson, A. M. 495 [G.E. 523]
Sauer, G. 417 [G.E. 413]
Sauer, W. 648 [G.E. 675]
Sauvage, J.-P. 764 [G.E. 813]
Schaad, L. J. 651
Schäfer, H. 570 [G.E. 594]
Schäfer, H. J. 247, 758 [G.E. 173, 777]
Schaffer, O. 112 [G.E. 136]
Schaumann, E. 493 [G.E. 486]
Scheikh-ol-Eslami, N. 568 [G.E. 593]
Schellhammer, C.-W. 665 [G.E. 693]
Scherberich, P. 330 [G.E. 372]
Scherer, O. J. 485, 629 [G.E. 485, 667]
Schildknecht, H. 427 [G.E. 421]
Schilling, P. 556 [G.E. 548]
Schiwy, W. 436 [G.E. 451]
Schlosser, M. 365 [G.E. 346]
Schlözer, R. 363 [G.E. 388]
Schlunegger, U. P. 679 [G.E. 731]
Schmadel, E. 94 [G.E. 115]
Schmetzer, J. 487 [G.E. 489]
Schmid, G. 53 [G.E. 34]
Schmid, G. 645 [G.E. 673]
Schmid, H.-G. 433, 434 [G.E. 454, 455]
Schmidbaur, H. 183, 438, 637 [G.E. 204, —, 630]
Schmidpeter, A. 489, 490 [G.E. 517, 519]
Schmidt, A. H. 823 [G.E. 879]
Schmidt, K. H. 266
Schmidt, M. 638 [G.E. 631]
Schmidt, R. R. 64, 581 [G.E. 69, 603]
Schmidt, U. 432, 523 [G.E. 454, 535]
Schmitz, H. 647 [G.E. 674]
Schneider, M. 707 [G.E. 717]
Scholl, F. 267
Schöllkopf, U. 629, 765 [G.E. 624, 814]
Schrader, B. 364 [G.E. 345]
Schrauzer, G. N. 514 [G.E. 579]
Schreiner, K. 366, 550 [G.E. 285, 589]
Schroeder, J. 665 [G.E. 693]
Schröer, U. 246 [G.E. 247]
Schuchardt, U. 706 [G.E. 715]
Schuckmann, W. 823 [G.E. 879]
Schuhbauer, N. 639 [G.E. 634]
Schulte, K.-W. 172 [G.E. 194]
Schulte-Frohlinde, D. 254, 430 [G.E. 250, 417]
Schulten, H.-R. 403, 561 [G.E. 425, 544]
Schultz, M.-L. 821 [G.E. 840]
Schumann, H. 368 [G.E. 354]
Schurig, V. 493 [G.E. 484]
Schuster, P. 115
Schwarz, A. 812 [G.E. 844]
Schweig, A. 172 [G.E. 194]
Schwesinger, R. 347, 348, 630, 632, 633 [G.E. 349, 350, 625, 626, 627]
Schwochow, F. 620 [G.E. 659]
Schwuger, M. J. 94 [G.E. 115]
Seebach, D. 15, 57, 634, 762 [G.E. 1, 37, 629, 812]
Sela, M. 266
Sellmann, D. 571, 753 [G.E. 595, 772]
Semmelhack, M. F. 718
Seng, F. 770
Seshadri, T. 699 [G.E. 742]
Seybold, G. 248, 703, 704 [G.E. 171, 710, 711]
Sheldrick, W. S. 435, 490 [G.E. 456, 519]
Sheline, R. K. 309, 314 [G.E. 332, 337]
Sherwood, J. N. 579
Shugar, D. 188
Siebert, W. 262 [G.E. 286]
Sieghold, H. 52 [G.E. 63]
Siemion, I. Z. 702 [G.E. 712]
Sieveking, S. 493 [G.E. 486]
Sigel, H. 394 [G.E. 391]
Simmons, E. L. 266
Simon, H. 106 [G.E. 111]
Skell, P. S. 195 [G.E. 215]
Slater, J. L. 309 [G.E. 332]
Sliwka, W. 539 [G.E. 556]
Slopianka, M. 560 [G.E. 551]
Snatzke, G. 109 [G.E. 133]
Sombroek, J. 564 [G.E. 591]
Sonoda, N. 636 [G.E. 668]
Šorm, F. 72
Spahić, B. 365 [G.E. 346]
Spirin, A. S. 113
Spohn, K.-H. 144 [G.E. 152]
Stauff, J. 105 [G.E. 132]
Stec, W. J. 108 [G.E. 134]
Steenken, S. 254, 430 [G.E. 250, 417]
Steglich, W. 58 [G.E. 64]
Steinfatt, M. 560 [G.E. 546]
Stenzel, W. 558 [G.E. 547]
Stephanatou, J. S. 169 [G.E. 169]
Steuber, F. W. 553, 553 [G.E. 587, 588]
Steudel, R. 655 [G.E. 683]
Stoddart, J. F. 168, 169 [G.E. 168, 169]
Stohler, F. 174 [G.E. 198]
Stork, K. 551 [G.E. 590]
Stork, W. 436 [G.E. 452]
Stotz, E. H. 190, 719
Strathmann, H. 457 [G.E. 476]
Stripp, B. 577
Sucrow, W. 560 [G.E. 551]
Süss, G. 700 [G.E. 710]
Sutcliffe, H. 771

TAJTELBAUM, J. 639 [G.E. 634]
Tan, E. M. 266
Tarassenko, P. V. 431 [G.E. 453]
Tarchini, C. 365 [G.E. 346]
Tattershall, B. W. 166 [G.E. 208]
Taube, R. 261 [G.E. 291]
Taylor, R. T. 496 [G.E. 488]
Thallmair, E. 753 [G.E. 772]
Tigler, D. 714 [G.E. 746]
Timms, P. L. 273 [G.E. 295]
tom Dieck, H. 173, 249, 250, 251 [G.E. 197, 244, 245, 246]
Tsay, Y.-H. 262 [G.E. 286]
Tschamber, Th. 567 [G.E. 545]
Tune, D. 185 [G.E. 205]
Turco, A. 72
Turner, J. J. 304 [G.E. 326]
Turro, N. J. 438

UGHETTO, G. 369 [G.E. 380]
Ugi, I. 59, 61, 823 [G.E. 66, 67, 847]
Ulm, K. 181 [G.E. 171]
Urban, R. 61 [G.E. 67]

VAHRENKAMP, H. 322 [G.E. 363]
Van Chau, L 365 [G.E. 346]
Van Ende, D. 700 [G.E. 709]
Van Meersche, M. 53 [G.E. 33]
Van Tamelen, E. E. 717
Vassilev, G. 438
Vazquez, D. 188
Vdovin, V. M. 373
Veith, M. 263 [G.E. 287]
Venanzi, L. M. 369, 563 [G.E. 380, 547]
Viehe, H. G. 53 [G.E. 33]
Vieweg, R. 579
Vogel, E. 420, 564, 566 [G.E. 412, 591, 592]
Vogt, G. 821 [G.E. 840]
Vögtle, F. 497, 559 [G.E. 522, 543]
Voigt, E. 103 [G.E. 109]
Vollhardt, K. P. C. 712 [G.E. 744]
Völz, H. G. 688 [G.E. 721]
von Schnering, H. G. 570 [G.E. 594]
von Seyerl, J. 434 [G.E. 455]
Vorbrüggen, H. 255, 421, 818 [G.E. 251, 417, 877]

WACHTER, M. 715 [G.E. 747]
Wagemann, W. 564 [G.E. 591]
Wallenfels, K. 187 [G.E. 139]
Walling, C. 577
Walsh, A. D. 503
Walter, W. 427, 493 [G.E. 420, 486]
Warshel, A. 503
Watanabe, K. 820 [G.E. 880]
Watson, W. P. 813 [G.E. 841]
Weber, H. 562 [G.E. 550]
Wegener, G. 758 [G.E. 777]
Wegner, Ch. 424 [G.E. 419]
Wehner, E. 498 [G.E. 521]
Weidenbruch, M. 642 [G.E. 670]
Weigand, W. 181 [G.E. 171]
Weigert, W. M. 330 [G.E. 372]
Weinmaier, J. H. 489, 490 [G.E. 517, 519]
Weinreb, S. M. 718
Weiss, A. 268
Weiss, B. 646 [G.E. 674]
Weiss, R. 567 [G.E. 545]
Weisshuhn, M. C. 422 [G.E. 416]
Weissmann, C. 187
Werner, H. 185 [G.E. 205]
Wiberg, N. 177, 178 [G.E. 202, 203]
Wiechert, R. 65, 417 [G.E. 70, 413]
Wieland, Th. 702 [G.E. 712]
Wieser, K. 69, 70 [G.E. 72, 73]
Wiezer, H. 258 [G.E. 254]
Williams, T. P. 503
Winter, W. 170 [G.E. 172]
Winterfeldt, E. 357 [G.E. 385]

Wissing, H. 440
Witte, H. 268
Witte, L. 361 [G.E. 387]
Wittmann, H. G. 113
Wöber, G. 772
Wolfbeis, O. 278 [G.E. 300]
Wolmershäuser, G. 485 [G.E. 485]
Woltermann, A. 713 [G.E. 745]
Wünsch, E. 653
Wurster, B. 72

YAMAMOTO, K. 170 [G.E. 170]

ZACHMANN, H. G. 651
Zak, H. 432 [G.E. 454]
Zambonelli, L. 369 [G.E. 380]
Zbiral, E. 188
Zeller, K.-P. 32 [G.E. 52]
Zhdanov, R. I. 649
Zhenodarova, S. M. 649
Zimmermann, I. 491 [G.E. 520]
Zingaro, R. A. 652
Zobova, N. N. 71

SUBJECT INDEX

FP = Full paper (review article) CR = Conference report
SC = Short communication LA = Literature abstract
PR = Patent abstract
G.E. = Reference to Volume *87* (1975) of the German Edition of Angewandte Chemie.
References are given for Review Articles, Short Communications, and Conference Reports only.

ABSOLUTE configuration, Determination of ~ of amines (SC) 109 [G.E. 133]
Structure and ~ of an optically active square pyramidal molybdenum complex (SC) 353 [G.E. 379]
Acetoacetate, Detection of the trans-enol in methyl ~ by ^{1}H- and ^{13}C-NMR spectroscopy (SC) 260 [G.E. 283]
Acetonedicarboxylic acid and its derivatives (PR) 73
Acetylenes, Cyclobutenylideneammonium salts from cycloadditions of keteniminium salts to ~ (SC) 569 [G.E. 552]
Transition metal catalyzed cyclizations of ~. General synthesis of indans and tetralins (SC) 712 [G.E. 744]
Acetylenecarboxylic esters, Stable pyrazolium betaines by addition of 1,1-dialkylhydrazine (SC) 560 [G.E. 551]
Acids, Principle of hard and soft ~ and bases (LA) 438
Säuren und Basen (Book Review) 440
Acrylonitriles, Additions to the C=O group of ketenes: β-substituted α-trimethylsiloxy-~ (SC) 179 [G.E. 195]
Actinoid, Spectral evidence for lanthanoid and ~ carbonyl compounds (FP) 309 [G.E. 332]
Actinoid carbonyl compounds, Spectral evidence for lanthanoid carbonyl compounds and ~ (FP) 309 [G.E. 332]
Actinomycins, Three-dimensional structure (FP) 375 [G.E. 400]
Acylation, σ-Complex intermediates in ~ and sulfonylation of 1,3,5-tripyrrolidinobenzene—preparation, reactions, and structure (SC) 62 [G.E. 71]
Aging, Covalent modifications of nuclear proteins (LA) 577
Alterations of skeletal muscle enzymes (LA) 649
Impaired hormonal regulation of enzyme activity (LA) 717
Air pollution, Mechanisms of photochemical ~ (FP) 1 [G.E. 18]
Aldehydes, Conversion of 1,2-diols into ~ induced by photolysis of alkylcobaloximes: a model system for dioldehydrase (SC) 813 [G.E. 841]
Aliphatic nucleophilic substitutions, Experimental evidence for a novel limiting mechanism (SC) 59 [G.E. 66]
Alkaloids, Synthesis of Cephalotaxus ~ (LA) 717
Alkenes, [2+2]-Cycloaddition with allenes (SC) 709 [G.E. 740]
Alkenylidenecyclopropanes, Isomerizations catalyzed by Lewis acids (SC) 360 [G.E. 381]
Alkoxides, Quaternary hydroxyalkylammonium ~ and phenoxides (PR) 577
N-Alkylidenethiocarboxamide, Detection of valence tautomerism between 2H-1,3-thiazete and ~ (SC) 767 [G.E. 816]
Alkynes, [3+2]-Cycloadditions of mesoionic 1,3-oxathiol-4-ones to ~. A new entry to the furan series (SC) 422 [g.E. 416]
Alkynolates, Lithium phenylethynolate and its reaction with carbonyl compounds to give β-lactones (SC) 765 [G.E. 814]
Allenes, 4H-1,2-Oxazete N-oxides from 1,1-di-tert-butyl-~ (SC) 69 [G.E. 72]
[2+2]-Cycloaddition to alkenes (SC) 709 [G.E. 740]
Amines, Umpolung of amine reactivity. Nucleophilic α-(secondary amino)-alkylation via metalated nitrosamines (FP) 15 [G.E. 1]
Determination of the absolute configuration (SC) 109 [G.E. 133]
Aromatic poly-~ in production of polyurethane plastics (PR) 73
Amino acids, Hetero Cope rearrangements in cyclization of allyl and propargyl esters of N-acyl ~ to oxazolin-5-ones (SC) 58 [G.E. 64]
Chain-extended and α-branched α-~ by alkylation of metalated α-[bis(alkylthio)-methyleneamino] acid esters (SC) 426 [G.E. 450]
p-Aminobenzoic acid, Industrial preparation (LA) 373
α-Amino carbanions, Metalated dialkyl N-alkyliminocarbonates: new masked α-thio carbanions and ~ (SC) 424 [G.E. 449]
Aminophosphonic acids, Cyclic ~ (PR) 827
2-Amino sugar oligosaccharides, Building units for oligosaccharides. Synthesis of α-glycosidically linked ~ (SC) 558 [G.E. 547]
Aminyl free radicals (FP) 783 [G.E. 823]
Ammonia, Conversion into ketimine ligands—a simple method for synthesis of ketimine complexes (SC) 753 [G.E. 772]
Ammonioamidates (PR) 770
Analytical chemistry, Methoden der Analytischen Chemie (Book Review) 269
Recent analytical developments in the petroleum industry (Book Review) 504
Analytical methods, Field desorption mass spectrometry (FP) 403 [G.E. 425]
Detection of fragment genesis in the mass spectrometer: DADI mass spectrometry as an aid in the structure analysis of organic compounds (FP) 679 [G.E. 731]
Annulene, Topomerization of the cis,cis,cis,-trans-[9]-~ anion (SC) 562 [G.E. 550]
syn-1,6:8,13-Bismethano[14]-~ (SC) 564 [G.E. 591]
Annulenone, 2-Hydroxy-4,10-methano[11]-~—a 10 π analog of α-tropolone (SC) 566 [G.E. 592]
Anodic oxidation of cyclopropane derivatives (SC) 247 [G.E. 173]
Anthracene, Photo-Diels-Alder reactions (SC) 491 [G.E. 520]
Anthranilide, Synthesis and conformational behavior of N,N′,N″-trimethyltri-~ (SC) 169 [G.E. 169]
Anthraquinone α-methyl ethers (PR) 650
Antiaromaticity, ESR proof of ~ of a cyclopropenyl radical (SC) 550 [G.E. 589]
Antibiotics, Tetracyclines: chemistry, biochemistry, and structure-activity relations (FP) 721 [G.E. 751]
Anti-inflammatory steroids, Synthesis of novel ~ (SC) 65 [G.E. 70]
Antimony compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
Addition of P—H, As—H, and Sb—H groups to an N=N double bond (SC) 643 [G.E. 671]
Antiviral agents, Progress in the field of ~ (LA) 188
Arsabenzene, 4-Hydroxy-~—an "arsaphenol" (SC) 710 [G.E. 743]
Arsaphenol, 4-Hydroxyarsabenzene—an "~" (SC) 710 [G.E. 743]
Arsenic compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
Addition of P—H, As—H, and Sb—H groups to an N=N double bond (SC) 643 [G.E. 671]
Arsinidene complexes, Stabilization of phenylarsanediyl, C_6H_5As, in $C_6H_5As[Cr(CO)_5]_2$ (SC) 433 [G.E. 454]
Structure and electronic spectrum of $C_6H_5As[Cr(CO)_5]_2$ 434 [G.E. 455]
Arsorane, Methoxytetramethyl-~, $(CH_3)_4AsOCH_3$ (SC) 183 [G.E. 204]
Asymmetric membranes, Preparation and applications (FP) 452 [G.E. 476]
Atoms, Die Struktur der Atome und Moleküle (Book Review) 74
Autoimmune diseases, Induced ~ (LA) 266
2-Azaazulenes, Synthesis of 2H-cyclohepta[c]-pyrrol-6-ones. Route to ~ (SC) 821 [G.E. 840]
1-Aza-2-cyclopentadienone salts, Stable solutions in thionyl chloride/antimony pentachloride (SC) 63 [G.E. 38]
1,2λ^5-Azaphosphiridine, 1,2-Cycloadditions of "phosphazenes" having unusual coordination number: λ^5-phosphirane and ~ (SC) 363 [G.E. 355]
Azides, Reactions of vinyl ~ (FP) 775 [G.E. 831]
Aziridines (PR) 73
Aziridinimines, diaziridinimines, diaziridinones, and carbodiimides by photolysis of 2-tetrazolines (SC) 428 [G.E. 422]
Azomethine oxides, 1,3-Dipolar cycloaddition of nitrones (LA) 649
Azuleno[1,2,3-cd]phenalene, Synthesis and properties (SC) 170 [G.E. 170]

BACTERIA, Systems of carbohydrate utilization in ~ (CR) 187 [G.E. 139]
Defence against phytocidal ~ (PR) 503
Bases, Principle of hard and soft acids and ~ (LA) 438
Säuren und Basen (Book Review) 440
Benzene, As dienophile in Diels-Alder reaction (SC) 181 [G.E. 201]
1—5-η-Benzothiadiborolenetricarbonyl-iron—a complex having a fixed π-electron system in the ~ ring (SC) 262 [G.E. 286]
Photoaddition of vinyl acetate (SC) 552 [G.E. 540]
Photochemical cycloaddition to vinylene carbonate (SC) 698 [G.E. 708]
Benzene derivatives, Preparation of ~ containing an isocyanatomethyl side chain (PR) 718
Benzene trisulfide, cis-Trithiatris-σ-homobenzene (cis-"~") (SC) 252 [G.E. 248]
Benzofuran, 2,3-Dihydro-7-methoxy-~ derivatives (PR) 188
Benzofuroxan, Syntheses with ~ (LA) 770
Benzoic acids, Halogenated o-benzoyl-~ (PR) 189
Benzopyrans (PR) 439
Benzothiazoles, 2-(Difluoromethylthio)-~ (PR) 504
1-Benzothiepin 1-oxides, The first ~ (SC) 812 [G.E. 843]
Benzoylbenzoic acids, Halogenated o-~ (PR) 189
Benzyl radicals, Conformation of sterically hindered ~ and cations: comparison of ESR findings and conclusions from space-filling models (SC) 366 [G.E. 285]
Bicyclo[1.1.0]butane, Intramolecular interaction of cyclopropylidene with the ~ system (SC) 765 [G.E. 815]
Bicyclo[3.2.0]hept-2-enes, Non-equilibrating diradicals: stereochemistry of the thermal reorganization of methyl-substituted ~ (SC) 257 [G.E. 252]
Bicyclo[2.2.2]octadienones, Photochemical rearrangement and fragmentation (SC) 761 [G.E. 782]
Bicyclooctanes, Simple synthesis of 1-halo-~ (SC) 824 [G.E. 878]
Biochemistry, Comprehensive ~ (Book Review) 719
Biochemie der Pflanzen (Book Review) 772
trans-Bishomobenzene, Facile conversion of 3-

norcarene into ~ (SC) 496 [G.E. 488]
syn-1,6:8,13-Bismethano[14]annulene (SC) 564 [G.E. 591]
Bismuth compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
Bonding, Properties of sulfur-sulfur bonds (FP) 655 [G.E. 683]
Borabenzene, New route to alkali-metal borinates and to complex derivatives of ~ (SC) 184 [G.E. 196]
Borazines, N-Halo-~ (SC) 709 [G.E. 741]
Borinates, New route to alkali-metal ~ and to complex derivatives of borabenzenes (SC) 184 [G.E. 196]
Boron compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
1,3,2,4-Diazaphosphaboretidines: a four-membered boron-nitrogen-phosphorus heterocycle (SC) 56 [G.E. 34]
1—5-η-Benzothiadiborolenetricarbonyl-iron—a complex having a fixed π-electron system in the benzene ring (SC) 262 [G.E. 286]
Pentacyclic derivative of cyclododecaborazane (SC) 359 [G.E. 382]
Brevicomin, Synthesis by Kolbe electrolysis (SC) 758 [G.E. 777]
Bridgehead olefins, Methods for preparation (FP) 528 [G.E. 568]
Buffers for pH and metal ion control (Book Review) 190
Butadiene, Enantiomerization of optically stable substituted ~-s (SC) 708 [G.E. 715]
Butadiene complex, Bis(1,3-butadiene)monocarbonylmanganese—a paramagnetic ~ (SC) 351 [G.E. 351]
Crystal and molecular structure of bis(1,3-butadiene)monocarbonylmanganese (SC) 352 [G.E. 353]
2-Butenylene diacetate (PR) 650
tert-Butoxycarbonyl group, Selective acidic cleavage (SC) 818 [G.E. 877]

CARBANIONS, Metalated dialkyl N-alkyliminocarbonates: new masked α-amino and α-thio ~ (SC) 424 [G.E. 449]
Chain-extended and α-branched α-amino acids by alkylation of metalated α-[bis(alkylthio)methyleneamino] acid esters (SC) 426 [G.E. 450]
Carbene complexes, Synthesis of bis(dimethylamino)carbenetetracarbonyliron (SC) 367 [G.E. 288]
Constitutional and configurational stability of a carbamoyl-tetracarbonyliron anion complex (SC) 487 [G.E. 489]
Carbenes, Chemistry of phosphoryl-~ (FP) 222 [G.E. 259]
3,5-Di-tert-butyl-4-oxo-2,5-cyclohexadien-1-ylidene by 1,5-elimination (SC) 64 [G.E. 39]
Insertion of a carbon atom into olefinic double bonds: synthesis of fluorodienes and fluoroalkenes (SC) 365 [G.E. 346]
Synthesis of the naphthol skeleton from pentacarbonyl[methoxy(phenyl)carbene]-chromium(0) and tolan (SC) 644 [G.E. 672]
Carbenium ion stabilization, Theoretical investigation of ~ by trifluoroacetic acid (SC) 641 [G.E. 632]
Carbodiimides, Aziridinimines, diaziridinimines, diaziridinones, and ~ by photolysis of 2-tetrazolines (SC) 428 [G.E. 422]
Carbohydrates, Systems of utilization in bacteria (CR) 187 [G.E. 139]
2,3-Unsaturated sugars and their derivatives (LA) 769
β-Carboline derivatives, Facile entry to 1,4-disubstituted ~. Total synthesis of N^a-methylbrevicollin (SC) 357 [G.E. 385]
Carbonyl compounds, Flipping of CO ligand groups in metal ~ and its frequency in $Fe(CO)_5$ (FP) 314 [G.E. 337]
Thermal cyclization of unsaturated ~ (LA) 373
Carboxylic acid, 1,2,3,4,5-pentanepenta-~ (PR) 718
Carbyne complexes, Cationic ~—tetracarbonyl-trans-(trimethylphosphane)(methylcarbyne)chromium(I) tetrahaloborates from tetracarbonyl-trans-(trimethylphosphane)-[methoxy(methyl)carbene]chromium(0) and boron trihalides (SC) 345 [G.E. 359]
Transfer of carbyne ligands from chromium to cobalt (SC) 346 [G.E. 360]
trans-Bromo(diethylaminocarbyne)tetracarbonylchromium (SC) 760 [G.E. 781]
Carriers, Selective transport of alkali metal cations through a liquid membrane by macrobicyclic ~ (SC) 555 [G.E. 542]
Catalysis, Soluble metal complexes of polymers for ~ (SC) 493 [G.E. 484]
Formation of O^- centers by homolytic decomposition of OH^- groups on magnesium oxide (SC) 568 [G.E. 593]
Homogeneous catalytic activation of C—H bonds (LA) 649
~ in strongly acidic media and the Wallach rearrangement (LA) 717
Catalyst for ring-opening polymerization of cyclopentene (PR) 114
Catalysts for preparation of polyurethane foams (PR) 188
Catalysts latent below 50°C (PR) 770
Cephalosporin derivatives (PR) 114
Cephalotaxus alkaloids, Synthesis (LA) 717
Ceramics, Painting of ancient ~ (FP) 602 [G.E. 639]
Chalcogen compounds, Vibrational spectra of transition metal ~ (LA) 266
Chemistry, Mehr Wissen über Chemie (Book Review) 440
Chemiluminescence of the exhaust gases of an internal combustion engine (SC) 105 [G.E. 132]
Chemotaxis as a model for sensory systems (LA) 187
Chlorination, Tertiary phosphane/tetrachloromethane, a versatile reagent for ~, dehydration, and P—N linkage (FP) 801 [G.E. 863]
Chlorine compounds, Synthesis of polychloro compounds with chlorinated functional groups (LA) 71
Chloromolybdate(VI)—a halomolybdate having tetrahedral coordination (SC) 574 [G.E. 599]
Chloroplast membranes and coupling factor conformations (LA) 770
Chroman and chromene compounds (PR) 718
Chromatography, Bonded stationary phases in ~ (Book Review) 772
Chromene and chroman compounds (PR) 718
Chromium complexes, [Bis(diphenylphosphino-η-benzene)chromium]tetracarbonyl-metal complexes of chromium, molybdenum, and tungsten (SC) 174 [G.E. 198]
Cationic carbyne-metal complexes—tetracarbonyl-trans-(trimethylphosphane)(methylcarbyne)chromium(I) tetrahaloborates from tetracarbonyl-trans-(trimethylphosphane)[methoxy(methyl)carbene]chromium(0) and boron trihalides (SC) 345 [G.E. 359]
Transfer of carbyne ligands from chromium to cobalt (SC) 346 [G.E. 360]
Tricarbonyl-(penta- and 2,4,6-tri-methylpyridine)chromium(0)—true pyridine π-complexes (SC) 639 [G.E. 634]
Synthesis of the naphthol skeleton from pentacarbonyl[methoxy(phenyl)carbene]-chromium(0) and tolan (SC) 644 [G.E. 672]
trans-Bromo(diethylaminocarbyne)tetracarbonylchromium (SC) 760 [G.E. 781]
Tetraisopropylchromium (SC) 760 [G.E. 781]
Circular dichroism, Determination of the absolute configuration of amines (SC) 109 [G.E. 133]
Clusters, Formation of Ad-layers and ~ on condensation of metal vapors on solid surfaces (FP) 212 [G.E. 233]
Cobaloximes, Nonenzymatic model reaction for the coenzyme B_{12}-catalyzed rearrangement of methylmalonyl-CoA into succinyl-CoA (SC) 822 [G.E. 877]
Conversion of 1,2-diols into aldehydes induced by photolysis of alkyl-~: a modul system for dioldehydrase (SC) 813 [G.E. 841]
Cobalt complexes, Transfer of carbyne ligands from chromium to cobalt (SC) 346 [G.E. 360]
Stereoselective hydrogen exchange at the methylene group of glycine in the ΛR-(N-benzylglycinato)bis(ethylenediamine)cobalt-(III) ion (SC) 495 [G.E. 523]
Phthalocyaninecobalt(I) salts, "supernucleophilic" vitamin B_{12} models stable in neutral medium (SC) 825 [G.E. 847]
Colorimetry, Optical properties of pigments—objective methods for testing and evaluation (FP) 688 [G.E. 721]
Combustion engine, Chemiluminescence of the exhaust gases of an internal ~ (SC) 105 [G.E. 132]
Complex cations, Reaction of transition metal carbonyl halides with $AgAsF_6$ in liquid SO_2: a key reaction for the preparation of novel ~ (SC) 640 [G.E. 669]
Complexes, Transition metal atoms in the synthesis of binuclear ~ (FP) 292 [G.E. 314]
Sulfur atoms as ligands in metal ~ (FP) 322 [G.E. 363]
Soluble metal ~ of polymers for catalysis (SC) 493 [G.E. 484]
Vibrational structure in electronic spectra of coordination compounds (LA) 113
New results of the photochemistry of ~ of the heavier transition metals (LA) 114
van der Waals molecules (LA) 827
Complexing agents, Chemical and biological functions of membrane-active (LA) 113
Configuration, Atlas of stereochemistry (Book Review) 440
Conformation, Conformational behavior of 6H,12H,18H-5,11,17-trithiatribenzo[a,e,i]-cyclododecene (SC) 168 [G.E. 168]
Synthesis and conformational behavior of N,N',N''-trimethyltrianthranilide (SC) 169 [G.E. 169]
Determination of ~ of conjugated dienes by means of vibrational frequencies (SC) 364 [G.E. 345]
Change in ~ of a cystine peptide on transition from the crystal to solution (SC) 429 [G.E. 448]
Twist and chair ~ of the diphenyl esters of, respectively, cis- and trans-dithiodihydrazidodimetaphosphoric acid (SC) 554 [G.E. 541]
Cope rearrangement, Hetero ~ in cyclization of allyl and propargyl esters of N-acyl amino acids to oxazolin-5-ones (SC) 58 [G.E. 64]
Low temperature thermal and photochemical formation of diallylic 1,3-diradicals. ~ of cis-1,2-divinylcyclopropane (SC) 707 [G.E. 717]
Copper complexes, Ternary Cu^{2+}-complexes: stability, structure, and reactivity (FP) 394 [G.E. 391]
Corrosion protection, Schutz gegen atmosphärische Korrosion (Book Review) 771
Corticosterone, Impaired hormonal regulation of enzyme activity during aging (LA) 717
Coupling factor conformations and chloroplast membranes (LA) 770
p-Cresols, Selective oxidation of the methyl group of ~ by base-catalyzed oxygenation (SC) 356 [G.E. 386]
Crystals, Ionenkristalle, Gitterdefekte und Nichtstöchiometrische Verbindungen (Book Review) 115
Crystal structure, Molecular structure and ~ of bis(1,3-butadiene)monocarbonylmanganese (SC) 352 [G.E. 353]
Structure and absolute configuration of an optically active square pyramidal molybdenum complex (SC) 353 [G.E. 379]
Cumulenes, Synthesis of a stable alkylideneketenimine and an alkylidenethioketene (SC) 53 [G.E. 34]
Cumulogy, Synthesis of a stable substituted thiacumulene: the concept of ~ (SC) 53 [G.E. 33]
Cyanide complexes, Mixed cyanide phosphane complexes of transition metals (LA) 72
Cyanotrihydridoborate, Uses (LA) 503
Cyclization, Thermal ~ of unsaturated carbonyl compounds (LA) 373
Cycloaddition, [2+2]-~ of allenes to alkenes

(SC) 709 [G.E. 740]
Thermal ~ between 3,6-diphenyl-s-tetrazine and 9-oxabicyclo[6.1.0]nona-2,4,6-triene; construction of the oxonino[4,5-d]pyridazine frame (SC) 814 [G.E. 842]
Unusual ~ of tetracyanoethylene to dispiro-[2.0.2.4]deca-7,9-diene (SC) 816 [G.E. 842]
~ of aliphatic and aromatic acyl isocyanates (LA) 71
1,3-Dipolar ~ of nitrones (LA) 649
2-Cycloalkene-1,4-diols, Synthesis of bicyclic γ-lactones from ~ (SC) 103 [G.E. 109]
Cyclobutadiene, Novel ~-rhodium(I) complex (SC) 170 [G.E. 172]
Photoelectron spectrum and structure of tri-tert-butyl-~ (SC) 172 [G.E. 194]
Unusual chemical behavior of tri-tert-butyl-~ (SC) 648 [G.E. 675]
New stable ~-s (SC) 704 [G.E. 711]
Cyclobutanes, Ring contractions and expansions of vicinally disubstituted ~ and cyclopropylmethyl compounds (FP) 473 [G.E. 505]
Synthesis from olefins (LA) 71
Cyclobutene, Nucleophilic attack on the 3-phenyl-4-sulfidocyclobutenediylium-1,2-diolate anion (SC) 823 [G.E. 879]
Cyclobutenones, New synthesis (SC) 499 [G.E. 491]
Vinylketenes from ~ by electrocyclic ring opening (SC) 500 [G.E. 491]
Cyclobutenylideneammonium salts from cycloadditions of keteniminium salts to acetylenes (SC) 569 [G.E. 552]
β-Cyclodextrin, Selective photochemical Fries rearrangement of phenyl acetate in the presence of ~ (SC) 820 [G.E. 880]
Cyclododecaborazane, Pentacyclic derivative (SC) 359 [G.E. 382]
2H-Cyclohepta[c]pyrrol-6-ones, Synthesis. Route to 2-azaazulenes (SC) 821 [G.E. 840]
2,5-Cyclohexadien-1-ylidene, 3,5-Di-tert-butyl-4-oxo-~ by 1,5-elimination (SC) 64 [G.E. 39]
2,5,7-Cyclooctatriene-1,4-dione (SC) 418 [G.E. 414]
Cyclopentene, Catalyst for ring-opening polymerization of ~ (PR) 114
Cyclophanes, [2.2.2.2](1,2,4,5)Cyclophane (SC) 107 [G.E. 138]
Cyclophosphazenes, Formation in an "anomalous Kirsanov reaction" (SC) 826 [G.E. 875]
Cyclopolyaromatics, Synthesis of heterocyclic ~ containing similar kinds of nuclei (SC) 713 [G.E. 745]
Synthesis of heterocyclic ~ containing different kinds of nuclei (SC) 714 [G.E. 746]
Cyclopropane, Anodic oxidation of derivatives (SC) 247 [G.E. 173]
Isomerizations of alkenylidene-~-s catalyzed by Lewis acids (SC) 360 [G.E.381]
Low temperature thermal and photochemical formation of diallylic 1,3-diradicals. Cope rearrangement of cis-1,2-divinyl-~ (SC) 707 [G.E. 717]
Cyclopropenyl radical, ESR proof of the antiaromaticity (SC) 550 [G.E. 589]
Cyclopropylidene, Intramolecular interaction with the bicyclo[1.1.0]butane system (SC) 765 [G.E. 815]
Cyclopropylmethyl compounds, Ring contractions and expansions of vicinally disubstituted cyclobutanes and ~ (FP) 573 [G.E. 505]
Cysteine peptides, 2-Nitro-1-phenylethyl: a new protecting and chiroptical reporter group for ~ (SC) 817 [G.E. 876]
Cystine peptide, Change in conformation of a ~ on transition from the crystal to solution (SC) 429 [G.E. 448]

DECAMOLYBDATE, Anion structure of ammonium ~ $(NH_4)_8Mo_{10}O_{34}$ (SC) 644 [G.E. 634]
Decarbonylation, Synthesis and thermal ~ of 2,3-furandiones (SC) 636 [G.E. 668]
Dehydration, Tertiary phosphane/tetrachloromethane, a versatile reagent for chlorination, ~, and P—N linkage (FP) 801 [G.E. 863]
Dehydrohalogenation, Reductive ~ of β-halogenated fatty acids and stereoselective hydrogenation of α-halogenated α,β-unsaturated fatty acids by Clostridium kluyveri (SC) 106 [G.E. 111]
Density gradient, Metrizamide, a new ~ medium (LA) 577
2-Deoxystreptamine, Simple and productive total syntheses of ~ and (±)-hyosamine (SC) 632 [G.E. 626]
Desulfurization of flue gases, Selenium-catalyzed formation of sulfate and sulfur from sulfite (SC) 638 [G.E. 631]
Detergents, Replacement of phosphates in ~—possibilities and limits (FP) 94 [G.E. 115]
Dialkyl carbonates (PR) 770
cis-Diazabis-σ-homobenzene. Synthesis and $2\sigma \rightarrow 2\pi$ isomerization to 1,4-diaza-2,5,7-cyclooctatriene derivatives (SC) 348 [G.E. 350]
1,4-Diazabutadiene, Reductive fixation of cis- and trans-~ (SC) 249 [G.E. 244]
Unsymmetrical coordination of a symmetrical ~ to iron(0) (SC) 251 [G.E. 246]
1,4-Diaza-2,5,7-cyclooctatriene, cis-Diazabis-σ-homobenzene. Synthesis and $2\sigma \rightarrow 2\pi$ isomerization to ~ derivatives (SC) 348 [G.E. 350]
Diazadiphosphetidines by reaction of amino-iminophosphanes with iminophosphoranes (SC) 768 [G.E. 810]
1,3,2,4-Diazaphosphaboretidines: a four-membered boron-nitrogen-phosphorus heterocycle (SC) 56 [G.E. 34]
Diazaphosphiridine 3-oxide, 1,2,3-Tri-tert-butyl-~ (SC) 486 [G.E. 487]
Diaziridinimines, Aziridinimines, ~, diaziridinones, and carbodiimides by photolysis of 2-tetrazolines (SC) 428 [G.E. 422]
Diaziridinones, Aziridinimines, diaziridinimines, ~, and carbodiimides by photolysis of 2-tetrazolines (SC) 428 [G.E. 422]
Diazirines as photochromic valence isomers of α-diazo carbonyl compounds (SC) 103 [G.E. 109]
α-Diazo carbonyl compounds, Wolff rearrangement (FP) 32 [G.E. 52]
Diazirines as photochromic valence isomers of ~ (SC) 103 [G.E. 109]
Diazomethane, Metal-stabilized C-protonated ~: a methanediazonium complex (SC) 355 [G.E. 358]
5H-Dibenz[c,e]azepine, Synthesis by elimination of methanesulfinic acid (SC) 265 [G.E. 289]
Dictionary, Römpps Chemie-Lexikon (Book Review) 651
Dicyclopropylidenemethane, Simple synthesis (SC) 821 [G.E. 874]
4,5-Didehydrotropone, Formation and trapping (SC) 711 [G.E. 742]
Diels-Alder reaction, Benzene as dienophile in ~ (SC) 181 [G.E. 201]
Photo-~ of anthracene (SC) 491 [G.E. 520]
Dienes, Determination of conformation of conjugated ~ by means of vibrational frequencies (SC) 364 [G.E. 345]
Dienophile, Benzene as ~ in Diels-Alder reaction (SC) 181 [G.E. 201]
L-3-(3,4-Dihydroxyphenyl)alanine, Facile synthesis of ~ (L-Dopa) and related compounds (SC) 361 [G.E. 379]
Diimine, $(C_5H_8N_2)Fe(CO)_9$—an iron cluster containing a cis-~ unit (SC) 182 [G.E. 206]
Diketene, Novel reactions (LA) 188
1,4-Dilithiobutane and vinyllithium from ethylene and lithium (SC) 259 [G.E. 254]
Dimethoxybenzene, Formation of radical cations from 1,2- and 1,4-~ by electron transfer to Tl^{2+} and Ag^{2+} in aqueous solution. A pulse radiolysis and in situ radiolysis EPR study (SC) 430 [G.E. 418]
α,α-Dioxa-β-thiatris-σ-homobenzene, Chemistry of cis-trioxatris-σ-homobenzene, ~, and β-oxa-α,α-dithiatris-σ-homobenzene (SC) 253 [G.E. 249]
Dioldehydrase, Conversion of 1,2-diols into aldehydes induced by photolysis of alkylcobaloximes: a model system for ~ (SC) 813. [G.E. 841]
Dipole, X-ray structure analysis of a stable ~ (SC) 493 [G.E. 486]
Diradicals, Non-equilibrating ~: stereochemistry of the thermal reorganization of methyl-substituted 6-methylenebicyclo[3.2.0]hept-2-enes (SC) 257 [G.E. 252]
Low temperature thermal and photochemical formation of diallylic 1,3-~. Cope rearrangement of cis-1,2-divinylcyclopropane (SC) 707 [G.E. 717]
Disulfur monoxide as complex ligand (SC) 645 [G.E. 673]
Dithiadiazole, 5-Oxo-1,3λ⁴,2,4-~—a five-membered heterocyclic ketone (SC) 498 [G.E. 521]
Dithiodihydrazidodimetaphosphoric acid, Twist and chair conformation of the diphenyl esters of, respectively, cis- and trans-~ (SC) 554 [G.E. 541]
Divinylallene, Synthesis of 1,3,4,6-heptatetraene (~) (SC) 501 [G.E. 492]
L-Dopa, Facile synthesis of ~ and related compounds (SC) 361 [G.E. 379]
Drugs, Perinatal enzyme capacity for degradation of ~ and other xenobiotics (LA) 577

ELECTROANALYTICAL chemistry (Book Review) 771
Electrochemistry, Anodic oxidation of cyclopropane derivatives (SC) 247 [G.E. 173]
Electrochemical entry to 9,10-homonaphthodiquinone (SC) 420 [G.E. 412]
Mechanism of electrochemical pinacolization. First asymmetric synthesis in a chiral medium (SC) 634 [G.E. 629]
Electron transfer, Formation of radical cations from 1,2- and 1,4-dimethoxybenzene by to Tl^{2+} and Ag^{2+} in aqueous solution. A pulse radiolysis and in situ radiolysis EPR study (SC) 430 [G.E. 418]
Electroorganic chemistry, Elektroorganische Chemie (Book Review) 441
Emodin, Biomimetic synthesis of skyrin (SC) 819 [G.E. 846]
Enantiomerization of optically stable substituted butadienes (SC) 708 [G.E. 715]
Energy, Stereochemistry of reaction paths as determined from crystal structure data—a relationship between structure and ~ (FP) 460 [G.E. 461]
Transfer and storage of ~ by molecules (Book Review) 579
Enol, Detection of the trans-~ in methyl acetoacetate by ^1H- and ^{13}C-NMR spectroscopy (SC) 260 [G.E. 283]
Enones, Michael addition of metalated thioacetals to cyclic ~ (SC) 57 [G.E. 37]
Enzymatic analysis, Methods of ~ (Book Review) 268
Enzyme mechanisms, Investigation of ~ with nucleoside phosphorothioates (FP) 160 [G.E. 179]
Enzymes, Pyruvate dehydrogenase multienzyme complex (FP) 591 [G.E. 614]
Specificity of ~ of D-glucose metabolism toward anomers (LA) 72
Perinatal enzyme capacity for degradation of drugs and other xenobiotics (LA) 577
Alterations of skeletal muscle ~ during aging (LA) 649
Rate-determining step of enzyme-catalyzed reactions (LA) 769
Enzyme—Gewinnung—Analyse—Regulation (Book Review) 374
Epoxide resins, 3-Amino-4-(aminomethyl)pyrrolidines as hardening agents for ~ (PR) 578
Epoxides, New synthetic route to di- and trisubstituted ~ (SC) 350 [G.E. 347]
New route to ~ (SC) 700 [G.E. 709]
ESR spectroscopy, Conformation of sterically hindered benzyl radicals and cations: comparison of ESR findings and conclusions from space-filling models (SC) 366 [G.E. 285]
Ester shift, Substituent effect on a [1,5] sigmatropic ~ (SC) 553 [G.E. 587]
Ethanedithioamides, C—N twisted ~ in electron-rich complexes (SC) 250 [G.E. 245]
Etherification, Alkylation of Tl^I alkoxides. A useful modification of Williamson ~ (SC) 762 [G.E. 812]
Ethers, Preparation of aryl-alkyl ~ and thio-~

(SC) 370 [G.E. 357]
Ethylene, Insertion into a platinum(II)-hydrido-complex containing a bidentate ligand spanning trans-positions (SC) 563 [G.E. 547]
Preparation of ~-propylene-diene terpolymers (PR) 650
Radical and ionic polymerization (PR) 650
Evolution, Comprehensive biochemistry (Book Review) 190
Eutrophication, Replacement of phosphates in detergents—possibilities and limits (FP) 94 [G.E. 115]
Exhaust gases, Chemiluminescence of ~ of an internal combustion engine (SC) 105 [G.E. 132]

FATTY acids, Reductive dehydrohalogenation of β-halogenated ~ and stereoselective hydrogenation of α-halogenated α,β-unsaturated ~ by Clostridium kluyveri (SC) 106 [G.E. 111]
Fenton's reagent (LA) 577
Field desorption mass spectrometry (FP) 403 [G.E. 425]
Applications to inorganic chemistry: salts (SC) 561 [G.E. 544]
Flame-protection agents, 1,2-Oxaphospholane-5-phosphonic esters suitable as ~ (PR) 770
Flame-resistance (PR) 650
Flavin adenine dinucleotide, Inhibition of monoamine oxidase by propargylamine: structure of the inhibitor complex (SC) 110 [G.E. 137]
Fluorescent dyestuffs, Heterocycles as structural units in new optical brighteners (FP) 665 [G.E. 693]
Fluorine compounds, Fluorination of cyanogen chloride and N-chlorodichloromethyleneamine (SC) 166 [G.E. 208]
Fluoroalkenes, Insertion of a carbon atom into olefinic double bonds: synthesis of fluorodienes and (SC) 365 [G.E. 346]
Fluorocarbons, Reactions with metal atoms (FP) 287 [G.E. 309]
Fluorocyclotriphosphazenes, Substituted ~ (PR) 718
Fluorodienes, Insertion of a carbon atom into olefinic double bonds: synthesis of ~ and fluoroalkenes (SC) 365 [G.E. 346]
Foams, Preparation from aqueous silicate solution (PR) 189
Formaldehyde, UV spectra and excited states (LA) 503
Four component condensation, Asymmetrically induced ~ with extremely high stereoselectivity and multiplication of stereoselectivity (SC) 61 [G.E. 67]
Fragmentation, Detection of fragment genesis in the mass spectrometer: DADI mass spectrometry as an aid in the structure analysis of organic compounds (FP) 679 [G.E. 731]
Free radicals, Aminyl ~ (FP) 783 [G.E. 823]
Fries rearrangement, Selective photochemical ~ of phenyl acetate in the presence of β-cyclodextrin (SC) 820 [G.E. 880]
Furan, [3 + 2]-Cycloadditions of mesoionic 1,3-oxathiol-4-ones to alkynes. A new entry to the ~ series (SC) 422 [G.E. 416]
2,3-Furandiones, Synthesis and thermal decarbonylation of ~ (SC) 636 [G.E. 668]

GENE expression, Control at the transcription level (LA) 188
Geochemistry, ~ of stable isotopes (FP) 75 [G.E. 104]
Organic compounds in nature: limits of our knowledge (FP) 507 [G.E. 527]
Germanium compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
Chloro(di-tert-butylphosphino)germanediyl and -stannanediyl: stable germanium(II) and tin(II) organophosphorus compounds (SC) 368 [G.E. 354]
Germylmercury, Disilylmercury and di-~ (SC) 167 [G.E. 207]
Glucocorticoids, Age-related changes in binding of ~ by rat splenic leukocytes (LA) 577
Glucose, Ribose-~ exchange in purine nucleosides (SC) 815 [G.E. 839]
Specificity of enzymes of D-~ metabolism toward anomers (LA) 72
Glutamate dehydrogenase, Function in rat liver (LA) 503
Glutardialdehyde (PR) 114
Glycine, Stereoselective hydrogen exchange at the methylene group of ~ in the AR-(N-benzylglycinato)bis(ethylenediamine)cobalt-(III) ion (SC) 495 [G.E. 523]
Synthesis of tert-alkyl-substituted ~-s (SC) 629 [G.E. 624]
Glycol ethers, Mono- or polyalkylene ~ (PR) 828
1,2-Glycols, Phosphorous esters (PR) 114
Glycosides, Preparation with polymeric acid-binding reagents (SC) 715 [G.E. 747]

1-HALOBICYCLOOCTANES, Simple synthesis (SC) 824 [G.E. 878]
N-Haloborazines (SC) 709 [G.E. 741]
Halomalondialdehydes, Preparation, structure, and reactions (FP) 86 [G.E. 124]
Hardening agents, 3-Amino-4-(aminomethyl)-pyrrolidines as ~ for epoxide resins (PR) 578
Hazards in using perchloric acid (SC) 647 [G.E. 635]
Helicenes, Novel simple synthesis (SC) 418 [G.E. 415]
Hemoglobin, Recent results of ~ research (LA) 72
1,3,4,6-Heptatetraene, Synthesis of ~ (divinylallene) (SC) 501 [G.E. 492]
Herbicides, New group of ~ (PR) 771
Heterocycles, Heterocyclic systems having eight π-electrons. Synthesis, properties, and significance (FP) 581 [G.E. 603]
As structural units in new optical brighteners (FP) 665 [G.E. 693]
Synthesis of heterocyclic cyclopolyaromatics containing similar kinds of nuclei (SC) 713 [G.E. 745]
Synthesis of heterocyclic cyclopolyaromatics containing different kinds of nuclei (SC) 714 [G.E. 746]
Cyclophosphazene formation in an "anomalous Kirsanov reaction" (SC) 826 [G.E. 875]
Synthesis with organophosphorus compounds (LA) 188
Synthesis by ring transformation reactions of isooxazoles (LA) 266
Hexamethyl-trans-σ-tris-homobenzene, Valence isomerization (SC) 371 [G.E. 383]
Hexenes, Dimerization of propylene to linear ~ (SC) 104 [G.E. 110]
High pressure kinetics in organic and macromolecular chemistry (FP) 137 [G.E. 186]
Histidine, Observation of residues in proteins by NMR spectroscopy (LA) 502
Homobenzene, Chemistry of cis-trioxatris-σ-~. A simple total synthesis of streptamine (SC) 630 [G.E. 625]
Simple and productive total syntheses of 2-deoxystreptamine and (±)-hyosamine (SC) 632 [G.E. 626]
Productive synthesis of trans-trioxatris-σ-~ (trans-"benzene trioxide") (SC) 633 [G.E. 627]
9,10-Homonaphthodiquinone, Electrochemical entry to ~ (SC) 420 [G.E. 412]
Homotropone, Hexamethyl-tris-σ-~ from 3,3-dimethylcyclopropene and carbon monoxide (SC) 706 [G.E. 715]
Hormones, Hormonal regulation of phosphoenol pyruvate carboxykinase (LA) 577
Impaired hormonal regulation of enzyme activity during aging (LA) 717
Hydration, Covalent ~—new results using ^{13}C-NMR spectroscopy (SC) 354 [G.E. 356]
Hydrazines, Stable pyrazolium betaines by addition of 1,1-dialkyl-~ to acetylenecarboxylic esters (SC) 560 [G.E. 551]
Addition of P—H, As—H, and Sb—H groups to an N=N double bond (SC) 643 [G.E. 671]
Hydrazinoribose—an intermediate for the specific formation of natural nucleosides and their derivatives (SC) 64 [G.E. 69]
Hydrocarbons, New method for synthesis of many-membered hydrocarbon rings (SC) 559 [G.E. 543]
Recent analytical developments in the petroleum industry (Book Review) 504
Hydrogenation, Reductive dehydrohalogenation of β-halogenated fatty acids and stereoselective ~ of α-halogenated α,β-unsaturated fatty acids by Clostridium kluyveri (SC) 106 [G.E. 111]
Hydrogen bonding (Book Review) 651
Hydrogen exchange, Stereoselective ~ at the methylene group of glycine in the AR-(N-benzylglycinato)bis(ethylenediamine)cobalt-(III) ion (SC) 495 [G.E. 523]
4-Hydroxyarsabenzene—an "arsaphenol" (SC) 710 [G.E. 743]
Hyosamine, Simple and productive total syntheses of 2-deoxystreptamine and (±)-~ (SC) 632 [G.E. 626]
Hypoglycine, Biochemistry (LA) 113
Hyperconjugation, C—N ~ in a π-radical twisted through 90° (SC) 553 [G.E. 588]

IMMUNOLOGY, New approaches to immunosuppression (LA) 72
Immunological research in the last decade (LA) 266
Indans, Transition metal catalyzed acetylene cyclizations. General synthesis of ~ and tetralins (SC) 712 [G.E. 744]
"Indigo diimine"—a tautomer with unsymmetrical structure (SC) 52 [G.E. 63]
Inorganic chemistry, Practical ~ (Book Review) 771
Insect hormones and bioanalogs as potential insecticides (LA) 72
Insertion of an ethoxycarbonylmethylene moiety into a Ni—N bond of meso-tetraphenylporphinatonickel(II) (SC) 567 [G.E. 545]
Insulin, Impaired hormonal regulation of enzyme activity during aging (LA) 717
Intermediates, Reactive ~ in organic chemistry (Book Review) 652
Iron cluster, $(C_5H_8N_2)Fe(CO)_9$—an ~ containing a cis-diimine unit (SC) 182 [G.E. 206]
Iron complexes, μ-Carbonylbis(cyclobutadienecarbonyliron), a complex containing an iron-iron triple bond—model for unusual behavior of $Fe(CO)_4$ in solution? (SC) 54 [G.E. 35]
Unsymmetrical coordination of a symmetrical 1,4-diazabutadiene to iron(0) (SC) 251 [G.E. 246]
1—5-η-Benzothiadiborolenetricarbonyliron—a complex having a fixed π-electron system in the benzene ring (SC) 262 [G.E. 286]
Synthesis of bis(dimethylamino)carbenetetracarbonyliron (SC) 367 [G.E. 288]
Constitutional and configurational stability of a carbamoyl-tetracarbonyliron anion complex (SC) 487 [G.E. 489]
Simple synthesis of $[C_5H_5Fe(CO)dppe]^+$ and its photochemical conversion into the dinitrogen complex $[\{C_5H_5Fe(dppe)\}_2N_2]^{2+}$ (SC) 571 [G.E. 595]
Isocyanates, Cycloadditions of aliphatic and aromatic acyl ~ (LA) 71
Preparation of benzene derivatives containing an isocyanatomethyl side chain (PR) 718
N,N,N′,N′-Tetramethyl-2,2′-oxydiethylamine (PR) 578
Isocyanato-s-triazines, Preparation of mono- or di-~ (PR) 189
Isocyanide complexes, Oxidative addition of isocyanide dichlorides to metal complexes (SC) 369 [G.E. 290]
Isocyanide dichlorides, Oxidative addition to metal complexes (SC) 369 [G.E. 290]
Isocyanides, Synthesis of tert-alkyl-substituted glycines (SC) 629 [G.E. 624]
Transformation of carbonyl into isocyanide ligands via carbamoyl intermediates (SC) 757 [G.E. 776]
Isomerizations of alkenylidenecyclopropanes catalyzed by Lewis acids (SC) 360 [G.E. 381]
Isooxazoles, Synthesis of heterocycles by ring transformation of ~ (LA) 266
Isothiazolo[3,4-d]pyrimidines, 3-Amino-~ (PR) 827
Isothiocyanate, Dichlorofluoromethanesul-

fenyl ~ (SC) 698 [G.E. 707]
Isothiocyanato acyl chlorides, Synthesis from lactams (SC) 502 [G.E. 517]
Isotopes, Geochemistry of stable ~ (FP) 75 [G.E. 104]
Itaconic acid (PR) 267

JAHN-Teller effects, Theory and manifestations (LA) 438

KETENE, Additions to C=O group of ~-s: β-substituted α-trimethylsiloxyacrylonitriles (SC) 179 [G.E. 195]
Novel reactions of di-~ (LA) 188
Ketenimine, Synthesis of a stable alkylidene-~ and an alkylidenethioketene (SC) 53 [G.E. 34]
N-Halo-~-s (PR) 650
Keteniminium salts, Cyclobutenylideneammonium salts from cycloadditions of ~ to acetylenes (SC) 569 [G.E. 552]
Ketenylidenetriphenylphosphorane, Simple synthesis of ~ and its thioanalogs (SC) 634 [G.E. 630]
Ketimine complexes, Conversion of ammonia into ketimine ligands—a simple method for synthesis of ~ (SC) 753 [G.E. 772]
Ketones (PR) 72
Kinetics, High pressure ~ in organic and macromolecular chemistry (FP) 137 [G.E. 186]
Rate-determining step of enzyme-catalyzed reactions (LA) 769
Formale Kinetik (Book Review) 719
Specialist periodical reports. Reaction ~ (Book Review) 828
Kirsanov reaction, Cyclophosphazene formation in an "anomalous ~" 826 [G.E. 875]
Kolbe electrolysis, Synthesis of brevicomin (SC) 758 [G.E. 777]

LACTAMS, Isomerization polymerization of ~ (FP) 43 [G.E. 43]
Synthesis of isothiocyanato acyl chlorides from ~ (SC) 502 [G.E. 517]
Lactones, Synthesis of bicyclic γ-~ from 2-cycloalkene-1,4-diols (SC) 103 [G.E. 109]
Lithium phenylethynolate and its reaction with carbonyl compounds to give β-~ (SC) 765 [G.E. 814]
Synthesis of α-methylene ~ (LA) 437
Lanthanoid, Spectral evidence for ~ and actinoid carbonyl compounds (FP) 309 [G.E. 332]
Lanthanoid carbonyl compounds, Spectral evidence for actinoid carbonyl compounds and ~ (FP) 309 [G.E. 332]
Laser-evaporation of metals and its application to organometallic synthesis (FP) 278 [G.E. 300]
Lasers, Chemical and biochemical applications of ~ (Book Review) 829
Lattice defects, Ionenkristalle, Gitterdefekte und Nichtstöchiometrische Verbindungen (Book Review) 115
Leukocytes, Age-related changes in glucocorticoid binding by rat splenic ~ (LA) 577
Ligand, Dimethylphosphinomethanide ion, $(CH_3)_2PCH_2$. Novel ~ for transition metals (SC) 637 [G.E. 630]
Disulfur monoxide as complex ~ (SC) 645 [G.E. 673]
Ligand exchange, Flipping of CO ligand groups in metal carbonyl compounds and its frequency in $Fe(CO)_5$ (FP) 314 [G.E. 337]
Ligand field theory, Ligandenfeldtheorie (Book Review) 115
Lipids and membranes (LA) 72
Lithium compounds, Vinyllithium and 1,4-dilithiobutane from ethylene and lithium (SC) 259 [G.E. 254]
Dilithium-nickel-olefin-complexes. Novel bimetal complexes containing a transition metal and a main group metal (SC) 752 [G.E. 809]
Synthesis and reactions of simple organo-~ from weakly acidic C—H compounds (LA) 438

MAGNESIUM oxide, Formation of O^- centers by homolytic decomposition of OH^- groups on ~ (SC) 568 [G.E. 593]
Magnetochemistry, Magnetochemie (Book Review) 268
Manganese complexes, Bis(1,3-butadiene)-monocarbonylmanganese—a paramagnetic butadiene complex (SC) 351 [G.E. 351]
Crystal and molecular structure of bis(1,3-butadiene)monocarbonylmanganese (SC) 352 [G.E. 353]
Preparation of the trinuclear triphenylcyclotriphosphane complex $(C_6H_5)_3P_3$-$[Mn(CO)_2C_5H_5]_3$ by demetalation of $C_5H_5(CO)_2MnP(C_6H_5)Li_2$ (SC) 572 [G.E. 597]
Malondialdehydes, Preparation, structure, and reactions of halo-~ (FP) 86 [G.E. 124]
Mass spectrometry, Field desorption ~ (FP) 403 [G.E. 425]
Detection of fragment genesis in the mass spectrometer: DADI mass spectrometry as an aid in the structure analysis of organic compounds (FP) 679 [G.E. 731]
Applications of field desorption ~ to inorganic chemistry: salts (SC) 561 [G.E. 544]
Mathematics, Mathematik für Naturwissenschaftler und Ingenieure (Book Review) 190
Mathematik für Chemiker (Book Review) 651
Matrix photochemistry, Photochemistry in matrices and its relevance to atom synthesis (FP) 304 [G.E. 326]
Membranes, Asymmetric ~: preparation and applications (FP) 452 [G.E. 476]
Selective transport of alkali metal cations through liquid ~ by macrobicyclic carriers (SC) 555 [G.E. 542]
Lipids and ~ (LA) 72
Chloroplast ~ and coupling factor conformations (LA) 770
Protein mobility in ~ (LA) 827
Mercury compounds, Disilylmercury and digermylmercury (SC) 167 [G.E. 207]
Mercury(II) tropolonate, Structure (SC) 358 [G.E. 384]
Metal atoms, Relationships between the chemistry of dispersed metals and chemical syntheses with ~ (FP) 193 [G.E. 213]
Reactions of transition ~ with organic substrates (FP) 195 [G.E. 215]
Isolation and reactions of ~ in matrices (FP) 199 [G.E. 220]
Reactions between ~ and gases during the production of thin films in high vacuum (FP) 207 [G.E. 227]
Synthetic reactions of ~ at temperatures of 10 to 273 °K (FP) 273 [G.E. 295]
Laser evaporation of metals and its application to organometallic synthesis (FP) 278 [G.E. 300]
Reactions of ~ with fluorocarbons (FP) 287 [G.E. 309]
Transition ~ in the synthesis of binuclear complexes (FP) 292 [G.E. 314]
Spectral evidence for lanthanoid and actinoid carbonyl compounds (FP) 309 [G.E. 332]
Metal vapors, Formation of Ad-layers and clusters on condensation of ~ on solid surfaces (FP) 212 [G.E. 233]
Production and condensation in large quantities (FP) 218 [G.E. 239]
Metamorphosis inhibitors (LA) 373
Methanediazonium complex, Metal-stabilized C-protonated diazomethane: a ~ (SC) 355 [G.E. 358]
Methanesulfinic acid, Synthesis of 5H-dibenz-[c,e]azepine by elimination of ~ (SC) 265 [G.E. 289]
4,10-Methano[11]annulenone, 2-Hydroxy-~—a 10 analog of α-tropolone (SC) 566 [G.E. 592]
5-Methylaminomethyl-2-thiouridine, Synthesis of ~, a rare nucleoside from t-RNA (SC) 255 [G.E. 251]
N^a-Methylbrevicollin, Facile entry to 1,4-disubstituted β-carboline derivatives. Total synthesis of ~ (SC) 357 [G.E. 385]
Methylmalonyl-CoA, Nonenzymatic model reaction for the coenzyme B_{12}-catalyzed rearrangement of ~ into succinyl-CoA (SC) 822 [G.E. 877]
Metrizamide, a new density gradient medium (LA) 577
Michael additions of metalated thioacetals to cyclic enones (SC) 57 [G.E. 37]
Microencapsulation (FP) 539 [G.E. 556]
Microorganisms, Fixation of atmospheric nitrogen by ~ (FP) 80 [G.E. 97]
Reductive dehydrohalogenation of β-halogenated fatty acids and stereoselective hydrogenation of α-halogenated α,β-unsaturated fatty acids by Clostridium kluyveri (SC) 106 [G.E. 111]
Mobility, ^{13}C Spin-lattice relaxation times and the ~ of organic molecules in solution (FP) 144 [G.E. 152]
Molecules, Die Struktur der Atome und Moleküle (Book Review) 74
Molybdates, Chloromolybdate(VI): a halomolybdate having tetrahedral coordination (SC) 574 [G.E. 599]
Anion structure of ammonium deca-~ $(NH_4)_8Mo_{10}O_{34}$ (SC) 644 [G.E. 634]
Molybdenum complex, [Bis(diphenylphosphino-η-benzene)chromium]tetracarbonylmetal complexes of chromium, molybdenum, and tungsten (SC) 174 [G.E. 198]
Structure and absolute configuration of an optically active square pyramidal ~ (SC) 353 [G.E. 379]
$[(n\text{-}C_4H_9)_4N]_2Mo_5Cl_{13}$—a compound with the cluster group $[Mo_5Cl_8^{4}]$ (SC) 570 [G.E. 594]
Monoamine oxidase, Inhibition by propargylamine: structure of the inhibitor complex (SC) 110 [G.E. 137]
Multienzyme complex, Pyruvate dehydrogenase ~ (FP) 591 [G.E. 614]
Multisurface chemistry, En route to ~ (FP) 790 [G.E. 851]

NAPHTHODIQUINONE, Electrochemical entry to 9,10-homo-~ (SC) 420 [G.E. 412]
Naphthol, Synthesis of ~ skeleton from pentacarbonyl[methoxy(phenyl)carbene]chromium(0) and tolan (SC) 644 [G.E. 672]
Natural products, Organic compounds in nature: limits of our knowledge (FP) 507 [G.E. 527]
~ chemistry (Book Review) 504
Nickel, Importance as a trace element in organisms (LA) 72
Nickel complexes, Insertion of an ethoxycarbonylmethylene moiety into a Ni—N Bond of meso-tetraphenylporphinatonickel(II) (SC) 567 [G.E. 545]
Nickel(II) compounds, Lithium tetraphenyl- and tetramethylniccolate(II) 261 [G.E. 291]
Nickel-olefin complexes, Dilithium-~. Novel bimetal complexes containing a transition metal and a main group metal (SC) 752 [G.E. 809]
Nickel plating, Chemical ~ (FP) 614 [G.E. 652]
Nitrogenase, Nonenzymatic simulation of ~ reactions and the mechanism of biological nitrogen fixation (FP) 514 [G.E. 579]
Nitrogen complex, Simple synthesis of $[C_5H_5Fe(CO)dppe]^+$ and its photochemical conversion into the di-~ $[\{C_5H_5Fe(dppe)\}_2N_2]^{2+}$ (SC) 571 [G.E. 595]
Nitrogen compounds, 1,2,4λ⁴,3,5-Trithiadiazol-1-one. N_2S_3O—the first oxide of a five-membered sulfur-nitrogen ring (SC) 258 [G.E. 254]
Cyclic nitrogen derivatives of tetra- and divalent tin (SC) 263 [G.E. 287]
Pentacyclic derivative of cyclododecaborazane (SC) 359 [G.E. 382]
Nitrogen fixation, Fixation of atmospheric nitrogen by microorganisms (FP) 80 [G.E. 97]
Nonenzymatic simulation of nitrogenase reactions and the mechanism of biological ~ (FP) 514 [G.E. 579]
Nitrones, 1,3-Dipolar cycloadditions (LA) 649
2-Nitro-1-phenylethyl: a new protecting and chiroptical reporter group for cysteine peptides (SC) 817 [G.E. 876]
2-(o-Nitrophenyl)-1,3-propanediol (PR) 503

Nitrosamines, Umpolung of amine reactivity. Nucleophilic α-(secondary amino)-alkylation via metalated ~ (FP) 15 [G.E. 1]
Nitroso compounds, Stable 4H-1,2-oxazetes by intramolecular cyclization of α,β-unsaturated ~ (SC) 70 [G.E. 73]
Nitrosyl group, Introduction into coordination compounds (LA) 503
NMR spectroscopy, ^{13}C Spin-lattice relaxation times and the mobility of organic molecules in solution (FP) 144 [G.E. 152]
Detection of the trans-enol in methyl acetoacetate by ^{1}H- and ^{13}C-~ (SC) 260 [G.E. 283]
Covalent hydration—new results using ^{13}C-~ (SC) 354 [G.E. 356]
Influence of the distance of the proline carbonyl from the β and γ carbon on the ^{13}C chemical shifts (SC) 702 [G.E. 712]
Observation of histidine residues in proteins by ~ (LA) 502
Topics in carbon-13 ~ (Book Review) 828
Nonactic acid, Highly stereoselective synthesis of racemic ~ and synthesis of dextrorotatory (2S,3S,6R,8R)-~ (SC) 432 [G.E. 454]
3-Norcarene, Facile conversion into trans-bishomobenzene (SC) 496 [G.E. 488]
D-Norgestrel, Synthesis (SC) 417 [G.E. 413]
N-Phosphonomethylaminocarboxylic acids (PR) 267
Nuclear fission, What do we know about ~? (FP) 117 [G.E. 77]
Nucleic acids, Biosynthesis of ribo-~ (FP) 445 [G.E. 497]
Nucleophilic substitutions, Experimental evidence for a novel limiting mechanism of aliphatic ~ (SC) 59 [G.E. 66]
Nucleoside phosphorothioates, Investigation of enzyme mechanisms with ~ (FP) 160 [G.E. 179]
Nucleosides, Hydrazinoribose—an intermediate for the specific formation of natural ~ and their derivatives (SC) 64 [G.E. 69]
New catalysts for synthesis of ~ (SC) 421 [G.E. 417]
Synthesis of 5-methylaminomethyl-2-thiouridine, a rare nucleoside from t-RNA (SC) 255 [G.E. 251]
Nucleotides, Investigation of enzyme mechanisms with nucleoside phosphorothioates (FP) 160 [G.E. 179]
Chemical methods of oligonucleotide synthesis (LA) 649
Nylon, Impact-resistant modified polyamides of the type of ~-6 or -6,6 (PR) 650

OLEFINS, Methods for preparation of bridgehead ~ (FP) 528 [G.E. 568]
New modification of the ozone cleavage reaction (SC) 716 [G.E. 748]
Synthesis of cyclobutanes from ~ (LA) 71
Addition of radicals to ~ in the presence of redox systems (LA) 717
Oligonucleotide synthesis, Chemical methods (LA) 649
Oligosaccharides, Building units for ~. Synthesis of α-glycosidically linked 2-amino sugar ~ (SC) 558 [G.E. 547]
Optical activity of oriented molecules (SC) 176 [G.E. 200]
Optical brighteners, Heterocycles as structural units in new ~ (FP) 665 [G.E. 693]
Oriented molecules, Optival activity (SC) 176 [G.E. 200]
Orbitals, Orbitale organischer Moleküle (Book Review) 191
Organic chemistry, Organische Chemie I and II (Book Review) 440
Oxadiazaphospholines, Synthesis of oxazaphospholinobenzooxaazaphospholines and -~—compounds having pentacoordinated phosphorus as bridgehead of a bicyclo[3.3.0]octane skeleton (SC) 489 [G.E. 517]
β-Oxa-α,α-dithiatris-σ-homobenzene, Chemistry of cis-trioxatris-σ-homobenzene, α,α-dioxa-β-thiatris-σ-homobenzene, and ~ (SC) 253 [G.E. 249]
7-Oxanorbornadiene—3-Oxaquadricyclane (SC) 753 [G.E. 772]
1,2-Oxaphospholane-5-phosphonic esters suitable as flame-protection agents (PR) 770
3-Oxaquadricyclane—7-oxanorbornadiene (SC) 753 [G.E. 772]
1,3-Oxathiol-4-ones, [3 + 2]-Cycloadditions of mesoionic ~ to alkynes. A new entry to the furan series (SC) 422 [G.E. 416]
Oxazaphospholine, Synthesis of oxazaphospholinobenzo-~-s and -oxadiazaphospholines—compounds having pentacoordinated phosphorus as bridgehead of a bicyclo[3.3.0]octane skeleton (SC) 489 [G.E. 517]
Distortion of the trigonal-bipyramidal ligand arrangement in bicyclophosphoranes—structure of 2,3,8,8-tetraphenyl-[1,3,2λ⁵]oxazaphospholino[2,3-b]benzo[d]-1,3,2λ⁵]-~ (SC) 490 [G.E. 519]
4H-1,2-Oxazete N-oxides from 1,1-di-tert-butylallenes (SC) 69 [G.E. 72]
4H-1,2-Oxazetes, Stable ~ by intramolecular cyclization of α,β-unsaturated nitroso compounds (SC) 70 [G.E. 73]
Oxazolin-5-ones, Hetero Cope rearrangements in the cyclization of allyl and propargyl esters of N-acyl amino acids to ~ (SC) 58 [G.E. 64]
Oxidation, Selective ~ of the methyl group of p-cresols by base-catalyzed oxygenation (SC) 356 [G.E. 386]
Oxonino[4,5-d]pyridazine, Thermal cycloaddition between 3,6-diphenyl-s-tetrazine and 9-oxabicyclo[6.1.0]nona-2,4,6-triene; construction of the ~ frame (SC) 814 [G.E. 842]
2-Oxothiazole-5-carboxylic acid derivatives (PR) 114
Oxygenation, Selective oxidation of the methyl group of p-cresols by base-catalyzed ~ (SC) 356 [G.E. 386]
Ozone cleavage, New modification of the ~ reaction (SC) 716 [G.E. 748]
Ozonolysis, Mechanism (FP) 745 [G.E. 765]

PAINTING of ancient ceramics (FP) 602 [G.E. 639]
Palladium(0) catalysts, Hexamethyl-tris-σ-homotropone from 3,3-dimethylcyclopropene and carbon monoxide (SC) 706 [G.E. 715]
Palladium complexes, Preparation and structure of novel binuclear ~ containing a metal-metal bond: μ-(η-C_5H_5)-μ-(η-C_4H_7)Pd_2L_2 (SC) 185 [G.E. 205]
Synthesis of sulfinato-O,S complexes of palladium(II) (SC) 256 [G.E. 251]
D-Penicillamine—production and properties (FP) 330 [G.E. 372]
Pentacyclo[6.4.0.0^{2,7}.0^{4,11}.0^{5,10}]-dodecane, tetraasterane (SC) 180 [G.E. 174]
Pentanepentacarboxylic acid, 1,2,3,4,5-~ (PR) 718
4-Pentenylamine, Platinum-promoted cyclization (SC) 369 [G.E. 380]
Peptides, Influence of the distance of the proline carbonyl from the β and γ carbon on the ^{13}C chemical shifts (SC) 702 [G.E. 712]
Peptide synthesis, Asymmetrically induced four component condensation with extremely high stereoselectivity and multiplication of stereoselectivity (SC) 61 [G.E. 67]
Houben-Weyl: Methoden der organischen Chemie (Book Review) 653
Perchloric acid, Hazards in use (SC) 647 [G.E. 635]
2-(Perfluoroalkyl)ethyl iodides, Fatal accident with ~ (SC) 181 [G.E. 171]
Pest-control agents (PR) 439
Petroleum industry, Recent analytical developments in the ~ (Book Review) 504
Phages, Life cycle of RNA ~ (LA) 187
Phenol oxidation, Biomimetic synthesis of skyrin (SC) 819[G.E. 846]
Phenoxides, Quaternary hydroxyalkylammonium alkoxides and ~ (PR) 577
Phenyl acetate, Selective photochemical Fries rearrangement of ~ in the presence of β-cyclodextrin (SC) 820 [G.E. 880]
Phosphane complexes, Mixed cyanide-~ of transition metals (LA) 72
Phosphanediyls, Formation, detection, and reactions (FP) 523 [G.E. 535]
Phosphanes, Tertiary phosphane/tetrachloromethane, a versatile reagent for chlorination, dehydration, and P—N linkage (FP) 801 [G.E. 863]
Stabilization of unknown ~: secondary amino- and alkoxy-~ as complex ligands (SC) 571 [G.E. 596]
Preparation of the trinuclear triphenylcyclotriphosphane complex ($C_6H_5)_3P_3$-[$Mn(CO)_2C_5H_5]_3$ by demetalation of $C_5H_5(C\overset{O}{}O)_2MnP(P_6H_5)Li_2$ (SC) 572 [G.E. 597]
Diazadiphosphetidines by reaction of aminoimino-~ with iminophosphoranes (SC) 768 [G.E. 810]
Bis(hydroxymethyl)methylphosphane oxide (PR) 267
Phosphane sulfide, Isomerization of dimethyl-~ on transition metals (SC) 416 [G.E. 447]
Phosphates, Replacement of ~ in detergents—possibilities and limits (FP) 94 [G.E. 115]
2-Phospha-1-tetrazene, 1-tert-Butyl-3-trimethylsilyl-4,4-dimethyl-~ (SC) 629 [G.E. 667]
Phosphazenes, 1,2-Cycloadditions of "~" having unusual coordination number: λ⁵-phosphirane and 1,2λ⁵-azaphosphiridine (SC) 363 [G.E. 355]
Substituted fluorocyclotri-~ (PR) 718
Phosphinidene complex, $C_6H_5P[Mn(CO)_2C_5H_5]_2$: a ~ with trigonal planar coordinated phosphorus(I) (SC) 705 [G.E. 714]
Phosphinidenes, Formation, detection, and reactions (FP) 523 [G.E. 535]
Phosphinomethanide ion, Dimethyl-~ $(CH_3)_2PCH_2$. Novel ligand for transition metals (SC) 637 [G.E. 630]
λ⁵-Phosphirane, 1,2-Cycloadditions of "phosphazenes" having an unusual coordination number: ~ and 1,2λ⁵-azaphosphiridine (SC) 363 [G.E. 355]
Phosphoenol pyruvate carboxykinase, Hormonal regulation (LA) 577
Phosphonic acids, α-Chlorobenzylidenediphosphonic acid (chloro(phenyl)methane-1,1-diphosphonic acid) (PR) 189
Cyclic amino-~ (PR) 827
Phosphonic esters, Aminoalkyl-~ (PR) 189
Phosphorane, Extreme perturbation of π-systems by ylidic substituents (SC) 173 [G.E. 197]
Simple synthesis of ketenylidenetriphenyl-~ and its thioanalogs (SC) 634 [G.E. 630]
λ⁵-Phosphorins, 1,1-Dimethoxy-2,6-diphenyl-λ⁵-phosphorin-4-carbaldehyde and -4-carbonitrile (SC) 111 [G.E. 135]
4-(Acetylamino)-1,1-dialkoxy-2,6-diphenyl-~ (SC) 112 [G.E. 135]
Phosphorous esters of 1,2-glycols (PR) 114
Phosphorus compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
1,3,2,4-Diazaphosphaboretidines: a four-membered boron-nitrogen-phosphorus heterocycle (SC) 56 [G.E. 34]
New route to phosphoro- and phosphinothiocyanatidates (SC) 108 [G.E. 134]
Phosphorus(V) having trigonal planar coordination (SC) 261 [G.E. 284]
Chloro(di-tert-butylphosphino)germanediyl and -stannanediyl: stable germanium(II) and tin(II) organophosphorus compounds (SC) 368 [G.E. 354]
1,2,3-Tri-tert-butyldiazaphosphiridine 3-oxide (SC) 486 [G.E. 487]
Synthesis of oxazaphospholinobenzooxazaphospholines and -oxadiazaphospholines—compounds having pentacoordinated phosphorus as bridgehead of a bicyclo[3.3.0]octane skeleton (SC) 489 [G.E. 517]
Distortion of the trigonal-bipyramidal ligand arrangement in bicyclophosphoranes—structure of 2,3,8,8-tetraphenyl[1,3,2λ⁵]-oxazaphospholino[2,3-b]benzo[d][1,3,2λ⁵]-oxazaphospholine (SC) 490 [G.E. 519]
Addition of P—H, As—H, and Sb—H groups to an N=N double bond (SC) 643 [G.E. 671]
1λ⁴,2,4,3λ⁵-Thiadiazaphosphetidine: a sulfur-nitrogen-phosphorus four-membered ring compound (SC) 769 [G.E. 810]
Cyclophosphazene formation in an "anoma-

lous Kirsanov reaction" (SC) 826 [G.E. 875]
Synthesis of heterocycles with organophosphorus compounds (LA) 188
Phosphorylcarbenes, Chemistry (FP) 222 [G.E. 259]
Photoaddition of vinyl acetate to benzene (SC) 552 [G.E. 540]
Photochemical reactions, A classification (LA) 438
Photochemistry, Mechanisms of photochemical air pollution (FP) 1 [G.E. 18]
~ in matrices and its relevance to atom synthesis (FP) 304 [G.E. 326]
~ of organic solids (FP) 386 [G.E. 439]
En route to multisurface chemistry (FP) 790 [G.E. 851]
Sudden polarization in the zwitterionic Z_1 excited states of organic intermediates. Photochemical implications (SC) 575 [G.E. 599]
Photochemical cycloaddition of benzene to vinylene carbonate (SC) 698 [G.E. 708]
Carbonylrhenium clusters by photoreaction of $Re_2(CO)_{10}$ with water (SC) 700 [G.E. 710]
Photochemical rearrangement and fragmentation of bicyclo[2.2.2]octadienones (SC) 761 [G.E. 782]
New results of ~ of complexes of the heavier transition metals (LA) 114
Photo-Diels-Alder reactions of anthracene (SC) 491 [G.E. 520]
Photoelectron spectroscopy, Photoelectron spectrum and structure of tri-tert-butyl-cyclobutadiene (SC) 172 [G.E. 194]
~ of tetrazene (SC) 178 [G.E. 203]
Phthalic anhydride, Isomer-free 3,4,5,6-tetrahydro-3-methyl-~ (PR) 189
Phthalocyaninecobalt(I) salts, "supernucleophilic" vitamin B_{12} models stable in neutral medium (SC) 825 [G.E. 847]
Phthaloyl peroxide as an efficient source of singlet oxygen (SC) 560 [G.E. 546]
Pigments, Painting of ancient ceramics (FP) 602 [G.E. 639]
Optical properties of ~—objective methods for testing and evaluation (FP) 688 [G.E. 721]
Pinacolization, Mechanism of electrochemical ~. First asymmetric synthesis in a chiral medium (SC) 634 [G.E. 629]
Plastics, Transparent ~ reinforced by glass fibers (PR) 73
Plastics analysis, Atlas der Kunststoff-Analyse (Book Review) 267
Plastics handbook, Kunststoff-Handbuch (Book Review) 579
Platinum complexes, Platinum-promoted cyclization of 4-pentenylamine (SC) 369 [G.E. 380]
Platinum(II)-hydrido complex, Insertion of ethylene into a ~ containing a bidentate ligand spanning trans-positions (SC) 563 [G.E. 547]
Polarization, Sudden ~ in the zwitterionic Z_1 excited states of organic intermediates. Photochemical implications (SC) 575 [G.E. 599]
Polyalkylene and monoalkylene glycol ethers (PR) 828
Polyamides, Impact-resistant modified ~ of nylon-6 or -6,6 type (PR) 650
Polyamidimides with elastic properties (PR) 267
Polyanions, $Sn_{10}O_4S_{20}^{8-}$: a new type of polyanion (SC) 436 [G.E. 451]
Polychloro compounds, Synthesis of ~ with chlorinated functional groups (LA) 71
Polyenes as four-stage redox systems (SC) 556 [G.E. 548]
Polyether, Polyfunctional chiral macrocyclic ~ derived from L-(+)-tartaric acid (SC) 764 [G.E. 813]
Polyethylene carbonates, Copolymerization of ethylene oxide or propylene oxide with carbon dioxide (PR) 189
Polymerization, Isomerization ~ of lactams (FP) 43 [G.E. 43]
Catalyst for ring-opening ~ of cyclopentene to form polymers (PR) 114
Radical and ionic ~ of ethylene (PR) 650
Polymers, Microencapsulation (FP) 539 [G.E. 556]
Soluble metal complexes of ~ for catalysis (SC) 493 [G.E. 484]
Low-molecular ~ containing terminal hydroxy groups (PR) 267
Process for the preparation of ethylene-propylene-diene ter-~ (PR) 650
Polyols, Protected ~ (PR) 503
~ for preparation of flame-resistant polyurethanes (PR) 578
Polypropylene carbonates, Copolymerization of ethylene oxide or propylene oxide with carbon dioxide (PR) 189
Polyurethane, N,N,N',N'-Tetramethyl-2,2'-oxydiethylamine (PR) 578
Polyurethane foam, Catalysts for preparation of ~ (PR) 188
Polyurethane plastics, Aromatic polyamines for production of ~ (PR) 73
Polyurethanes, Development of smoke from burning polyvinyl chloride or ~ (PR) 267
Polyols for preparation of flame-resistant ~ (PR) 578
Polyvinyl chloride, Development of smoke from burning ~ or polyurethanes (PR) 267
Porphyrinogen, A N,N',N'',N'''-tetramethyl-~ (SC) 424 [G.E. 449]
Porphyrins, Preparation and reactivity of sterically crowded ~ (SC) 361 [G.E. 387]
Insertion of an ethoxycarbonylmethylene moiety into a Ni—N bond of meso-tetraphenylporphinatonickel(II) (SC) 567 [G.E. 545]
Programmed learning, Programmierte Prüfung. Chemie, Physik, Physikalische Chemie (Book Review) 651
Proline, Influence of the distance of the ~ carbonyl from the β and γ carbon on the ^{13}C chemical shifts (SC) 702 [G.E. 712]
Propargylamine, Inhibition of monoamine oxidase by ~: structure of the inhibitor complex (SC) 110 [G.E. 137]
~ (PR) 73
Propylene, Dimerization to linear hexenes (SC) 104 [G.E. 110]
Preparation of ethylene-~-diene terpolymers (PR) 650
Propylene diacetate ("propylene glycol diacetate") (PR) 114
Prostaglandins (FP) 337 [G.E. 143]
Protecting groups, 2-Nitro-1-phenylethyl: a new protecting and chiroptical reporter group for cysteine peptides (SC) 817 [G.E. 876]
Selective acidic cleavage of the tert-butoxycarbonyl group (SC) 818 [G.E. 877]
Protein mobility in membranes (LA) 827
Proteins, Covalent modifications of nuclear ~ during aging (LA) 577
Protein synthesis, Inhibitors (LA) 188
Purine nucleosides, Ribose-glucose exchange in ~ (SC) 815 [G.E. 839]
3H-Pyran-2,4-diones, Synthesis and thermal decarbonylation of 2,3-furandiones (SC) 636 [G.E. 668]
Pyrazolium betaines, Stable ~ by addition of 1,1-dialkylhydrazines to acetylenecarboxylic esters (SC) 560 [G.E. 551]
Pyridinecarbaldehydes, Vinylogous ~ by Wittig reaction (SC) 486 [G.E. 486]
Pyridine π-complexes, Tricarbonyl-(penta- and 2,4,6-trimethylpyridine)chromium(0)—true ~ (SC) 639 [G.E. 634]
Pyrroles, Synthesis of linear tri- and tetra-~ of biogenetic significance (SC) 423 [G.E. 418]
Synthesis of 2H-cyclohepta[c]pyrrol-6-ones. Route to 2-azaazulenes (SC) 821 [G.E. 840]
Pyrrolidines, 3-Amino-4-(aminomethyl)-~ as hardening agents for epoxide resins (PR) 578
Pyruvate dehydrogenase multienzyme complex (FP) 591 [G.E. 614]

RADICAL anion intermediates, Substitution reactions which proceed via ~ (FP) 734 [G.E. 797]
Radical anions, Formation of cis- and trans-semidione ~ by addition of acyl radicals to α-oxo carboxylic acids (SC) 254 [G.E. 250]
Radical cations, Formation from 1,2- and 1,4-dimethoxybenzene by electron transfer to Tl^{2+} and Ag^{2+} in aqueous solution. A pulse radiolysis and in situ radiolysis EPR study (SC) 430 [G.E. 418]
Radical chemistry, Einführung in die Radikalchemie (Book Review) 439
Radicals, Aminyl free ~ (FP) 783 [G.E. 823]
Non-equilibrating di-~: stereochemistry of the thermal reorganization of methyl-substituted 6-methylenebicyclo-substituted 6-methylenebicyclo[3.2.0]hept-2-enes (SC) 257 [G.E. 252]
Mode of formation of triphenylverdazyl from triphenylverdazylium salts or from triphenylformazan (SC) 431 [G.E. 453]
ESR proof of the antiaromaticity of a cyclopropenyl radical (SC) 550 [G.E. 589]
C—N Hyperconjugation in a π-radical twisted through 90° (SC) 553 [G.E. 588]
Addition to olefins in presence of redox systems (LA) 717
Reaction mechanisms, Reaktionsmechanismen der Organischen Chemie. Ein Seminarbuch (Book Review) 115
Reaction paths, Stereochemistry of ~ as determined from crystal structure data—a relationship between structure and energy (FP) 460 [G.E. 461]
Rearrangement, A ~ in the λ^5-phosphorin series analogous to the Claisen-~ [G.E. 136]
Preparative aspects of Ag^+ (LA) 769
Redox systems, Polyenes as four-stage ~ (SC) 556 [G.E. 548]
Reducing agent, Use of sodium cyanotrihydridoborate (LA) 503
Rhenium compounds, Carbonylrhenium clusters by photoreaction of $Re_2(CO)_{10}$ with water (SC) 700 [G.E. 710]
Rhodium(I) complex, Novel cyclobutadiene-~ (SC) 170 [G.E. 172]
Ribonucleic acids, Biosynthesis (FP) 445 [G.E. 497]
Ribose-glucose exchange in purine nucleosides (SC) 815 [G.E. 839]
Ribosomes, Structural transformations (LA) 113
Active sites (LA) 113
Ring contractions and expansions of vicinally disubstituted cyclobutanes and cyclopropylmethyl compounds (FP) 473 [G.E. 505]
Ring expansions and contractions of vicinally disubstituted cyclobutanes and cyclopropylmethyl compounds (FP) 473 [G.E. 505]
Rodenticides, New group of ~ (PR) 439
Rubber, Flowing powder filler-containing ~ mixes (PR) 190

SEDIMENTS, Organic compounds in nature: limits of our knowledge (FP) 507 [G.E. 527]
Selenium, ~-catalyzed formation of sulfate and sulfur from sulfite (SC) 638 [G.E. 631]
~ (Book Review) 652
Selenium compounds, New synthetic route to di- and trisubstituted epoxides (SC) 350 [G.E. 347]
New route to epoxides (SC) 700 [G.E. 709]
Semiconductors, Organic ~ (Book Review) 374
Semidione radical anions, Formation of cis- and trans-~ by addition of acyl radicals to α-oxo carboxylic acids (SC) 254 [G.E. 250]
Silanes, Synthesis of tri-tert-butyl-~ (SC) 642 [G.E. 670]
Silicate foam materials (water glass foams) (PR) 114
Silicates, Zeolites—synthesis, structure, and applications (FP) 620 [G.E. 659]
Foams from aqueous solutions of ~ (PR) 189
Silicon complexes, Preparation of $[SiCl_2bipy_2](ClO_4)_2$ by oxidation of $SiCl_2bipy_2$ (SC) 699 [G.E. 742]
Silicon compounds, New element-carbon (p-p)π bonds (FP) 232 [G.E. 269]
New catalysts for synthesis of nucleosides (SC) 421 [G.E. 417]
Selective acidic cleavage of the tert-butoxycarbonyl group (SC) 818 [G.E. 877]
Unstable silicon analogs of unsaturated compounds (LA) 373

Silylmercury, Di-~ and digermylmercury (SC) 167 [G.E. 207]
Silyl shift, 1,3-S,N-~ in silylated thioamides (SC) 427 [G.E. 420]
Singlet oxygen, Phthaloyl peroxide as an efficient source of ~ (SC) 560 [G.E. 546]
Skyrin, Biomimetic synthesis (SC) 819 [G.E. 846]
Smog, Mechanisms of photochemical air pollution (FP) 1 [G.E. 18]
Soils, Organic compounds in nature: limits of our knowledge (FP) 507 [G.E. 527]
Solids, Photochemistry of organic ~ (FP) 386 [G.E. 439]
Spectroscopy, Determination of conformation of conjugated dienes by means of vibrational frequencies (SC) 364 [G.E. 345]
Vibrational structure in electronic spectra of coordination compounds (LA) 113
Applications of diffuse reflectance ~ (LA) 266
Vibrational spectra of transition metal chalcogen compounds (LA) 266
Absorption ~ of organic molecules (Book Review) 191
Spreading alkaloid stenusin from the staphylinid Stenus comma (Coleptera: Staphylinidae) (SC) 427 [G.E. 421]
Spin density, Vinylaminyl oxides (vinyl nitroxides) with high ~ in the vinyl group (SC) 551 [G.E. 590]
Spin-lattice relaxation times, ^{13}C-~ and the mobility of organic molecules in solution (FP) 144 [G.E. 152]
Spirenes, [2π,6π]-~. Synthesis of the first member of a new class of compounds (SC) 646 [G.E. 674]
Spirocyclopropabenzene, Synthesis of first ~ (SC) 647 [G.E. 674]
Stannanediyls, Dialkyl-~ (dialkylstannylenes) (SC) 246 [G.E. 247]
New route to dialkyl-~, (dialkylstannylenes) and their preparative application (SC) 812 [G.E. 844]
Stannylenes, Dialkylstannanediyls (dialkyl-~) (SC) 246 [G.E. 247]
New route to dialkylstannanediyls, (dialkyl-~) and their preparative application (SC) 812 [G.E. 844]
Stenusin, The spreading alkaloid ~ from the staphylinid Stenus comma (Coleptera: Staphylinidae) (SC) 427 [G.E. 421]
Stereochemistry, ~ of reaction paths as determined from crystal structure data—a relationship between structure and energy (FP) 460 [G.E. 461]
Atlas of ~ (Book Review) 441
Stereoselectivity, Asymmetrically induced four component condensation with extremely high ~ and multiplication of ~ (SC) 61 [G.E. 67]
Streptamine, Chemistry of cis-trioxatris-σ-homobenzene. A simple total synthesis of ~ (SC) 630 [G.E. 625]
Structure, Stereochemistry of reaction paths as determined from crystal ~ data—a relationship between ~ and energy (FP) 460 [G.E. 461]
Substituent effects, Extreme perturbation of π-systems by ylidic substituents (SC) 173 [G.E. 197]
Substitutions, Proceeding via radical anion intermediates (FP) 734 [G.E. 797]
Experimental evidence for a novel limiting mechanism of aliphatic nucleophilic ~ (SC) 59 [G.E. 66]
Sulfenes (LA) 438
Sulfenyl isothiocyanate, Dichlorofluoromethane-~ (SC) 698 [G.E. 707]
4-Sulfidocyclobutenediylium-1,2-diolate, Nucleophilic attack on 3-phenyl-~anion (SC) 823 [G.E. 879]
Sulfinato-O,S complexes, Synthesis of ~ of palladium(II) (SC) 256 [G.E. 251]
Sulfite, Selenium-catalyzed formation of sulfate and sulfur from ~ (SC) 638 [G.E. 631]
Sulfones, Tetrachloro-4-cyanophenyl sulfoxides and ~ (PR) 771
Sulfonylation, σ-Complex intermediates in acylation and ~ of 1,3,5-tripyrrolidinobenzene—preparation, reactions and structure (SC) 62 [G.E. 71]
3-Sulfopropionic anhydride (LA) 373
Sulfoxides, Tetrachloro-4-cyanophenyl ~ and sulfones (PR) 771
Sulfur, Selenium-catalyzed formation of sulfate and ~ from sulfite (SC) 638 [G.E. 631]
Sulfur atoms as ligands in metal complexes (FP) 322 [G.E. 363]
Sulfur compounds, 1,2,4λ⁴,3,5-Trithiadiazol-1-one N_2S_3O—the first oxide of a five-membered sulfur-nitrogen ring (SC) 258 [G.E. 254]
Sulfur dioxide complexes, Reaction of transition metal carbonyl halides with $AgAsF_6$ in liquid SO_2: A key reaction for the preparation of novel complex cations (SC) 640 [G.E. 669]
Sulfur-nitrogen compounds, Synthesis of tetrasulfur pentanitride anion (SC) 485 [G.E. 485]
Sulfur-sulfur bonds, Properties (FP) 655 [G.E. 683]
Surface chemistry, Low-energy electrons and ~ (Book Review) 504
Synthetic methods, Umpolung of amine reactivity. Nucleophilic α-(secondary amino)-alkylation via metalated nitrosamines (FP) 15 [G.E. 1]
Preparation, structure, and reactions of halomalondialdehydes (FP) 86 [G.E. 124]
Chemistry of phosphorylcarbenes (FP) 222 [G.E. 259]
Ring contractions and expansions of vicinally disubstituted cyclobutanes and cyclopropylmethyl compounds (FP) 473 [G.E. 505]
Methods for preparation of bridgehead olefins (FP) 528 [G.E. 568]
Substitution reactions which proceed via radical anion intermediates (FP) 734 [G.E. 797]
Tertiary phosphane/tetrachloromethane, a versatile reagent for chlorination, dehydration, and P—N linkage (FP) 801 [G.E. 863]

TETRAASTERANE, pentacyclo-[6.4.0.0^{2,7}.0^{4,11}.0^{5,10}]dodecane (SC) 180 [G.E. 174]
Tetrachloromethane, Tertiary phosphane-~, a versatile reagent for chlorination, dehydration, and P—N linkage (FP) 801 [G.E. 863]
Tetracyanoethylene, Unusual cycloaddition to dispiro[2.0.2.4]deca-7,9-diene (SC) 816 [G.E. 842]
Tetracyclines: chemistry, biochemistry, and structure-activity relations (FP) 721 [G.E. 751]
Tetraethynylethylenes (SC) 498 [G.E. 490]
1,2,3,4-Tetrahydroquinazoline-4-carbohydrazides, New 3-substituted 4-hydroxy-2-oxo-~ (PR) 439
Tetraisopropylchromium (SC) 760 [G.E. 781]
Tetralins, Transition metal catalyzed acetylene cyclizations. General synthesis of indans and ~ (SC) 712 [G.E. 744]
N,N,N′,N′-Tetramethyl-2,2′-oxydiethylamine (PR) 578
Tetrapyrroles, Synthesis of linear tripyrroles and ~ of biogenetic significance (SC) 423 [G.E. 418]
Tetrasulfur pentanitride anion, Synthesis (SC) 485 [G.E. 485]
Tetrazene, Isolation (SC) 177 [G.E. 202]
Photoelectron spectrum (SC) 178 [G.E. 203]
s-Tetrazine, Thermal cycloaddition between 3,6-diphenyl-~ and 9-oxabicyclo[6.1.0]nona-2,4,6-triene; construction of the oxonino[4,5-d]pyridazine frame (SC) 814 [G.E. 842]
2-Tetrazolines, Aziridinimines, diaziridinimines, diaziridinones, and carbodiimides by photolysis of ~ (SC) 428 [G.E. 422]
Textbook, Lehrbuch der Organischen Chemie (Book Review) 191
Thallium(I) alkoxides, Alkylation of ~. Useful modification of Williamson etherification (SC) 762 [G.E. 812]
Polyfunctional chiral macrocyclic polyether derived from L-(+)-tartaric acid (SC) 764 [G.E. 813]
Thiacumulene, Synthesis of a stable substituted ~: concept of cumulogy (SC) 53 [G.E. 33]
Thiadiazaphosphetidine, 1λ⁴,2,4,3λ⁵-~. A sulfur-nitrogen-phosphorus four-membered ring compound (SC) 769 [G.E. 810]
1,2,3-Thiadiazoles, Flash thermolysis: a simple route to thioketenes (SC) 248 [G.E. 171]
Thiadiazolidine-3,4-diones, 2,5-Diaryl-1-(arylimino)-1λ⁴,2,5-~: new five-membered heterocycles (SC) 762 [G.E. 811]
2H-1,3-Thiazete, ~: a new heterocyclic system (SC) 766 [G.E. 816]
Detection of valence tautomerism between ~ and N-alkylidenethiocarboxamide (SC) 767 [G.E. 816]
Thiazines, 2-(Phenylhydrazino)thiazoline and -thiazine derivatives (PR) 828
Thiazolines, 2-(Phenylhydrazino)thiazoline and -thiazine derivatives (PR) 828
Thiazyl trifluoride, NSF_3 as ligand in transition metal complexes: (~)pentacarbonylrhenium hexafluoroarsenate (SC) 186 [G.E. 208]
Thioacetals, Michael additions of metalated ~ to cyclic enones (SC) 57 [G.E. 37]
Thioacyl chlorides, Aliphatic ~. Preparation and properties (SC) 703 [G.E. 710]
Thioamides, C—N twisted ethanedi-~ in electron-rich complexes (SC) 250 [G.E. 245]
1,3-S,N-Silyl shift in silylated ~ (SC) 427 [G.E. 420]
α-Thio carbanions, Metalated dialkyl N-alkyliminocarbonates: new masked α-amino carbanions and ~ (SC) 424 [G.E. 449]
Thiocyanatidates, New route to phosphoro- and phosphino-~ (SC) 108 [G.E. 134]
Thioethers, Preparation of aryl-alkyl ethers and ~ (SC) 370 [G.E. 357]
Thioketenes, Synthesis of a stable alkylideneketenimine and an alkylidene-~ (SC) 53 [G.E. 33]
Flash thermolysis of 1,2,3-thiadiazoles: a simple route to ~ (SC) 248 [G.E. 171]
Thiooxalic acids, Alkali metal salts of mono-, 1,1-di-, and 1,1,2-tri-~ (SC) 436 [G.E. 452]
Thiophenes, Nonclassical condensed ~ (LA) 718
Thiophosphinic acids, Isomerization of dimethylphosphane sulfide on transition metals (SC) 416 [G.E. 447]
Thiostannate, $Sn_{10}O_4S_{20}^{8-}$: a new type of polyanion (SC) 436 [G.E. 451]
Thiotritungstates, Crystalline compound with isolated $W_3S_9^{2-}$ ion: a thio analog of transition metal isopolyanions (SC) 573 [G.E. 598]
2-Thiouridine, Synthesis of 5-methylaminomethyl-~, a rare nucleodide from t-RNA (SC) 255 [G.E. 251]
Tin compounds, Dialkylstannanediyls (dialkylstannylenes) (SC) 246 [G.E. 247]
Cyclic nitrogen derivatives of tetra- and divalent tin (SC) 263 [G.E. 287]
Chloro(di-tert-butylphosphino)germanediyl and -stannanediyl: stable germanium(II) and tin(II) organophosphorus compounds (SC) 368 [G.E. 354]
$Sn_{10}O_4S_{20}^{8-}$: a new type of polyanion (SC) 436 [G.E. 451]
Titanium compounds, Use of low-valent ~ in organic chemistry (LA) 266
Tolan, Synthesis of the naphthol skeleton from pentacarbonyl[methoxy(phenyl)carbene]-chromium(0) and ~ (SC) 644 [G.E. 672]
Topomerization of the cis,cis,cis,trans-[9]annulene anion (SC) 562 [G.E. 550]
Toxic compounds, Fatal accident during work with 2-(perfluoralkyl)ethyl iodides (SC) 181 [G.E. 171]
Transition metal atoms, Reactions with organic substrates (FP) 195 [G.E. 215]
~ in the synthesis of binuclear complexes (FP) 292 [G.E. 314]
Transition metals, New results of the photochemistry of complexes of the heavier ~ (LA) 114
Transition state, High pressure kinetic investigations in organic and macromolecular chemistry (FP) 137 [G.E. 186]
Transport, Selective ~ of alkali metal cations through a liquid membrane by macrobicyclic carriers (SC) 555 [G.E. 542]
Trianthranilide, Synthesis and conformational

behavior of N,N',N''-trimethyl-~ (SC) 169 [G.E. 169]
1,4,7-Triaza-2,5,8-cyclononatriene, Chemistry of cis-triazatris-σ-homobenzene, $3\sigma \rightarrow 3\pi$ isomerization to the ~ system (SC) 347 [G.E. 349]
Triazatris-σ-homobenzene, Chemistry of cis-~. $3\sigma \rightarrow 3\pi$ isomerization to the 1,4,7-triaza-2,5,8-cyclononatriene system (SC) 347 [G.E. 349]
s-Triazines, Preparation of mono- or diisocyanato-~ (PR) 189
Trifluoroacetic acid, Theoretical investigation of carbenium ion stabilization by ~ (SC) 641 [G.E. 632]
Trimethylenemethane, Thermal diastereoisomerization of 3-methyl-6-ethylidene bicyclo[3.1.0]hexane: orthogonal versus planar (SC) 758 [G.E. 777]
Trioxatris-σ-homobenzene, Chemistry of cis-~, α,α-dioxa-β-thia- and β-oxa-α,α-dithiatris-σ-homobenzene (SC) 253 [G.E. 249]
Chemistry of cis-~. Simple total synthesis of streptamine (SC) 630 [G.E. 625]
Simple and productive total syntheses of 2-deoxystreptamine and (±)-hyosamine (SC) 632 [G.E. 626]
Productive synthesis of trans-~ (trans-"benzene trioxide") (SC) 633 [G.E. 627]
Triphenylmethane, Triply clamped helical ~ systems (SC) 497 [G.E. 522]
Triphenylverdazyl, Mode of formation from triphenylverdazylium salts or from triphenylformazan (SC) 431 [G.E. 453]
1,3,5-Tripyrrolidinobenzene, σ-Complex intermediates in acylation and sulfonylation of ~—preparation, reactions, and structure (SC) 62 [G.E. 71]
trans-σ-Trishomobenzene, Valence isomerization of hexamethyl-~ (SC) 371 [G.E. 383]
Tris-σ-homotropone, Hexamethyl-~ from 3,3-dimethylcyclopropene and carbon monoxide (SC) 706 [G.E. 715]
Triterpenoids, Total syntheses of tetra- and pentacyclic ~ (LA) 717
1,2,4λ^4,3,5-Trithiadiazol-1-one, N_2S_3O—the first oxide of a five-membered sulfur-nitrogen ring (SC) 258 [G.E. 254]
Trithiatris-σ-homobenzene, cis-~ (cis-"benzene trisulfide") (SC) 252 [G.E. 248]
Tropolonate, Structure of mercury(II) ~ (SC) 358 [G.E. 384]
Tropolone, 2-Hydroxy-4,10-methano[11]annulenone—A 10 π analog of α-~ (SC) 566 [G.E. 592]
Tungsten complexes, [Bis(diphenylphosphino-η-benzene)chromium]tetracarbonylmetal complexes of chromium, molybdenum, and tungsten (SC) 174 [G.E. 198]
Metal-stabilized C-protonated diazomethane: a methanediazonium complex (SC) 355 [G.E. 358]
Tungsten compounds, Crystalline compound with isolated $W_3S_9^{2-}$ ion: a thio analog of transition metal isopolyanions (SC) 573 [G.E. 598]

ULLMANN's encyclopedia of technical chemistry, Ullmanns Encyklopädie der Technischen Chemie (Book Review) 73, 268, 578
Umpolung of amine reactivity. Nucleophilic α-(secondary amino)-alkylation via metalated nitrosamines (FP) 15 [G.E. 1]
Urethanes, Thermal dissociation (PR) 189

VAN DER WAALS molecules (LA) 827
Vinyl acetate, Photoaddition to benzene (SC) 552 [G.E. 540]
Vinylaminyl oxides (vinyl nitroxides) with high spin density in the vinyl group (SC) 551 [G.E. 590]
Vinylene carbonate, Photochemical cycloaddition to benzene (SC) 698 [G.E. 708]
Vinylenedisulfonium salts, cis- and trans-~ (SC) 755 [G.E. 773]
Stereoselective reactions (SC) 756 [G.E. 775]
Vinylketenes from cyclobutenones by electrocyclic ring opening (SC) 500 [G.E. 491]
Vinyllithium and 1,4-dilithiobutane from ethylene and lithium (SC) 259 [G.E. 254]
Vision, Chemistry of ~ (LA) 503
Vitamin B_{12}, Phthalocyaninecobalt(I) salts, "supernucleophilic" ~ models stable in neutral medium (SC) 825 [G.E. 847]
Nonenzymatic model reaction for the coenzyme B_{12}-catalyzed rearrangement of methylmalonyl-CoA into succinyl-CoA (SC) 822 [G.E. 877]

WALLACH rearrangement, Catalysis in strongly acidic media and ~ (LA) 717
Water of crystallization, Structure of octaethylxanthoporphinogen dihydrate (SC) 435 [G.E. 456]
Weed killers (PR) 439
Willgerodt reaction (LA) 717
Wittig reaction, Vinylogous pyridinecarbaldehydes by ~ (SC) 486 [G.E. 486]
Wolff rearrangement of α-diazo carbonyl compounds (FP) 32 [G.E. 52]

XANTHOPORPHINOGEN, Structure of ~ dihydrate (SC) 435 [G.E. 456]

YLIDES, Extreme perturbation of π-systems by ylidic substituents (SC) 173 [G.E. 197]
Inorganic chemistry with ~ (LA) 438

ZEOLITES—their synthesis, structure, and applications (FP) 620 [G.E. 659]
Zwitterion, Sudden polarization in the zwitterionic Z_I excited states of organic intermediates. Photochemical implications (SC) 575 [G.E. 599]